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PRESEDENT MESSAGE

The Journey of the Batticaloa Medical Journal Portfolio

Batticaloa Medical Journal (BMJ) has been the official journal of Batticaloa Medical Association (BMA) and published annually since its inception. 2019 is a year of change for the Batticaloa Medical Journal Portfolio. We consulted our members, readers and authors over last couple of years about what they wanted from BMJ. One of the loudest messages we received was biannual publication and indexing. There was also demand for digital version and wider participation and circulation.

In a busy healthcare system, stretched to capacity, our aim is to provide a platform for molding through learning and dissemination of knowledge & experience of professionals.

The untiring efforts of our Editorial Board on defining the strategic priorities to advance BMJ has taken measures to build a digital platform which enable us for a wider attraction and circulation among Universities and Academic organizations of the Country. From this year BMJ will be published biannually which will pave way for indexing in coming years.

While extending my sincere appreciation on unparalleled hard work of our Editorial board, I wish all the very best for authors and readers of BMJ.

Dr.H.R. Thambawita
MBBS, MS, MIPC MRCS FCSSL
Consultant Surgeon
T.H. Batticaloa
President, Batticaloa Medical Association

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EDITORIAL

Motives behind Suicide terrorism

In the aftermath of the devastation of the Easter suicide attacks (4/21) in Sri Lanka that killed more than 250 people, there has been extensive shock that two of the nine suicide bombers were the children of a millionaire. Some of the attackers had studied abroad and their career forecasts seemed bright. What motives behind them?

Suicide terrorism is not a new phenomenon for Sri Lanka. In particular, the Liberation Tigers of Tamil Eelam (LTTE) developed suicide attacks to be so frightening and effective for a vastly towards fighting forces, military commanders, political leaders, and economic spots.

They used men, women, children, animals, boats, trucks and cars, on and off the battlefield. Their methods were studied and copied, notably in the Middle East. Their modus operandi was so influential that it provides some insight into the motivation of future suicide terrorists.

A suicide attack is a situation in which a person intentionally kills himself or herself for the purpose of killing others in the service of a political or ideological goal. It is the most dangerous example of asymmetrical battle. Because a suicide attack is a more lethal attack than a normal bombing, the media is kept focused on this attack and when there are more casualties it generates more fear, horror and anxiety within targeted communities. The psychological effects are out of proportion to the damage caused.

It is obvious that, suicide attacks are not carried out by individuals, but by an organization. An organization can select or strongly suggest where and when to send suicide bombers and attackers. In normal terrorist attacks, there are more chances for a terrorist to be caught on the spot and in a suicide attacks, it is less likely that a suicide member will be arrested. The individual attackers have a mixture of motivations and the combination of motivators varies between the individual attackers, their groups and their causes. Religious motives remain the most common factors for suicide attacks because in this cause, suicide bombers get many personal and family or social and worldly benefits.

The suicide terrorism record in Flinders University in Australia, the most wide-ranging in the world, holds information on suicide bombings in Iraq, Palestine-Israel, Afghanistan, Pakistan and Sri Lanka, which together accounted for 90 per cent of all suicide attacks between 1981 and 2006.The evidence from the database largely discredits the common wisdom that the personality of suicide bombers and their religion are the principal cause. It shows that though religion can play a vital role in recruiting and motivating potential future suicide bombers, the driving force is not religion but a cocktail of motivations including politics, humiliation, revenge, retaliation and altruism.

The organizations that are widely active in the world are part of a worldwide Islamic Jihad network, whose ideology is based on their harsh version of political Islam. It is one which has manipulated the message of Islam to reflect each group's rigid and extremely conservative and violent views, but they still call themselves Islamist Jihadi Organization. Jihadi inspirations are rooted in the way they interpret the divine message. In the means of, if you will conduct the terrorist act against a specific community, a certain relation or a certain country, you will go to Jannah (Paradise) or you will become martyrs and will get seventy virgin ladies in the paradise hereafter.

Typically, most suicide bombers are psychologically normal and are deeply united into social networks and emotionally attached to their national communities. The available data denotes that, suicide attackers are young and not so young, educated and not educated, from poor families and from relatively well-off ones. They are not what psychologists call 'suicidal types' but are psychiatrically normal, sane and probably logical. They are not depressed, impulsive, lonely, or helpless with a continuous history of being in situations of personal difficulty or economic despair.

Participating in a suicide mission is not about dying and killing alone but has a wider significance for achieving multiple purposes, from personal to communal. These include gaining community approval and political success, liberating the homeland, achieving personal redemption or honor; using martyrdom to effect the survival of the community, refusing to accept subjugation; seeking revenge for personal and collective humiliation, conveying religious or nationalistic faiths; expressing guilt, shame, material and religious rewards, escaping from intolerable everyday degradations of life under occupation, boredom, anxiety and defiance. The configuration of these purposes varies and is an outcome of specific circumstances of the political conflict behind the rise of suicide attacks as a tactic and a weapon.

The psychological impact of suicide terrorism is more fearful than any other form of attacks because victims become psychologically disabled and cannot react instantly. The main goal of terrorists is to generate the terror which transfers people's reactions from rational fear into irrational fear. Apart from the immediate death and destruction, a main goal, terrorists want to generate irrational fear and panic in the hearts and mind of the ordinary citizens of the state. In this situation, our main policy should be, to thwart the irrational fear which terrorists create within a targeted population. The causes of suicide bombings lie not in individual psychopathology but in broader social conditions. Understanding and knowledge of these conditions is vital for developing appropriate public policies and responses to protect the public.

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Leading Article

Initiation of insulin in type 2 Diabetes mellitus

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Abstract :

The advanced nature of Type 2 diabetes, insulin therapy is routinely required to achieve glycemic control. When lifestyle modifications and treatment with metformin with or without other oral antidiabetic drugs (OADs) have failed to achieve good control, sensible initiation of single dose basal insulin treatment is an appropriate, effective, and authorized strategy. As soon as, type 2 diabetes is clinically diagnosed, only 50 percent of normal beta-cell function is remains. However, beta-cells lost their mass about 4% by every year. Consequently, a considerable number of patients need insulin therapy after nine or more years of disease. Augmentation therapy with basal insulin is suitable if some beta-cell function remains. Replacement therapy with basal-bolus insulin is required for beta-cell overtiredness. Rescue therapy using replacement regimens for several weeks may reverse glucose toxicity.

Keywords: Insulin therapy in type 2 diabetes, and initiation of insulin in diabetes.

Introduction:

The current management of diabetes needs scrupulous glycemic control. Poorly control, and long-term diabetes donate significantly to the morbidity, mortality, and economic burden of diabetes(1). The advanced nature of Type 2 diabetes, insulin therapy is habitually required to achieve glycemic control. When lifestyle modifications and treatment with metformin with or without other oral antidiabetic drugs (OADs) have failed to achieve good control, sensible initiation of single dose basal insulin treatment is an appropriate, effective, and endorsed strategy. Type 2 diabetes is considered by progressive beta-cell failure(2). Indications for exogenous insulin therapy in patients with this condition include acute illness or surgery, pregnancy, glucose toxicity, contraindications to or failure to achieve goals with oral antidiabetic medications, and a need for flexible therapy. Augmentation therapy with basal insulin is useful if some beta-cell function remains. Replacement therapy with basal-bolus insulin is required for beta-cell overtiredness. Rescue therapy using replacement regimens for several weeks may reverse glucose toxicity. The aim of this review is highlighting when and how to start insulin in type 2 DM.

Pathophysiology of the Beta Cell:

The main pathophysiological faults leading to the development of T2DM are insulin resistance in muscle and liver cells, resulting in decreased glucose uptake and increased hepatic glucose output, coupled with failure of pancreatic beta cells to produce sufficient insulin to maintain normoglycemia and to prevent adipose fatty acid release. This 'glucolipotoxicity' leads to further impairment of the beta cells, and a progressive cycle of beta cell dysfunction and metabolic decline. When type 2 diabetes is clinically diagnosed, only 50 percent of normal beta-cell function remains. However, beta-cells lost their mass about 4% by every year. Consequently, a substantial number of patients need insulin therapy after nine or more years of disease.

Insulin secretion:

After meal glucose influx can be 20 to 30 times higher than hepatic production between meals. Phase 1 insulin release, lasting

10 minutes, suppresses hepatic glucose production and facilitates phase 2 release, which lasts two hours and covers mealtime carbohydrates. In type 2 diabetes, phase 1 release is absent, and phase 2 release is delayed and inadequate. The sharp spike of mealtime insulin release occurring in normal persons is delayed, prolonged, and insufficient in amount in patients with type 2 diabetes.

When to start insulin therapy:

Introducing insulin therapy in a patient newly diagnosed with T2DM is uncommon, but initial insulin therapy should be considered when there is significant weight loss, severe symptoms of hyperglycemia (FBS >250mg/dl) or the presence of significant ketonuria which is called glucose toxicity(3). The American Diabetes Association (ADA), in a consensus statement, has called for using insulin early in the disease if lifestyle management and monotherapy with metformin fail to control glucose or if lifestyle management is not adequate and metformin is contraindicated. The ADA's goal hemoglobin A1c level is less than 7% for most patients. However, The American Association of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE), in another consensus statement, use an algorithm stratified by hemoglobin A1c level, in which insulin is mostly reserved for when combination therapy fails.

Types of insulin

Insulin is branded as basal or bolus insulin based on the duration of action . Basal insulins include neutral protamine Hagedorn (NPH) or isophane insulin (Humulin N), ultralente (extended insulin zinc suspension), and the insulin analogue glargine (Lantus). Bolus or mealtime insulins include regular insulin (Humulin R) and the analogue forms aspart and lispro (Humalog). Premixed formulations incorporate NPH and regular or rapid-acting analogues.

Traditional insulins (i.e., regular, NPH, and ultralente) have two features that complicate therapy. First, their absorption profiles are erratic, creating day-to-day fluctuations in glycemic control. 9 Second, their delayed onset of action and peak activity require coordination of injection and meals. Regular insulin must be injected 30 to 60 minutes before the meal to match postprandial glucose influx. NPH may cause hypoglycemia during its peak at four to 10 hours after injection unless the patient remembers to eat. Premixed formulations of NPH and regular insulin provide a bimodal pattern of insulin activity that rigidly dictates meal size and timing for the next 12 hours.

Advantages of insulin analogue

These problems are avoided with analogue insulins (i.e., glargine, aspart, and lispro)— so named because one to three amino acids have been substituted in the human insulin protein, producing altered absorption rates and more reliable absorption profiles. Lispro and aspart are active within 15 minutes and peak in about one hour, mimicking normal mealtime insulin release. Glargine provides a peakless, continuous release over 24 hours that approximates a normal basal pattern. The analogue insulins cost 60 to 100 percent more than traditional insulins. Initiation of insulin reduce the episode of hypoglycemia(4).

How to start insulin in Sri Lankan context

Psychological insulin resistance is a real phenomenon. Individuals with diabetes often feel that insulin is the beginning of the end. They fear taking the injection and feel that there is a stigma associated with insulin. Insulin therapy can, in fact, be a real pain both literally and figuratively. It is intrusive, can limit spontaneity, and can interfere with daily activities. As a consequence, adhering to an insulin regimen has been difficult for many patients. Education promotes compliance. Patients need to know that type 2 diabetes tends to progress and that in time their treatment will have to be intensified, with higher doses of their current drugs and new drugs added or substituted, possibly including insulin. This information is best given early, ie, when the diagnosis is made, even if hyperglycemia is mild at that time.

Insulin Regimens

Theoretically, the ideal insulin therapy regimen should mimic normal physiologic insulin release. The insulin regimen should be tailored to the patient's degree of hyperglycemia, the risks associated with hypoglycemia, comorbid conditions, the ability to adhere to a routine and understand and master the information and skills, and the cost(5). However, early initiation of insulin in type 2 diabetes , significantly reduce the diabetic complications(6).

Augmentation therapy

Augmentation therapy is effective in patients with residual but insufficient beta-cell function, which is exhibited as failure to maintain the A1C goal while taking oral medications. Augmentation therapy usually is provided with basal insulin using bedtime NPH. NPH twice daily, ultralente once daily, or glargine once daily, adjusted to maintain a fasting plasma glucose level between 90 and 130 mg per dL(7). Ideally, basal insulin should have no pronounced peak in activity, a low risk of hypoglycemia, low within-patient variability, and a duration of action of approximately 24 hours to enable once-daily injections. Regardless, basal insulin analogs have pharmacokinetic and pharmacodynamic advantages over NPH insulin—namely, a less pronounced peak effect, less variable absorption profiles, and a longer duration of action. Insulin analogs are also associated with lower rates of hypoglycemia, particularly nocturnal hypoglycemia, compared with NPH(Table 1).

Augmentation also can be provided at mealtime using regular insulin , aspart, or lispro adjusted to maintain two-hour postprandial glucose levels of 180 mg per dL (10 mmol per L) or less. It is interesting that instead of single basal insulin injection, the same amount of insulin divided into several bolus injections offers fewer postprandial glucose fluctuations, a lower A1C level, and greater weight gain.

Replacement therapy

Replacement therapy using basal-bolus insulin regimens is indicated for patients who need intensive control or have failed augmentation therapy(7). The most convenient basal-bolus regimen uses split-mixed injection of NPH and regular insulin before breakfast and dinner but requires rigid adherence to a set meal size and time.

Basal coverage with glargine provides A1C levels similar to those of NPH, but with less nocturnal hypoglycemia. Basal insulins can normalize the fasting glucose but do not affect post-prandial glucose levels, and premixed insulin formulations may be useful in patients who need to cover both fasting and post-prandial glucose(table 1). Premixed insulin analogues are appropriate here and generally preferred over human insulin, given the lower hypoglycaemia risk

TABLE 1
Description of Onset, Peak, and Duration of Insulins

Insulin	*Onset*	*Peak (hours)*	*Usual effective duration (hours)*	*Usual maximum duration (hours)*	*Cost**
Bolus or mealtime insulin					
Aspart (NovoLog)	5 to 10 minutes	1 to 3	3 to 5	4 to 6	$59
Lispro (Humalog)	< 15 minutes	0.5 to 1.5	2 to 4	4 to 6	59
Regular (Humulin R, Novolin R)	30 to 60 minutes	2 to 3	3 to 6	6 to 10	28
Basal insulin					
NPH (Humulin N, Novolin N)	2 to 4 hours	4 to 10	10 to 16	14 to 18	28
Lente (insulin zinc suspension)	3 to 4 hours	4 to 12	12 to 18	16 to 20	
Ultralente (extended insulin zinc suspension)	6 to 10 hours	Peakless	18 to 20	20 to 24	28
Glargine (Lantus)	1 hour, 6 minutes	Peakless	24	24	51
Combinations					
50% NPH/50% regular	30 to 60 minutes	Dual	10 to 16	14 to 18	
70% NPH/30% regular (Humulin R 70/30, Novolin R 70/30)	30 to 60 minutes	Dual	10 to 16	14 to 18	28
75% NPL/25% lispro (Humalog 75/25)	< 15 minutes	Dual	10 to 16	14 to 18	59†
70% APS/30% aspart (NovoLog Mix 70/30)	10 to 20 minutes	2.4 ± 0.80	24	24	59

NPH = neutral protamine Hagedorn; NPL = neutral protamine lispro; APS = aspart protamine suspension.

**—Estimated cost to the pharmacist for one 10-ml vial based on average wholesale prices in Red book. Montvale, N.J.: Medical Economics Data, 2004. Cost to the patient will be higher, depending on prescription filling fee.*
†—20-mL volume only—cost shown is one half of the cost of a 20-mL vial.

Adapted with permission from Resource guide 2004. Insulin. Diabetes Forecast 2004;57:RG16.

Dosing

The principle of 'start low and go slow' is prudent. The primary aims are to ensure patients can manage injecting and avoiding Hypoglycemia. Starting insulin dose for augmentation is calculated as 0.15 units per kg per day. Another safe calculation is units of insulin per day equals fasting plasma glucose level in mmol per L. The starting dose for replacement therapy is 0.5 units per kg per day(7). Twofold to fourfold higher doses often are required for patients with insulin resistance. Volumes greater than 0.5 mL (50 units of U-100 insulin) should be split and injected in separate areas to facilitate absorption. Fifty to 60 percent of the total insulin dose should be provided as basal form and 40 to 50 percent as bolus form.

Problem in starting insulin

Several factors affect this decision, including whether the patient is willing to follow a complex insulin regimen (such as a basal-bolus regimen), his or her work schedule, other lifestyle factors, the duration of diabetes, the type or types of insulin used, coexisting medical conditions, the frequency of hypoglycemia, unawareness of hypoglycemia, age, prognosis, life expectancy, and cost. The glycemic goal should be individualized

Fix the Fasting First

Thus, in a patient whose predominant glycemic burden occurs overnight therefore starting with a low dose of basal insulin (0.15-0.20 units/kg/d) and adjusting the dose to achieve fasting blood glucose levels 110–130 mg/dl often proves an effective strategy. Basal insulins can normalize the fasting glucose but do not affect post-prandial glucose levels, and premixed insulin formulations may be useful in patients who need to cover both fasting and post-prandial glucose(8). Basal insulin can be commenced at a single low dose of (0.15-0.20 units/kg/d) or 8–10 units/day, typically at bedtime, targeting the morning fasting glucose. Most often, glargine(9) or detemir (Levemir) insulin is used. Detemir can also be given twice daily if needed. If cost is a concern, NPH insulin once daily at bedtime or twice daily is a reasonable alternative.

Adding prandial insulin to a basal regimen

Once we achieved fasting glucose need to be check the HbA1c, if it is high problems in the prandial glucose. In general, whether to add prandial insulin can be decided on the basis of the patient's record of blood glucose monitoring. Insulin could be added before breakfast if the pre-lunch glucose level is raised, or before

lunch if the dinnertime blood glucose level is elevated, or before dinner if the bedtime blood glucose level is elevated or a combination of these. A short acting insulin or rapid-acting insulin analog is commonly administered around the time of the largest meal of the day because extreme glycemic control is likely to be obtained during the highest postprandial glucose outing. Prandial insulin can be started at a low dose (4–6 units) and increased gradually. Titrate with 2-3 unit of soluble insulin in every 2-3 days, if post prandial blood glucose level more than 180mg/dl or if the difference between pre-prandial and postprandial glucose levels is greater than 50 mg/dL.

How to give bolus insulin in top of basal insulin

In the case of poor glycemic control on a high dosage of basal insulin, a judicious first step would be to change the regimen to a basal-bolus regimen (about 50% basal and 50%bolus) with no change or a small decrease in the total daily dosage of insulin to avoid hypoglycemia. For example, in a patient on 80 units of glargine or detemir insulin who has inadequate control, the regimen could be changed to 40 units of either glargine or detemir and 10 to 12 units of soluble insulin, lispro, aspart, or glulisine before each meal as the bolus component(7).

When to stop other medications

The halt of oral agents often mandates a 20–30-unit increase in the total daily dosage of insulin, and oral agents may continue to provide an insulin-sparing effect. In our practice is to continue at least metformin with insulin(10). Some physician withdraws the sulphonylurea component when pre-mixed insulin is used. Studies have shown combining incretin-based therapies with basal insulin provides complementary glucose lowering benefit. The additional weight-sparing effect of GLP1RAs may be of benefit to patients concerned about insulin-induced weight gain. Likewise, insulin-sparing effects have been shown with the combination of DPP-4 inhibitors(11), leading to less hypoglycemia.

Problem in starting insulin in SriLanka.

Some patients may not accept giving themselves four or five injections per day with a basal-bolus regimen. They may accept a simpler regimen, giving themselves three injections of a premixed insulin per day, one before each meal. Biphasic insulin aspart (a mix of aspart and protamine aspart) given twice a day or three times daily provided similar improvement in glycemic control with no difference in the frequency of hypoglycemia compared with a basal-bolus regimen of NPH and aspart.

Conclusion

Initiate insulin therapy in patients with T2DM can be introduced simply and safely and further titration intensification can also be so managed once the patient and physician are comfortable. The suitable choice of insulin schedule, based on patient factors and directed self-monitoring of blood glucose, together with a multidisciplinary approach. Treatment of Type 2 diabetes include the combined use of metformin DPP-4 inhibitors therapies with basal insulin analogs, a combination that has demonstrated improved glycemic control with the potential for reduced insulin dosing.

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REVIEW ARTICLE

Minimizing The Prescribing Errors Within The Inpatient Settings - A Systematic Review

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Abstract :

Medication errors have a worldwide incidence of 8.8%. Prescribing errors are the leading type of Medication errors and they contribute to a significant number of morbidity and mortality. This Systematic Review aimed to identify a better intervention to reduce the prescribing errors at inpatient set up which can be achieved with available minimum resources. Articles were searched through Pubmed/MedLine search engine and interventional studies were included for the review. The Review Manager 5.3 version was used for the Meta analysis. The main interventions to reduce the prescribing errors have been done at PICU, paediatric ward and the cancer center. The interventions have focused on Zero Tolerance Prescribing (ZTP) policy and Daily Feedback mechanism, Pharmacist's Feedback on Prescriptions, Standardizing the Prescribing Tools with Education program and on Continuous Feedback on Prescribing. The Meta analysis identified that all these interventions are effective in reducing prescribing errors (OR 0.43, 95% CI 0.39 to 0.47) and ZTP is much more effective among the all the interventions in reducing the any type of prescribing error (OR 0.10 95% CI 0.08-0.12) or clinical type of prescribing error (OR 0.38, 95% CI 0.30 to 0.49). The Zero Tolerance Prescribing policy with Feedback mechanism which can be adapted and implemented as a multidisciplinary intervention in resource limited inpatient settings can bring a sustainable reduction in prescribing errors.

Key words:

"prescribing errors", "minimizing prescribing errors", "safe prescribing", "medication errors"

Introduction

Medication errors are considered as severe problems worldwide. The rate of error and the side effects are unacceptable in nature. (Al-Dhawailie 2011) Medication error is defined as ' a failure in the treatment process that leads to, or has the potential to lead to, harm the patient. (Lavan 2016)The medication errors include prescribing errors, transcribing errors, dispensing errors and medicine administration errors. The terms Medication errors and the Prescribing errors can't be used interchangeably because both errors have different contributing factors and need different interventions. (Lavan 2016)The prescribing errors are the leading type of medication error among all these subcategories. (Thirumagal 2017) The prescribing errors can occur at any health care set up and it has an incidence of 8.8% worldwide and the chance of error is 70% high during hospital admissions. (Lavan 2016) The main contributing factors for the prescribing errors are prescriber knowledge on medications, patient's co morbidities and the responsibility of prescribing is placed on the most junior doctor. (Lavan 2016) The consequences of prescribing errors can be ranging from adverse drug reactions, drug interactions and mortality. In United States it is estimated that 7000 deaths occur annually due to prescribing errors. (Gordon 2012)

Education on prescribing perceived by the medical students and the junior doctors was found to be inadequate even though they undergo training on prescribing during the undergraduate educational process. With the purpose of reducing the errors WHO introduced Guide to Good Prescribing during the undergraduate educational process and the results of the intervention was promising. (Lavan 2016)The other measures which can reduce the errors are Medication reconciliation, Feedback from the pharmacists and the Improvement in the working environment. The role of information

and communication technology and the prescribing-assessment tools in reducing the errors are still not promising. (Lavan 2016)

A study carried out in Sri Lanka identified 35.5 % (n=142) of Medication errors among the 400 prescriptions assessed and the prescribing error was 32.5% (n=130) among the total. (Thirumagal 2017) The main prescribing errors were wrong frequency, prescribing duplications, unacceptable medicine combinations, omission error and the dosing error. This study further concluded that if the number of medicines increases in a prescription the chance of error also increases. In countries like Sri Lanka which are middle income countries and the health care resources are limited. The lack of medical officers, lack of other health staff and overcrowded wards can increase the errors furthermore and can lead to mix up of medication orders. (Thirumagal 2017) The usage of error prone abbreviations were found to be prevalent in Sri Lanka, where more than half of the abbreviations were unapproved and they could lead to medication errors. (Samaranayake 2014a)

Multiple interventions have been implemented to reduce the prescribing errors with regard to improve the knowledge, skill of physicians and to reduce human factor related errors. The outcome of these interventions has been different but they have contributed to minimize the errors. To assess the effectiveness of these various interventions and to identify a better intervention to reduce the prescribing errors this systematic review was conducted.

Table 1 Classification of prescribing errors (Lavan 2016)

Omission error	Deletion of a drug previously used
Commission error	Addition of a drug not previously used
Dosing error	Incorrect dose
Frequency error	Incorrect frequency
Form error	Incorrect form
Substitution error	A drug from one class substituted for another drug from the same class not previously used
Duplication error	Two drugs from the same class being prescribed

Objective

The main objective of this review was to identify a better intervention to reduce the prescribing errors at inpatient set up which can be achieved with available minimum resources.

Methodology

The relevant articles were searched using the Pubmed/ Medline using "Minimizing prescribing errors, reducing prescribing errors, interventions to reduce prescribing errors, methods to reduce prescribing errors, prescribing errors" up to year 2019. The articles which described the intervention with pre and post interventional data to minimize the prescribing errors were included for the review purpose. For this purpose the abstracts were screened. Articles which didn't have a pre interventional group or interventional study or which were not focusing on minimizing the prescribing errors were not included for the review. From the Pubmed search 04 interventional studies were selected for this review which were published during 2012 to 2019 period. The selected articles were imported to Review Manager 5.3 version for the Meta analysis. The Meta analysis was performed using the Review Manager 5.3 version. (Review Manager (RevMan) [Computer program]. Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014)

Table 2 Details of the selected studies for Meta analysis

Study ID	Title of the article
Booth 2012	Zero tolerance prescribing: a strategy to reduce prescribing errors on the paediatric intensive care unit
Gordon 2012	A novel system of prescribing feedback to reduce errors: A pilot study
Martinez - Anton 2012	Impact of an intervention to reduce prescribing errors in a pediatric intensive care unit
Moon 2019	Effects of pharmacist interventions on reducing prescribing errors of investigational drugs in oncology clinical trials

Characteristics of the studies

The details of different interventions from the selected studies are described below.

1. Booth 2012

Objective of the study: This study aimed to investigate simple, readily implemented and cost-effective strategies for reducing prescribing errors in the PICU, such as reducing interruptions and distractions and providing feedback and education.

Study Setting and Methodology: Prospective, non-blinded, pre- and post-intervention observational study was undertaken in a PICU over a period of 134 weeks.

Intervention:

Step1. Zero Tolerance Prescribing (ZTP): This was implemented for 12 weeks duration and the following steps were taken.

- Provision of a dedicated area for prescribing where prescribers cannot be interrupted except in emergency
- No prescriptions permitted outside of this area (including ward rounds)
- A formal set of rules to which all prescriptions must comply
- Nursing staff explicitly supported in not administering inadequate prescriptions
- The dedicated prescribing areas had the following features:
- Up-to-date editions of the standard UK paediatric drug dosing reference texts
- All PICU guidelines accessible in an alphabetized folder
- Laminated copies of key unit guidelines on a notice board above the desk
- Laminated copies of infusion guidelines and common PICU

drug regimens on the surface of the desk

- Calculators
- Lighting
- No telephone or computer terminal

Step 2- After implementing the ZTP policy for 12 weeks the daily anonymous feedback by the PICU specialist pharmacist on the previous day's prescribing errors was introduced on weekdays at the formal handover and daily medical ward round. The ZTP policy was continued during this period.

2. Gordon 2012

Objective of the study: To introduce a departmental prescribing feedback system to address the prescribing errors

Study Setting and Methodology: This was a before and after study design. This study was carried out at a district general paediatric inpatient department. There were 26 paediatric staff and all of them participated with a study ID. As the base line of the study all the staff was sent the trust prescribing guideline. A pharmacist visited the ward on a daily basis to assess the prescriptions.

Intervention: A baseline assessment of a whole ward sample of inpatient prescription charts were reviewed against the trust prescribing policy. After this a feedback poster was developed which included the general information and was displayed at the staff areas of the department and every three week over a period of 03 months the prescriptions were assessed. Subsequent feedback posters were developed depending on the assessment findings of the prescriptions and they included anonymous individual feedback using participant ID number. While the posters were displayed at the department they were emailed to each participant every time.

3. Martinez-Anton 2012

Objective of the study: To analyze the prevalence of drug prescribing errors and their clinical impact in a PICU, to standardize the sources of prescription, pocket tables with dosing guidelines, development of an updated prescription protocol and the implementation of an educational program for physicians on drug errors and correct prescribing strategies.

Study Setting and Methodology: The study was before- after design without a control group. The study was done at a PICU. The study consisted 04 months of pre interventional data collection, 12 months of intervention and 04 months of post interventional data collection.

Intervention: This included the following components.

Standardization of prescription sources

Pocket tables with dosing guidelines

Updated prescription protocol

Educational program on correct prescribing

4. Moon 2019

Objective of the study: This study aimed to investigate the effectiveness of pharmacist intervention in reducing and preventing prescribing errors of investigational drugs for cancer patients.

Study Setting and Methodology: The study was carried out at National Cancer Center, Korea. The pre interventional data was collected from December 2015 to June 2016. The intervention was performed by the pharmacists from July 2016 to February 2017. The data for the interventional period also collected to assess the prescriptions. The Electronic Medical Record System was used to collect data on both occasions.=

Intervention: The pharmacists actively performed the following interventions during the intervention period. They discussed prescribing method with investigators before the start of study and provided a prescribing guide via e-mail to the investigators and clinical research coordinators. The guide included

Elements of a prescription that are required by law

All information needed to dispense the drug according to study protocol

Common error types, precautions, a good order example (order sets)

Information about the investigational drug

Results and Discussion

The selected interventional studies were different in the nature of the interventions done and the outcome of the interventions also was different. But each of the intervention has shown reduction in prescribing errors. The individual outcome of each intervention is discussed below, Booth 2012 adjusted the weekly aggregates of errors for PICU bed occupancy during the weekdays and the errors were expresses as a rate per 1000 PICU occupied bed days (OBDs). The baseline combined prescribing error rate was 892 (95 % CI 765–1,019) errors per 1,000 PICU OBDs. This included 230clinical prescribing errors per 1,000 OBDs, 394 non-clinical prescribing errors per 1,000 OBDs, and 268 infusion prescription errors per 1,000 OBDs. The most common clinical errors were dosing error and incorrect dosing frequency. The main non-clinical errors were failure to use the generic name and failure to record patient allergy status. After introducing the Zero Tolerance Prescribing policy the combined error rate was reduced by 25%, the clinical error by 12.7%, the infusion error by 15.9% and the non-clinical error didn't show a significant improvement. While the daily feedback was introduced after the 12 weeks of ZTP implementation the findings showed a significant reduction in non-clinical errors but the clinical errors and the infusion errors remained reduced from baselines. The combination of ZTP and daily feedback reduced the combined errors by 44.5% from the initial baseline errors.

Gordon 2012 did a continuous assessment of drug orders every three week for a total of 12 weeks. The baseline assessment revealed 69 errors among the 784 possibilities of error which was 8.8% and after the intervention for 12 weeks it came down to 1.8% (12 errors among 656 possibilities).

Martinez-Anton 2012 assessed a total of 4019 prescriptions during both the pre interventional and post interventional periods. During the pre interventional period there was 761 errors among 2228 prescriptions which was 34.2% and after the intervention it

was 388 among 1791 prescriptions (21.7%). This was 36.5% reduction in prescribing error from the baseline. The dose errors and wrong element errors were diminished by 28.6% and 46.1 %, respectively after the intervention. The most frequent error for both periods was "administration route not specified," appearing in 30% and 20.8 % of prescriptions during pre interventional and post interventional periods respectively.

Figure 1 Forest plot of comparison: Reduction in the total errors

Moon 2019 considered 12387 drug orders during both pre interventional and post interventional periods. Prior to the intervention among the 6477 prescriptions there were 395 (6.1%) prescribing errors and after the intervention it came down to 278 errors among the 5910 prescriptions (4.7%).This showed a 25% reduction in overall errors. The clinical types of error which included wrong dosage, wrong duration, wrong dosage form and wrong administration schedule came down from 1.8% to 1.2%.

The outcome of the above mentioned interventions were Meta analyzed to identify the effectiveness of each intervention using the RevMan3.5 version. The effectiveness of each intervention in reducing the overall errors revealed the following results.

The extent of prescribing errors is severe worldwide and in Sri Lanka it had a prevalence of 32.5% at one study. (Thirumagal 2017) While there is lack of nationwide studies on prescribing errors in Sri Lanka the percentage of prevalence identified from one study is very high and in unacceptable rate. The health care system in Sri Lanka is resource limited for physical or human resources. The consequences of the prescribing errors are detrimental and they can be prevented with some extra effort. The interventions described above were mainly done in the paediatric ICU settings (02 Interventions), paediatric ward (01 Intervention) and in the cancer unit (One Intervention). But the principles of prevention which were implemented in the interventions can be followed at any inpatient settings.

The Zero Tolerance Prescribing and Daily feedback is identified as the better mechanism (Odd Ratio 0.10, 95% CI 0.08-0.12) to prevent the prescribing errors and when the feasibility of this intervention is assessed it can be implemented at any resource limited in patient set up. The prescribing physician can follow the principles in this intervention in the ward set up by completing the prescriptions after the daily ward rounds in a dedicated area. During the process the drug chart of the patients can be reviewed daily and the prescribing area/ physician desk can have the pharmacopeia, management guidelines, calculators and any other specific guidelines as per the requirement of the specialties. Further there can be a systematic feedback mechanism about the prescriptions which can be done by the senior physicians or specialized physicians to the junior doctors. The inputs from the hospital pharmacists can be obtained in routine interval for the feedback purpose. This intervention doesn't need any extra human or physical resources compared to other interventions such as feedback by the pharmacists, continuous feedback mechanism by posters and email, and educational program on safe prescribing. Further the outcome of these interventions is less compared to the ZTP. Even though the findings from Gordon 2012 had the Odd Ratio 0.19 (Figure 1) and can minimize the errors by nearly 81%. But the intervention needs frequent assessment of the prescription and systematic feedback with posters and individual notices which requires extra efforts.

Computer assisted prescribing hasn't provided a promising outcome yet (Lavan 2016) and the bar code assisted medicine dispensing system has increased the number of medication errors. (Samaranayake 2014) This gives an implication that prescriptions should be human generated either can be hand written or typed in the computer and there should be Zero Tolerance for the error.

Conclusion

This review was able to identify interventions which can be done in minimal resourced settings to reduce the prescribing errors in a sustainable manner. The reduction in prescribing error can lead to safe prescribing where the adverse effects and drug interactions can be brought to a minimum. Every hospitals and ward can do interval audit or assessment of the prescriptions and can identify the prevalence of prescribing errors and can adapt an intervention to minimize them, which can increase the quality of health care service further. A multidisciplinary approach involving the doctors, nurses and the pharmacists in the intervention as done in the Zero Tolerance Prescribing policy and feedback mechanism can bring the prescribing errors to a minimum which can be done in any resource limited inpatient setting.

Conflict of interests

Nothing to declare

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BRIEF ORIGINAL ARTICLE

Patient distribution in an urban community medical clinic and effective health care planning

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Abstract :

New medical specialties are constantly created; a large number of roles exist in patient care setting, and many different public and private organizations. All these roles in healthcare organizations are involved in the care of a single patient. However, decentralization of health care has to be implemented in order to provide quality and effective care to individuals with complex medical conditions. We have carried out a descriptive cross-sectional study to analyse the disease conditioned patients following a medical clinic in a tertiary care centre in June and July 2018. There were 1811 patients. The common conditions for patients followed up in the medical clinic are hypertension (56%), diabetes mellitus (53%) and ischemic heart disease (18%). Fifty one percent of patients were suffering from a single condition and 36 were suffering from two medical conditions. Due to the lack of non specialized centres for simple diseases like hypertension and bronchial asthma and due to the close proximity of the hospital, there's quite a follow up of patients within this clinic. We would like to suggest to a peripheral centre to be put up at the premises of tertiary centre or even outside to follow up simple conditions, where the burden in specialists' centres would be reduced.

Introduction

Epidemiological data can be useful in the design of new prevention strategies [1]. There is worldwide data available regarding the prevalence, morbidity and mortality of chronic diseases. Commonest medical conditions people are suffering with include cardiovascular conditions followed by diabetes mellitus [2]. Rising of the prevalence of Non Communicable disease is one of the major health challenges in Sri Lanka as it has caused the "double burden" [3]. Most of the medical clinics are overburdened by these patients. Physicians are treating them in outpatient clinics.

There are several types of government hospitals like the National Hospital of Sri Lanka, Teaching Hospitals, Provincial General Hospitals, District General Hospitals, Base Hospitals and Divisional Hospitals. Patients with all the types of diseases are presented to the medical clinics conducted by these hospitals (Annual health statistics, 2018). New medical specialties are constantly created; a large number of roles exists in patient care, and many different public and private organizations. All these roles in healthcare organizations are involved in the care of a single patient. However, decentralization of health care has to be implemented in order to provide quality and effective care to individuals with complex medical conditions. When this is the case, specialist centres would be providing care to basic conditions such as pure and simple hypertension, diabetes and asthma whereas the more complex conditions which require much more attention, are cast aside. This system is a classic example of the failure of the health care structure of this country, where we see specialities providing health care to unnecessarily straightforward conditions; this leads to these centres being overburdened and thus affects the complicated patients unfavourably. Therefore, this study is planned in such a way, to describe the type of patients followed up in a medical clinic in a tertiary care centre, in a Teaching Hospital.

Methods

A descriptive cross-sectional study was carried out the year of 2018, from June and July. All the medical clinic attendees

from the ward 21 and 22 clinics, conducted on Wednesday and Friday were included in the sample. The various disease conditions the patients were on treatment for were classified by the investigators with the help of patient medical records. These were recorded as percentages and with the use of 95% confidence intervals.

Results

There were 1811 patients present in both clinics. The following table describes the various disease conditions of the patients attending to the clinic.

Table 1. Different disease conditions classified

Condition	Frequency	%	95%	C.I.
IHD	326	18.0	16.2	19.8
DL	150	8.3	7.1	9.6
DM	965	53.3	50.9	55.6
HTN	1023	56.5	54.2	58.8
Stroke	50	2.8	2.1	3.5
Other CVS conditions	37	2.0	1.4	2.7
Renal diseases	24	1.3	0.1	1.9
CLCD	7	0.4	0.1	0.7
Arthritis and connective tissue diseases	53	2.9	2.2	3.5
GORD	8	0.4	0.1	0.9
COPD, Bronchiectasis	52	2.9	2.2	3.5
Asthma	85	4.7	3.7	5.7
Neurology	75	4.1	3.2	5.1
Haematology	23	1.3	0.1	1.9
Other Diseases	25	1.4	0.1	2.0

Table 2. Number of disease conditions patients are having who are attending to the medical clinic.

Number of diseases	frequency	%	95% CI
1 disease	933	51.52	49.2-53.8
2 diseases	656	36.22	34.1-38.4
3 Diseases	194	10.71	9.3-12.1
4 diseases	26	1.44	0.9-2.0
5 or more	1	0.06	0.05-0.20
Total	1811	100.00	

Discussion

The most common conditions of patients followed up in the medical clinic are as follows: hypertension (56%), diabetes mellitus (53%) and ischemic heart disease (18%). It is the same as the epidemiological data in the country. At the same time, all subspecialty conditions related to internal medicine were also followed up in the clinic. It's also important to note that nearly 933 patients with only one disease condition were also followed up in the sample. If we consider a 7-day clinic for one month with 5 doctors seeing patients in the clinic; that is nearly 52 patients that should be seen by one medical officer for 4 hours. It comes down to 7 minutes for one patient.

One finding clearly illustrates that conditions like pure and simple hypertension and bronchial asthma are followed up in our clinic due to the convenience of a nearby hospital and because of the lack of non specialized centres to follow up these patients. We would like to suggest to a peripheral centre to be put up at the premises of a tertiary centre or even outside to follow up simple conditions, where the burden in specialists' centres would be reduced.

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ORIGINAL ARTICLE

Pattern of anaemia among end-stage kidney disease

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Abstract :

Anaemia is one of the common complications associated with Chronic Kidney Disease (CKD) liable for the increase in the morbidity and mortality in such patients. Numerous factors have been attributed to cause renal anemia, amongst which hyperparathyroidism is one of the less recognized reasons. The excess amount of Parathyroid Hormone (PTH) secondary to CKD has been suggested to be a contributing factor for anaemia. The introduction of erythropoietin considerably improved anaemia in patients with CKD by relieving symptoms and avoiding complications associated with blood transfusion. The aim of the study is to see the prevalence of the anemia severity among CKD patients who are on regular dialysis. A descriptive, observational study was conducted at the dialysis unit at the Teaching Hospital Batticaloa, SriLanka. All cases attending the center for regular dialysis were included in this study. Majority of the dialysis patients 26 (62%) had hemoglobin in the range of 7-9g/dl, 7(16.7%) patients had hemoglobin of more than 10g/dl and 4(9.5%) patients had hemoglobin below 7g/dl. This study is clearly shown that almost all (100%) dialysis population had anemia. In conclusion, the use of iron therapies and erythropoiesis stimulating agents (ESAs) has allowed improvement in patients with anemia of CKD.

Key words:

Anemia among chronic kidney disease and anemia among hemodialysis patient

Introduction

Chronic kidney disease (CKD) contributes to the globally growing burden of non-communicable diseases, which represent the largest cause of death worldwide. Deficiency in the renal erythropoietin production in patients with CKD leads to anaemia and, subsequently, to severe restrictions to health and quality of life. Iron therapy, with or without concomitant administration of erythropoiesis-stimulating agents (ESAs), has been used in the management of anaemia in the chronic kidney disease (CKD) population for many years. Several studies have revealed the association of hyperparathyroidism with CKD [1]. Parathyroid hormone (PTH) is a major uremic toxin which may be blamable for long term consequences in CKD such as renal bone disease (osteodystrophy), vascular calcification, altered cardiovascular function, immune dysfunction and anaemia[2].However recently, the use of iron therapy as a means to delay the need for alternative anaemia management in the pre-dialysis population or to lower the required dosage of ESAs in the haemodialysis (HD) population has come to the fore [3]. Inadequate dietary iron uptake may be attributed by poor appetite or dietary restrictions, and intestinal bleeding may result in increased iron losses. The magnitude of this problem is exacerbated in patients receiving dialysis who experience significant additional iron losses due to blood residual in the dialyzer circuit after treatment[4].In addition to that, Patients with CKD getting treatment with erythropoietin are very prone to develop iron deficiency due to the increased demand for iron to support erythropoiesis, and certainly iron deficiency is the most commonly identified cause of hypo responsiveness to erythropoietin therapy in dialysis patients[5][6]. However, various pathophysiological mechanisms have been sketched by in vitro and in vivo studies, regarding the worsening effect of raised parathyroid levels on the haemoglobin levels, but no definitive mechanism has been recognized [7]. The CKD is divided into five

stages, classified according to the degree of the patient's renal function. Until the fourth stage of the disease, the so-called "conservative treatment" is recommended. In more advanced stages, called End-Stage Renal Disease (ESRD), i.e., when the kidneys can no longer maintain homeostasis of the body, the patient will depend on one of the modalities of Renal Replacement Therapy (RRT). Our study suggests that targeting hemoglobin levels in excess of 12.0 g/dL leads to small and not clinically meaningful improvements in health related quality of life(HQOL).However as a whole expert panel suggested that targeting treatment to hemoglobin levels that are in the range of 9.0 to 12.0 g/dL is preferred. Taken all the international guidelines and our clinical experiences together, we should consider administration of ESAs when the hemoglobin level becomes <11 g/dl in pre-dialysis patients and <10 g/dl in dialysis patients [8]. At present, suggested hemoglobin target levels for erythropoietin treatment in CKD in the USA are in the range of 11.0–12.0 g/dL and should not be greater than 13.0 g/ dL. In their clinical practice guidelines, the Kidney Disease Improving Global Outcomes (KDIGO) Work Group suggests erythropoietin should not be used to maintain hemoglobin concentration above 11.5 g/dL in adult patients with CKD, but recommends an individualization of therapy for some patients who may have improvements in quality of life with higher hemoglobin concentrations [9][10].The aim of the study is to see the prevalence of the anemia among ESRD patients who are on regular dialysis.

METHODOLOGY

A descriptive observational study was conducted with ESRD attending for the haemodialysis unit Teaching Hospital Batticaloa, SriLanka. All cases attending the study center for regular dialysis were included in this study. However, we included all data from adults age of 18 years and above 18 years and those who have been on dialysis for at least three-month duration. The study was conducted from mid of September 2017 to end of November 2017. We did not include the data from patients with carcinoma involving one or both kidneys and patients who undergone renal transplant. Finally, 42 ESRD patient's medical records were analyzed in this study.over a period of two and a half month from mid of September 2017 to end of November 2017,data were harvested from the medical records with the help of validated questionnaire. For this study and further its publication, consent was taken from the head of the institution. In this study anaemia was defined by a decrease in hemoglobin to <130 g/l in men and <120 g/l in women [11].

RESULTS

Out of 42 patients there were 25(59.5%) males and 17(40.5%) females (Table 1). There was a male: female ratio of 1.47:1. The youngest patient was 19 years of age and the oldest was 68 years of age. In this study nearly half of the patients20 (47.6%) were in the age group of 50-69 and another half of the patients 21(49.1%) were in the age group of 20-40(Table 1). Only 7(16.7%) out of 42 patients had a hemoglobin level of above 10g/dl. Majority of the dialysis patients 26 (62%) had hemoglobin in the range of 7-9g/dl. However, 4(9.5%) patients had hemoglobin below 7g/dl (Table 1).

Table 1 pattern of age, sex and haemoglobin

Sex	Frequency	%
Male	25	59.5
Female	17	40.5
Age		
<20	1	2.4
20-29	3	7.1
30-39	8	19.0
40-49	10	23.8
50-59	11	26.2
60-69	9	21.4
Age		
<20	1	2.4
20-29	3	7.1
30-39	8	19.0
40-49	10	23.8
50-59	11	26.2
60-69	9	21.4

DISCUSSION

The prevalence of anemia is higher among patients with chronic kidney disease (CKD) than among the general population. Moreover, anemia tends to be more severe in patients with more advanced CKD. The prevalence of anemia severity among dialysis patients haven't been evaluated in SriLanka. On the other hand, a study conducted among non-dialysis CKD patient in Korea, where the prevalence of anemia severity was 45.1% for Hb <13.0 g/dL, 18.8% for Hb <11.5 g/dL and 4.2% for Hb <10.0 g/dL, respectively[12].A similar study conducted by Aleix et al among non-dialysis patients, which revealed that the prevalence of anemia was 58.5%, however, only 14.9% of patients had hemoglobin levels less than 11g/dl[13].

However, this pattern has been totally changed in this study, majority of the dialysis patients 26 (62%) had hemoglobin in the range of 7-9g/dl, 7(16.7%) had hemoglobin of more than 10g/dl but less than 11g/dl and 4(9.5%) patients had hemoglobin below 7g/dl.. Normocytic normochromic anemia is one of the hallmarks of progressive chronic kidney disease (CKD). Normocytic normochromic anemia is defined by a decrease in hemoglobin to <130 g/l in men and <120 g/l in women [14]. According to this limit, our study is clearly shown that almost all (100%) dialysis population had anemia.

The treatment of anemia with erythropoietin in ESKD has revolutionized its treatment, but its use has been hardened by higher risks of cardiovascular morbidity and mortality. A recent meta-analysis found no difference in Hb concentrations between hemodialysis (HD) and peritoneal dialysis (PD) patients; however, treatment response to erythropoietin may vary depending on dialysis modality [15].

Erythropoietin therapy only is effective in the presence of sufficient iron to support increased erythropoiesis iron deficiency

is a major cause of erythropoietin hypo-responsiveness in patients with CKD. It is vital that iron deficiency should be addressed in patients prior to initiation of erythropoietin therapy [16]. The timing of iron therapy initiation, route of administration, and selection of treatment regimen should take into account a number of factors, including the severity of anemia, treatment goals, CKD stage and dialysis modality, comorbidities and concomitant patient health issues, as well as any relevant practical considerations. Intravenous administration of iron has been demonstrated to be more effective than oral administration with respect to the elevation of hemoglobin, ferritin and transferrin saturation levels in patients with ESRD [17].

CONCLUSION

Anaemia is a commonly diagnosed complication among patient's misery with chronic kidney disease. If left untreated, it may affect patient quality of life. There are several causes for anaemia in this patient population. As the kidney disease deteriorates, together with medications and dietary restrictions, patients may develop iron deficiency, resulting in reduction of iron supply to the bone marrow. The use of iron therapies and erythropoiesis stimulating agents (ESAs) has allowed improvement in patients with anemia of CKD. Newer therapies are under study, but this guideline will not make recommendations on agents such as hypoxia inducible factor stabilisers or hepcidin modulators as data remains preliminary. Chronic kidney disease patients may not be able to utilize their own body's iron stores effectively and hence, many patients, particularly those receiving haemodialysis, may require additional iron treatment, usually provided by infusion.

COMPETING INTERESTS

The author has no competing interests to declare

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CONSENT FOR PUBLICATION

Written informed consent was obtained from the parents for publication of this article

ETHICS APPROVAL

Not applicable

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ORIGINAL ARTICLE

Pattern of animal bites, a study conducted at Teaching Hospital Batticaloa in the East part of the SriLanka.

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Abstract :

An animal bite, especially dog bite is a major health and economic problems all over the world especially India, Bangladesh and SriLanka. Rabies is recognized as a one of the most neglected disease in developing countries, which cause to burden to rural and poor children. Incidence of an animal bites, especially dog bite increasing in the Batticaloa district in SriLanka. The objective of this article was identifying the current pattern of the animal bites and evaluate percentage use of anti-rabies vaccination.

Keywords: Animal bite, and dog bite in SriLanka.

Results: Total 923 animal bite victim were registered over a two months period from 1st of November to 31st of December 2018. Out of that 478 (51.8%) were males and 445(48.2%) were females. Among the animal bites, 700 (75.8%) were bitten by dogs, 213(23.1%) were bitten by cats, 5(0.5%) were bitten by rat and 1(0.1%) were reported as monkey bites. Remarkably, more than two-third of the bites 684(74.1%) were due to domestic dog and cat bites and 239(25.9%) were due to stray animals. It was obvious that 347(37.6%) of animal bites were reported at Batticaloa medical officer of health (MOH) area. In this study 886 (96%) of victims received anti-Rabies vaccination.

Introduction:

An animal bite, especially dog bite is a major health and economic problems all over the world especially in Asia and Africa. It is causing fear of anxiety and rabies. It is understandable that non-treated animal bite ends up with fatal outcome(1). Dogs are the main pool and route of the rabies in SriLanka. However, other mammals such as cat, monkey, wolves, foxes, jackals, mongoose, bats, and human also responsible for spread of rabies(2). Rabies is recognized as a one of the most neglected disease in developing countries, which cause to burden to rural and poor children. In SriLanka nearly 20-30 cases of rabies are reporting annually result of bites by unvaccinated dog(3).However, rabies virus or other lyssaviruses is responsible for nearly 50,000 deaths in each year in Asia(4).SriLanka is an Island situated in the Indian ocean closely with south end of the India. People from both sides are illegally do business for long period, which is high chance of getting rabies infected cats, rats and dogs are exchange both places. It is interesting that out of all Asian countries, rabies death rate are lowers in SriLanka, however rabies is still endemic and remains a substantial health problem. Even though SriLanka is a developing country, it spent huge amount of money for post exposure vaccination. In average, country spent nearly 175 US dollars per victim for post-exposure prophylaxis(5). According to the circular of ministry of health of SriLanka, stated that government spent nearly 50 million US dollars per annually for rabies control programme(6).

Regardless of economic burden and fear of rabies and anxiety, there is less information about the incidence of animal bite and rabies because of poor reporting system among rural population in SriLanka. Moreover, in our area many native medical practices are followed after dog bites, especially application of herbal extract, chilli paste and oil. Victims are usually got infected following bite or scratch by infected animals. Human to human transmission by bite is possible however , this mode of transmission is not been reported jet(7).The objective of this article was identifying the current pattern of the animal bites and estimate the use of anti-rabies vaccination.

Materials and Methods:

A descriptive-observational study was conducted at the accident emergency unit in the Teaching Hospital Batticaloa over a period of two months from 1st of November to 31st of December 2018. Accident emergency unit has well established post exposure vaccination unit with trained staffs. All the animal bites were registered and assessed for vaccination at the emergency department, where all demographic data, type of bites, type of animals and vaccination history were gathered and preserved in each patient's medical records. Post exposure vaccination was started once assessment has finished. This early assessment prevents the unnecessary delay of post exposure treatment. We harvested appropriate date from the patients' medical records with the help of pre-tested questionnaire. Before, collection of data the prepared questionnaire was pilot tested, and validity of its content and necessary corrections were made. This pre-tested questionnaire was filled by trained investigator. Data was entered and analyzed in SPSS (19) software.

Result:

A Total 923 animal bites victim were registered last two months of 2018, out of that 478 (51.8%) were males and 445(48.2%) were females (Table 1). Among the animal bites, 700 (75.8%) were bitten by dogs, 213 (23.1%) were bitten by cats, 5(0.5%) were bitten by rat and interestingly, 1(0.1%) were reported as monkey bite (Table 1). Remarkably, more than two-third of the bites 684(74.1%) were due to domestic animals and rest of the bites 239(25.9%) were due to stray animals. Among the animal bites more than half of the bites 551 (59.7%) occurred at legs and followed by hands 207 (22.4%).

Animal bites were reported in wide range of age groups, 345 (37.4%) of bites occurred in the age group of 30 -60, followed by 284 (30.8%) were under 16-year and 195(21.1%) were categorized in the age group of 17-29 (Table 1).Among the medical officer of health(MOH) area, 347(37.6%) of animal bites were reported at Batticaloa MOH area, 185 (20%) were in the Vavunatheevu area, followed by 160(17.3%) were in the Chenkalady area , 76(8.2%) were equally reported in the Eravur and Pattipala area(Table 2). In this study 886 (96%) of victims received anti-Rabies vaccination.

Table 1. Summary on patients underwent RCEx

Sex	Number of bites	(%)
Male	478	51.8
Female	445	48.2
Age categories	**Number of bites**	**%**
0-8	130	14.1
9-16	154	16.7
17-29	195	21.1
30-60	345	37.4
>60	99	10.7
Type of animals	**Number of bites**	**%**
Dog	700	75.8
Cat	213	23.1
Monkey	1	0.1
Rat	5	0.5
Pig	1	0.1
Dog and cat	1	0.1
Wild rat	2	0.2
Types of wound	**Number of bites**	**%**
Superficial	704	76.3
Multiple	55	6.0
Deep	114	12.4
Multiple and deep	22	2.4
Superficial and multiple	28	3.0

Table 2. Pattern of animal bites in different MOH area

MOH Area	Number of bites	Percentage (%)
Vavunatheevu	185	20.0
Eravur	76	8.2
Vakarai	5	0.5
Valaichenai	1	0.1
Chenkalady	160	17.3
Batticaloa	347	37.6
Kaluwanchikudy	16	1.7
Kiran	25	2.7
Kattankudy	6	0.7
Pattipala	76	8.2
Vellaveli	2	0.2
Arayampathy	24	2.6

Discussion:

The prevalence of dog bites is higher among other animal bites in the Batticaloa district in SriLanka. It carries major public health problem in this region. Emergency department in the Teaching Hospital Batticaloa, provides post-exposure prophylactic vaccine for animal bite. Nearly, 5714 were registered throughout the period of 2018 . Last two months of 2018, total 923 animal bite victims were registered, out of that 478 (51.8%) were males and 445(48.2%) were females. Among the animal bites, 700 (75.8%) were bitten by dogs, 213(23.1%) were bitten by cats, 5(0.5%) were bitten by rat and 1(0.1%) were reported as monkey bite. Similar study was conducted in India, where 63.7% of victims were bitten by dog(8).Furthermore, parallel study was conducted in Tamilnadu where 52% of bites were by

dogs(9). Moreover, similar observation was seen in a study, which was conducted by Karla Georges et al(10).Furthermore, another study was conducted in Kenya, where also males were more prone to get animal bite than females and dogs were involved for the 93% of animal bites(11).A similar study conducted at central part of the SriLanka , where pattern of sex differences were nearly same as our study(12).Almost all the studies clearly shown that males were more affected than female's counterpart, this is because males are more movable nature in this regions and dog bite were more common than other animals because peoples are rearing dogs in their home as a pet. Furthermore, cultural and religious believe in SriLanka that killing animals or do harm to the animals are consider as great sin. This is the reason people are petting animals in their home as hobby and ovoid their loneliness.

In our district, animal bites were reported in a wide range of age groups, 345 (37.4%) of bites noticed in the age group of 30 -60, followed by 284 (30.8%) were under 16 years old and next to that 195(21.1%) were in the age group of 17-29.It was obvious that more than 50% of victims were under age group of 17-60 .This is the productive age group naturally go for study, or work and to earn livelihood. Remarkably, more than two-third of the bites 684(74.1%) were due to domestic animals and rest of the bites 239(25.9%) were due to stray animals. Interestingly in our district ¾ of the bites were due to domestic animals. However, a similar study was conducted by Vishwanath G R et al, in India where 35.5% of animal bites were observed under 14-year -old age group, majority (60%) of bites were seen the age category of 15-65 and most of the bites were due to stray animals(13).This pattern clearly correlates with the time spent out of doors activities and risk for animal bite. However, according to the study conducted by Murugan vengatesan et al nearly 70% of the animal bites was happened in or around the houses(14).

In our study more than half of the bites 551 (59.7%) occurred at legs and followed by hands 207 (22.4%). Most 704(76.3%) of the bite injuries are superficial , only 114(12.4%) were deep injuries, and 55(6.0%) were multiple njuries.According to the Karla Georges et al study, 39.3% of victims had leg injuries(10).A similar study was conducted by Neera Marathe et al , where 60.8% of bites were observed in the lower limbs(15).

The medical administrative purposes, Batticaloa district has been divided number of medical officers of health (MOH) area. Some areas such as Eravur and Kattankudy where Muslim population are high, where incidence of dog bites was less compared with their population, this is because they have strong believe on petting animals is sin (Karaam).

In this study 886 (96%) of victims received anti-Rabies vaccination. Similar study was conducted at central part of the SriLanka where nearly 99% of animal bites were received post exposure rabies vaccination(12).However, Sangeetha S et al found that only 60.61% of victims received anti-rabies vaccine(8).In SriLanka, anti-rabies vaccines are freely available in the government sector and people receive post exposure prophylaxis without any delay. World Health Organization (WHO) designed the strategy for SriLanka to elimination of dog-related rabies death by 2030(16)(17).

Conclusion

In conclusion, animal bites especially dog bites possess major public health problem in the Batticaloa district in SriLanka. It also causing injuries and hospital visit to young generation and also big impact on the health care budget due to use of huge number of anti-rabies vaccination. This magnitude of the problem highlights that need for public awareness on the health challenged caused by animal bites. Though dogs were the major threat to the community, there are number of other animal bites also needed post exposure vaccination. It is sad to say that most of the domestic animals are not received any immunization or not followed up by vetenary clinics. In future need, more public health education regarding immediate management of dog bite cases and take more action on eradicate the stray dogs in the Batticaloa district. Furthermore, system should be developed where local and state health department should link with local or state vetenary department and take action to control stray animals and immunize domestic animals. Government should implement low and legislation regarding strict immunization policy to all domestic animals.

Abbreviations

MOH: Medical Officer of Health, THB: Teaching Hospital Batticaloa.

Ethical approval

We did not get ethical approval, as the study was on the hospital record, which did not disclose the identity of the patients and we did not involve with any animal bite victims, we only took the permission from the director, Teaching Hospital Batticaloa SriLanka.

Authors contributions

MU: conceived the research idea, guided it and contribute 2/3 of the research work. KTS: data collection and entry. Both authors made significant contribution to design and interpretation of data and writing the manuscript.

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Competing interests

Authors declare that they have no competing interests.

Availability of data and materials

All the data were presented in the main paper.

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CASE REPORT

Therapeutic plasmapheresis as a bridge to liver transplantation in fulminant Wilson disease

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Abstract :

Wilson disease is an autosomal recessive disorder of copper metabolism that leads to the accumulation of copper mainly in the liver, cornea, brain, and kidney. Rarely, Wilson disease can present as fulminant hepatic failure with direct agglination test (DAT) negative hemolytic anemia and renal failure. In the absence of liver transplantation, this disease is uniformly fatal. This report describes the successful use of plasmapheresis for a patient with fulminant Wilson disease as a bridge to transplantation. Five daily therapeutic plasmapheresis procedures using fresh frozen plasma as a replacement fluid were performed over 6 days. Serum bilirubin fraction, liver enzymes and hemolysis were significantly reduced, and renal functions were improved. The patient's clinical status improved, and he remained clinically stable without a liver transplant. Plasmapheresis can be a successful medical treatment in fulminant Wilson disease and should be considered as a therapeutic measure to stabilize a patient by decreasing serum copper, reducing hemolysis, and helping to prevent renal tubular injury from copper and copper complexes until liver transplantation is possible.

Introduction

Wilson's disease (WD) is an inherited metabolic disorder caused by mutations in the copper transporting enzyme P-type ATPase gene [1] .WD is characterized by the accumulation of copper in the liver, brain, kidney and corneas, leading to hepatic or neurologic manifestations in the majority of patients [2]. A minority of patients develop fulminant hepatic failure (FHF) accompanied by a hemolytic crisis [1,3]. It can result in death within 1 or 2 weeks if a liver transplantation is not performed.[4]

It has been reported that orthotopic liver transplantation is essential for a favorable outcome in patients with fulminant Wilson's disease (FWD).[5-8] However, it is limited by the lack of donor liver and an emergency liver transplantation cannot be performed in most cases at the time of diagnosis. Rapid and exact diagnosis by means of clinical, biochemical and genetic analysis and the immediate use of drug therapy with copper chelators are important for a favorable outcome in patients with FWD.

However, medical therapy is rarely effective in patients presenting with acute liverfailure resulted from WD, mainly due to the time required to remove toxic copper from the patients. It is worthwhile to explore a more effective therapeutic strategy for these patients. Several prediction systems for FWD and liver transplantation decision making have been developed. New Wilson's index,[9] Child-Pugh score and model for end stage liver disease (MELD) scores are useful tools for decision making on liver transplantation. A score of new Wilson's index greater than 11 is always fatal without liver transplantation.[10] Patients with a Child-Pugh score of ≥7, which places the patients in Child-Pugh class B or C, should be on the liver transplant waiting list.

Cirrhotic patients who have experienced gastrointestinal bleeding caused by portal hypertension or a single episode of spontaneous bacterial peritonitis (SBP) would meet the minimal liver transplant criteria irrespective of their Child-Pugh score.

Furthermore, patients with fulminant hepatic failure regardless of etiology of the onset of stage 2 hepatic encephalopathy meet the minimal criteria for liver transplantation.[11] Patients with a higher MELD and higher Child-Pugh score are at greater risk of death without liver transplantation.[12,13]

We report a case of acute Wilson's disease that rapidly progressed to life threatening multi organ failure and discuss the

presentation, diagnosis, and acute management options that can bridge patients to liver transplantation with an optimized comprehensive treatment including corticosteroid, copper-chelating agents (dimercaptopropansulfonate sodium, DMPS) administration and therapeutic plasma exchange (TPE) exerted positive effects on patients with FWD whose prognosis had been unfavorably judged by the prediction systems for FWD and liver transplantation decision-making. It is reasonable to reevaluate the prediction systems and the therapeutic strategy for patients with FWD, especially in the case of donor liver shortage and an emergency liver transplantation cannot be performed.

Case Report

A 18 year old boy was presented to local hospital with fever and yellowish discolorations of the sclera for 3days duration, Fever was sudden onset, intermittent spick without chills and rigors, responded to Paracetamol. On 3rd day of fever, he noticed yellowish discoloration of the sclera and palm, Yellowish discoloration was progressively deepened and ended up with tea colored urine, but no pale stools. He had epigastric pain without nausea or vomiting and had loss of appetite without weight loss. He was treated as viral hepatitis with cholestatic phase and discharged on 6th day of illness.

He readmitted two weeks following discharge with history of leg swelling, abdominal distention and persistent yellowish discoloration. He was re-evaluated and transferred to our hospital for further management.

On the third day following admission he got episodic dystonic movements involved his facial muscles, he became drowsy and transferred to medical intensive care unit(ICU). At ICU he was incubated electively.

He denied substance abuse and multiple sexual partners or unprotected sex, history of recent paracetamol overdose, history of blood transfusion and history of outside food intake . He is a non smoker and non alcoholic and no family history of liver disease.

He was deeply Icteric and pale , his blood pressure was 119/79 mmHg, heart rate was 105 beats per minute, respiratory rate was 20 breaths per minute, and oxygen saturation was 99% on ambient air(figure-1). He was alert and oriented a mildly distended abdomen without shifting dullness, and pitting edema of the lower extremities. On4th day GCS < 8/15(intubated later), developed flapping tremors , constructional apraxia and exaggerated deep tendon reflexes with down going planter.

Laboratory initially revealed mildly elevated transaminases with increased bilirubin, hypoal buminemia, and elevated international normalized ratio (INR) indicative of hepatocellular liver injury with impaired liver synthetic function (figure- 2). Further testing revealed negative results for Hepatitis A (IgM and IgG), Hepatitis B (surface antigen, e antigen, and core IgG), Hepatitis C (IgM and IgG), anti-nuclear antibody, and anti-smooth muscle antibody, making viral and autoimmune disease extremely unlikely. His serum ceruloplasmin level was low at 8 mg/dL (normal 22–50 mg/dL), without availability of serum and urine copper levels.

The findings of acute hepatitis and low ceruloplasmin level prompted a slit-lamp ophthalmologic exam revealing copper deposition in Descemet's membrane of the cornea consistent with the Kayser-Fleischer (KF) ring, confirming the diagnosis of Wilson's disease on progressive days .

Clinical deterioration ensued with increasing abdomen distention and development of hepatic encephalopathy. Hemolysis developed on day 5 with nadir hemoglobin of 7.2 g/dL, high LDH, undetectable haptoglobin, and negative direct Coomb's test, in addition to worsening hepatic function. The patient was subsequently placed on mechanical ventilation. The Plasmapheresis using fresh frozen plasma (FFP) was initiated to reduce the high serum copper level that was believed to be producing hemolysis and renal tubular damage.

He was started corticosteroid with liver failure regime and received plasmapheresis removing a total of approximately 5cycles, in addition to one unit RBC pack cell transfusion for anemia. The liver biopsy was performed with interval of 1 month. The explanted liver grossly had a tan-yellow hue with nodularity. Histologic findings revealed chronic inflammatory changes and extensive bridging fibrosis. A tissue copper quantification was not performed due to unavailability. He was discharged on standard immunosuppressive therapy but is expected to have no further complications related to copper overload.

Figure-1 admission clinical appearance.

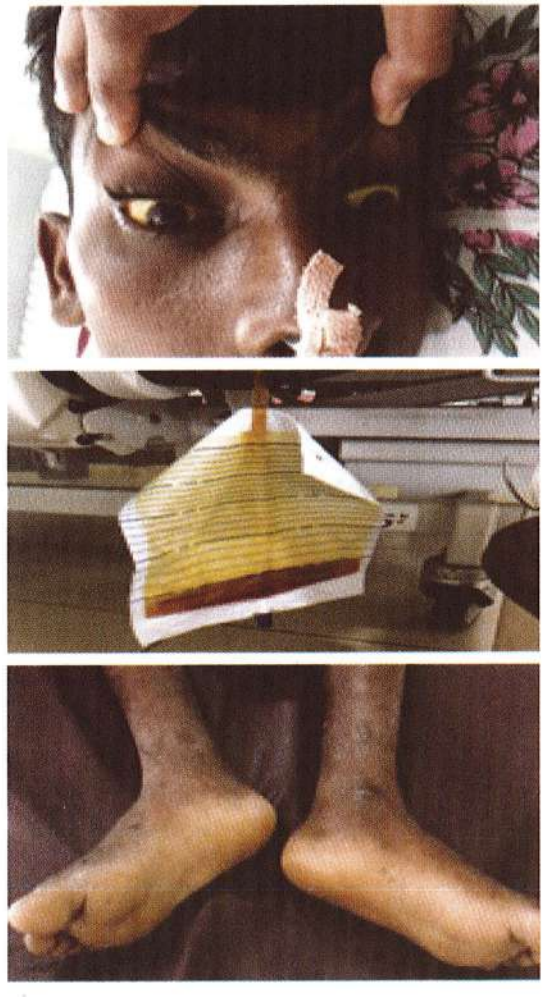

Figure-1 admission clinical appearance.

Investigation	Admission	ICU	Plasmapheresis started				
			D1	D2	D3	D4	D5
AST IU/L	831	567	527	275	251	225	183
ALT IU/L	434	311	257	135	150	155	163
ALP IU/L	226	280	152	142	142	120	98
Total protein	7.6	7.2	7.7	5.9	6.6	5.6	4.9
Serum albumin	2.4	2.1	3.4	3.4	2.6	2.7	2.5
INR	1.24	2.62	2.69	2.23	3.08	2.2	1.85
Total bilirubin	36	616	567	419	415	376	286
Direct bilirubin	12	156	396	262	228	216	198
Gamma GT	68	78	64	70	80	78	84
BU	20	91	94	75	45	32	12
Scr	1.1	1.4	2.1	1.8	1.0	0.8	0.9

Discussion

In Fulminant Wilson disease plasma exchange is rare Recommendation (Category TPE Grade 1C level evidence). Number of reported patients:<100 in world wield.

Wilson's disease is an autosomal recessive genetic disorder resulting from a mutation in the ATP7B, which encodes a copper transporting ATPase protein, leading to impaired biliary copper excretion, resulting in copper accumulation in the liver, brain, cornea, and kidney. Copper's incorporation into ceruloplasmin is also impaired. Birth incidence rates are 1/30,000– 40,000. It has been estimated that 1% of the population are carriers. The disease usually presents between ages 5 and 35 years. Children present with asymotomatic liver deposits of copper, teenagers with liver disease, and adults with neurological symptoms.

The spectrum of liver disease includes asymptomatic liver function test (LFT) abnormalities, hepatitis, cirrhosis, and acute liver failure (ALF). Neurological symptoms include Parkinsonism, dystonia, cerebellar, and pyramidal symptoms. History of behavioral disturbances is present in half of patients with neurological disease. The appearance of Kayser– Fleischer rings (copper deposits in the outer rim of the cornea) and direct antiglobulin test negative hemolytic anemia are relatively common. The hemolysis appears to be primarily due to copper-induced oxidant stress to RBC enzyme pathways and membrane damage. ALF is typically accompanied by hemolytic crisis and multiorgan failure with rapid clinical deterioration, and is nearly always fatal without liver transplantation (LT). No laboratory test is diagnostic but suggestive results include low serum ceruloplasmin, increased 24-h urinary copper excretion, and elevated serum copper. The gold standard for diagno- sis is a liver biopsy showing elevated copper content. A genetic test for ATP7B is available.

Current management/treatment Asymptomatic patients should be treated, since the disease is almost 100% penetrant. Low-copper diets are recommended. Zinc acetate is nontoxic and stimulates metallothioneine which reduces dietary and enterohepatic absorption of copper. It is the therapy of choice for asymptomatic patients or patients with hepatitis or cirrhosis, but without evidence of hepatic decompensation or neurologic/psychiatric symptoms. Zinc is also first choice in pediatric and pregnant patients. Chelation therapy (penicillamine, trientine) increases urinary copper excretion. Trientine has replaced penicillamine as the primary chelator due to less toxicity. If penicillamine is given, it should always be accompanied pyridoxine (25 mg/day). Chelation can be used as a temporizing agent to treat the enormous release of copper into the blood stream in ALF with renal failure; however substantial removal is not achieved for at least 1–3 months. Other methods have been used to reduce copper load in an attempt to stabilize patients including hemofiltration, albumin dialysis, and the Molecular Adsorbents Recirculating System (MARS). For initial neurologic therapy, tetrathiomolybdate is emerging as the drug of choice because of its rapid action, preservation of neurologic function, and low toxicity. Anticopper therapy must be life-long. LT is potentially curative and is the main stay of therapy for patients with ALF.

Disease severity is estimated using a prognostic score which is based on a combination of laboratory values, most commonly LFTs and coagulation status (INR/PT). Liver transplantation (LT) reverses most of the clinical and biochemical pathological manifestations of the disease within few months.

Rationale for therapeutic plasmapheresis Donor organs for Liver transplantation are not always available and temporizing treatments must be aimed at treating the release of massive amounts of copper into circulation. In this scenario, TPE can be beneficial as it rapidly remove significant amount of copper from the circulation average of 20 mg per TPE treatment. Decreased serum copper may decrease hemolysis, prevent progression of renal failure, and provide clinical stabilization. TPE can also remove large molecular weight toxins (aromatic amino acids, ammonia, endotoxins) and other factors which may be responsible for hepatic coma.

In most reported cases, TPE was used as a bridge to Liver Transplantation. Interestingly, recent reports showed that TPE combined with chelating agents improved ALF and eliminated need for LT. In addition, the widespread availability of TPE technology makes it a more accessible reasonable choice of therapy. Plasma replacement rapidly corrects coagulopathy. Plasma/albumin combination is also possible as use of albumin alone will worsen coagulopathy. TPV Frequency: daily or every other day Replacement fluid: Plasma, albumin.

Duration and discontinuation/number of procedures Serum copper reduction in most CRs had been achieved rapidly and maintained after the first two treatments. However, the total number of TPE performed is variable, depending on LT availability or recovery. Specific laboratory tests for the disease (serum copper, 24-h urinary copper excretion) are not routine testing thus are not helpful to guide effectiveness and the frequency of the treatment. In most cases judgment is based on clinical parameters and routine testing (improved encephalopathy and LFTs & controlled hemolysis).

Wilson's disease patients; however, with fulminant disease and rapidly progressive renal failure, the benefit is unclear. There have been reports of the use of D-penicillamine in combination with

plasmapheresis in the acute setting with successful outcomes . Nonetheless, the mortality rate in patients with fulminant liver failure approaches 100% without emergent liver transplant.

Liver transplantation is indicated for patients with Wilson's disease in the setting of fulminant liver failure or chronic liver disease unresponsive to medical management. Liver transplantation results for Wilson's disease appear to be excellent with multiple studies reporting 5-year survivals >85% andexcellent long-term prognosis. The largest of these series was reported from France, including 121 patients transplanted for Wilson's disease between 1985 and 2009, with the reported survival rate of 87% at 5, 10, and 15 years following transplantation

Conclusion

Wilson's disease should be suspected in young patients presenting with fulminant liver failure of unknown etiology. In this setting, plasmapheresis is effective for stabilization of clinical and laboratory parameters and served as a bridge to liver transplant. This case further supports the use of serum copper-reducing modalities in the setting of fulminant Wilson's disease.

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CASE REPORT

Diabetic Ketoacidosis in Type 2 Diabetes Mellitus "look under the sheet please."

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Abstract :

DKA is a cardinal feature of type 1 diabetes, which has led to the widespread errant perception that it is a complication unique to type 1 diabetes due to insulin deficiency. [1] It can be the first presentation of diabetes. This accounts for about 6% of cases. Diagnostic criteria for DKA include presence of blood glucose >250 mg/dL, arterial pH of ≤7.30, bicarbonate level of ≤18 mEq/L, and adjusted for albumin anion gap of >10–12. [2] However, it has been repeatedly reported that DKA does occur in patients with type 2 diabetes. Moreover, it can occur even in patients who were previously insulin independent.

Studies evaluating consecutive admissions for DKA at large academic centers observed that 21.7% had type 2 diabetes. [3] Nearly 70% of the admissions involved discontinuation of medications, and almost half had an identifiable infection when an intensive search was undertaken.

Case history

A 44-year-old female was admitted to the emergency department of Teaching Hospital, Batticaloa with sudden onset of dyspnoea abdominal pain and dizziness. She had been on treatment for type 2 Diabetes mellitus for 8 years and not taken treatment for past 6 days. Clinical examination revealed a dehydrated with a heart rate of 122 beats/min, temperature of 37°C. Her blood pressure was 85/55 mmHg. She was tachypnoeic and dyspnoeic with a respiratory rate of 36 breaths/minute. There were no focal neurological deficits. Respiratory examination was normal other than the dyspnoea and tachypnoea. Abdomen was soft and non-tender; bowel sounds were present. Electrocardiogram (ECG) showed a sinus tachycardia. Arterial blood gas revelaed a pH of 6.97with a bicarbonate level of 12 mmol/l. Arterial pO2 and pCO2 levels were 91 mm Hg and 22 mm Hg, respectively. Random plasma glucose was Hi index and urine Ketone bodies were not done due to unavailability of the test. Potassium was 3.1 mmol/L, and the renal and liver function tests were normal. Neutrophilic leucocytosis was there and serum lactate level was 3mmol/L. She was started on rapid fluid boluses with 9% saline infusions and fixed rate intravenous insulin at the same time. With fluid, insulin and potassium infusions she was improved. Patient was counseled on diabetic treatment and discharged from the hospital 3 days later.

Discussion

Ketoacidosis occurs in diabetics as a function not only of severe insulin deficiency, but also due to elevated glucagon levels. Insulin is an anabolic hormone. Severe insulin deficiency results in decreased glucose utilization by muscle and an unregulated increase in lipolysis. This leads to an enhanced delivery of gluconeogenetic precursors (glycerol and alanine) to the liver. Furthermore, removal of the normal suppressive effect of insulin causes glucagon elevation.

Glucagon is a catabolic hormone. Glucagon promotes gluconeogenesis, decreases oxidation of free fatty acids to triglycerides, and promotes hepatic ketogenesis. Importantly, the concentration of insulin required to suppress lipolysis is only one-tenth of that required to promote glucose utilization. Typically, moderate insulin deficiency (as observed in patients with type 2 diabetes) is associated with sufficient insulin to block lipolysis (and therefore ketoacid formation), but not enough to promote glucose utilization. This leads to hyperglycemia without formation of the ketoacids.

DKA occurs in the setting of absolute or relative insulin deficiency combined with increased levels of counter-regulatory hormones, such as glucagon, catecholamines, cortisol, and growth hormone. Insufficient insulin and elevated counterregulatory hormones contribute to the hyperglycemia through glycogenolysis, gluconeogenesis, and decreased peripheral use of glucose. Volume

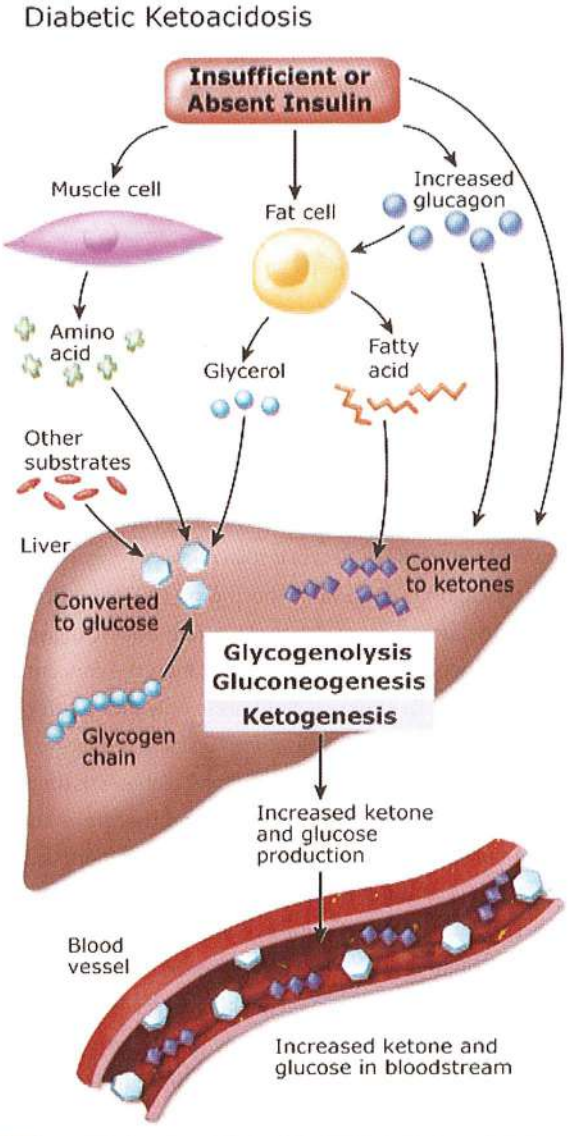
depletion is probably the principal factor that results in the marked hyperglycemia seen in DKA. The metabolic acidosis that develops in DKA is primarily the result of accumulation of the metabolic acids, acetoacetic acid and β-hydroxybutyric acid, in the plasma. These ketoacids develop as a consequence of the lipolysis and proteolysis that occur when elevated glucagon-insulin ratios cause increased hepatic levels of carnitine and decreased malonyl–coenzyme A concentrations.

When DKA occurs in patients with type 2 diabetes, the presumed mechanism of ketoacidosis is the combination of relative insulin deficiency and increased secretion of glucagon (as well as other counter-regulatory hormones such as cortisol, catecholamines, and growth hormone) in response to stress from

1. overwhelming infection,
2. infarction of tissue, or
3. other severe illness.

The elevated catecholamines further suppress insulin secretion to perpetuate a downward spiral. The increased glucagons-to-insulin ratio causes a mismatch that promotes unregulated lipolysis and proteolysis with subsequent uninterrupted formation of ketoacids.

Image 1. Pathogenesis of diabetic ketoacidosis



Diagnosis is based on biochemical criteria. However, hyperglycaemia may not always be present and low blood ketone levels (<3 mmol/L) do not always exclude DKA.[1] On the other hand, euglycaemic diabetic ketoacidosis (EDKA) is a rare complication of treatment with SGLT2 inhibitors in patients with type 2 diabetes.[2] Uncertainty remains about its precise mechanistic basis, but the physiological derangement is acute and profound, yet reversible with cessation of the drug. It is reminiscent of other "non type 1" presentations with DKA such as ketosis prone diabetes, except that glucose levels are usually normal. Impaired beta cell glucose sensing that mimicked a state of hypoglycaemia could theoretically lead to abrupt and transient cessation of insulin secretion. GLUT2 mediates glucose sensing in beta cells. In other tissues such as enterocytes, GLUT2 mediated glucose transport is controlled by SGLT1. Although the affinity of SGLT1 for SGLT2 inhibitors is low, hypothetically a rare variant within the SGLT family with a hitherto unrecognised role in GLUT2 mediated glucose sensing might have an affinity for the SGLT2 inhibitor ligand and thus give rise to acute, severe but reversible euglycaemic DKA in susceptible patients.

Conclusion

DKA is not a unique feature of type 1 diabetes. Though much more common in type 1 diabetes, it does occur in patients with type 2 diabetes, as illustrated by many case reports. However, it is rare for DKA to occur in type 2 diabetes in the absence of some precipitating event. When DKA occurs in an individual with type 2 diabetes, the clinician should "look under the sheets" and initiate an intensive search for the precipitating factor. Once identified, the trigger should be treated promptly and appropriately. You may also not find a trigger sometimes.

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CASE REPORT

Heart block following a kerosene oil poisoning

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Abstract :

Kerosene oil is commonly used in all part of Srilanka as fuel for cooking and lighting lamps. In Srilanka both accidental and intentional ingestion of kerosene for suicidal attempt is the commonest reason for poisoning. Here we report a case of 30-year-old female presented with intentional kerosene oil poisoning complicated with varying degrees of heart blocks. Finally she made a complete recovery from cardio toxicity after a successful management.

Introduction

Kerosene oil is produced by distillation of crude oil and it is a liquid mixture of chemicals (1). It is commonly used in all part of Srilanka as fuel for cooking and lightening lamps especially among low socio economic people. Kerosene is containing aliphatic hydrocarbon and it is also known as paraffin (1). Poisoning commonly results from ingestion or inhalation. In Srilanka both accidental and intentional ingestion of kerosene for suicidal attempt is the commonest reason for poisoning than inhalation.

Accidental ingestion of kerosene is common among children less than five years and can result in aspiration pneumonitis (2, 5). Inhalation is more common among adolescents and can results in ventricular fibrillation usually without warning symptoms.

Hydrocarbon toxic potential mainly depends on its viscosity (1, 2). Low viscosity hydrocarbons can spread rapidly over large surface areas and are more likely to cause aspiration pneumonitis (2). The toxicity is further determined by lipophilicity, volatility and surface tension (1).

Kerosene oil poisoning mainly affects central nervous system and respiratory system (2). Rarely does it affect myocardium and kidneys (2). The common manifestations of the poisoning are tachypnea, haemoptysis, and shortness of breath with chemical pneumonitis, gagging, bronchitis and bronchopneumonia. Sometimes it can lead to pneumothorax, pneumome diastinum, pneumatocele and subcutaneous emphysema.

Case Report

A 30-year-old young female was transferred from a local hospital to our emergency unit after one hour following ingestion of Kerosene oil (around 30ml) with a suicidal intention. At the time of presentation she was symptomatic and had burning type of central chest pain and epigastric pain, nausea, left sided pleuritic type of chest pain and difficulty in breathing.

On examination, she was alert and conscious. She was tachypnoeic with the respiratory rate of 30/minute and reduced saturation, 87% on air. The saturation picked up to 96 % with 5l oxygen. She was tachycardic with the heart rate of 130 beats per minute and the ECG revealed sinus tachycardia (Figure 1). She was hypotensive and severely dehydrated with the blood pressure of 80/60 mmHg. Bilateral basal crepitations were present on chest auscultation. Other systemic examination was not significant.

Initial ABG, serum electrolytes and basic blood investigations were normal. Urgent chest Xray revealed bilateral basal consolidations suggestive of chemical pneumonitis. Urgent focus Ultra sound scan of the chest revealed no evidence of pleural effusions or free fluid in the thoracic cavity.

Initial fluid resuscitation has been done with intravenous crystalloids. Oxygen supplementation continued via face mask to maintain the saturation more than 94%. She was given intravenous steroids and proton pump inhibitors. Intravenous antibiotics, Ceftriaxone and Metronidazole, were started empherically.

During her ward stay, after 24hours of admission she started to deteriorate and became severely dyspnoeic despite current treatment. Her oxygen saturation was 90% with 10l/minute oxygen via facemask and respiratory rate was 40/min with high fever spikes. On chest auscultation, reduced bilateral air entry and increased basal crepitations were noted. ABG showed respiratory acidosis with reduced arterial oxygenation (PaO2 -76%). Focus ultrasound chest revealed bilateral mild pleural effusion and mild free fluid in the thoracic cavity. Repeated chest X-ray showed pneumomediastinum and bilateral basal pneumonitis. The possibility of oesophageal rupture excluded by urgent contrast enhanced CT thorax.

She was given intensive care unit care with noninvasive ventilation (CPAP) and she was stable for 6 hours before developing respiratory arrest. Thereafter she was intubated and ventilated.

On day four of poisoning she developed bradycardia with the heart rate fluctuating between 35 - 50 beats per minute. ECG revealed sinus pauses and varying degrees of nodal block (Figure 2). Thereafter she was treated with isoprenalene infusion for 3days as per cardiology opinion. The possibility of severe bradycardia due to hydrocarbon toxicity and AV node depression kept. Her 2DEcho was normal.

On day eight she recovered from bradycardia and isoprenalene tailed off. On day nine she was extubated and transferred to ward. On day twelve she made a significant recovery from fever and basal pneumonitis. She was discharged on the same day (day 12) with a plan of reviewing in one week.

Figure1-Sinus tachycardia

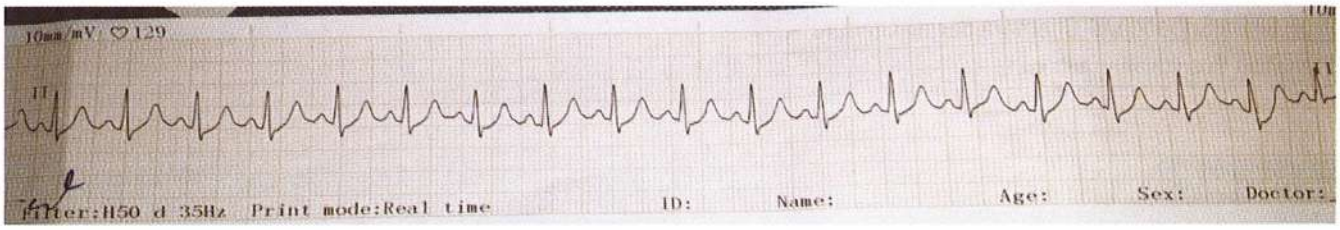
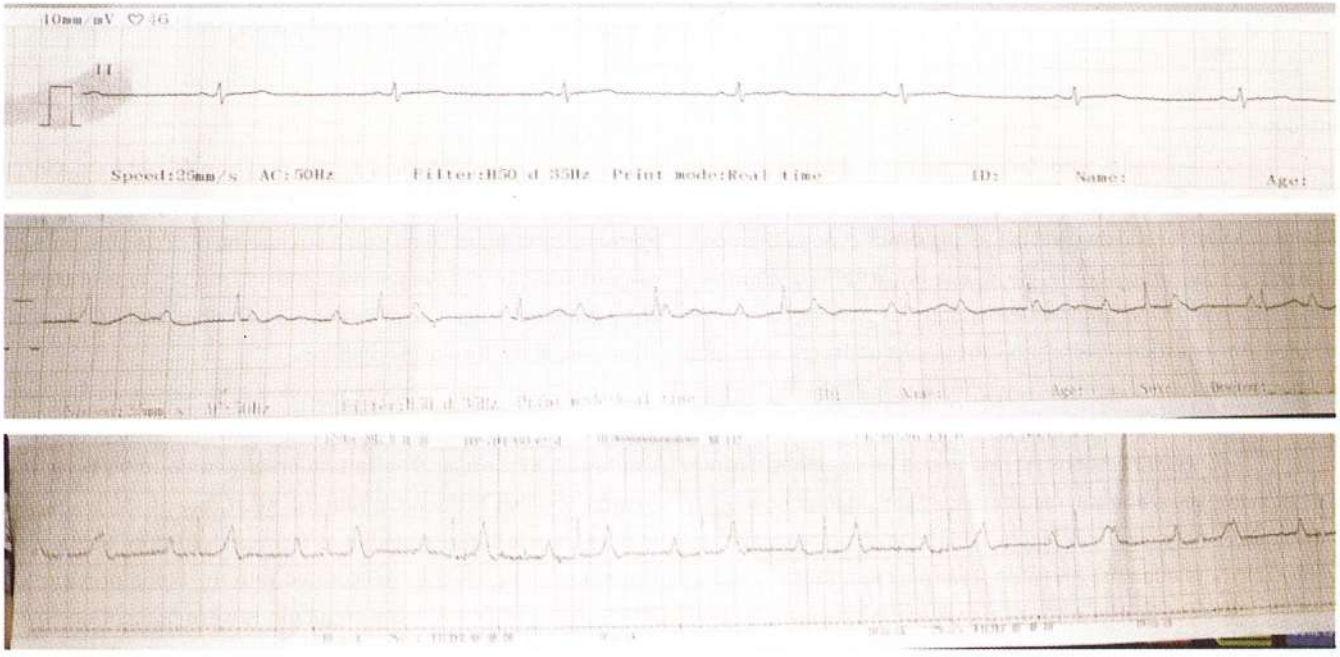


Figure2-Following three rhythm strips are showing varying degrees of atrioventricular blocks.



Discussion

In developed countries there are alternative energy sources rather than kerosene for cooking and lightening lamps used by people. But in developing countries still this is not the case and kerosene is freely available for the above purposes. Therefore accidental and suicidal kerosene poisoning are mostly found in developing countries like Srilanka (4, 7).

Kerosene is a liquid mixture of chemicals produced from distillation of crude oil (1, 7). If someone ingested it accidentally or intentionally, that person stands the risk of having chemical pneumonitis, hydrocarbon induced heart block and the risk of oesophageal perforation. Like most of the chemicals, the amount of kerosene associated with adverse health effects must be above certain levels. But the threshold toxicity value is still not clearly available.

The toxicity of the hydrocarbons mainly related to their viscosity, volatility, surface tension and chemical activity of the side chains (1-3). It can affect any system of the body even though pulmonary system and central nervous system are most commonly getting affected (2). Usually the onset of

respiratory symptoms after kerosene oil exposure can occur soon after to within 10hours (8). Within one hour of ingestion, radiological manifestations may appear and commonly consists of right basal followed by perihilar infiltration (8). Most of the patients will have interstitial and bilateral chemical pneumonitis. (6)

Usually respiratory system exposure to kerosene vapor may cause nonspecific signs such as cough, vomiting, difficulty in breathing, fever, dizziness and headache. The most frequent adverse effect of any hydrocarbon poisoning is aspiration, which can cause significant lung parenchymal damage by inducing an inflammatory response(4).It might result in hemorrhagic exudative alveolitis and loss of surfactant function(4). Type II pneumocytes are most commonly affected during inhalation of kerosene, resulting in decreased surfactant production (4). This decrease in surfactant results in alveolar collapse, ventilation - perfusion mismatch, and hypoxemia (4). Further complications in the lungs include pneumothorax, pneumatocele, and bronchopleural fistula (4). High grade fever can heighten kerosene toxicity by inducing narcotic effects like narcolepsy, cataplexy and death especially in children.

Numerous cases of cardiac arrhythmias and sudden cardiac death have been reported due to hydrocarbon toxicity. Hydrocarbons such as kerosene have complex effects on the heart. At low levels of exposure they sensitize the myocardium to the effects of catecholamines (11). This will lead to arrhythmias and sudden cardiac death (10, 11). They might have negative inotropic dromotrophic and chronotropic effect on myocardium but with unknown mechanism . It appears to be due to altered function of calcium, potassium, and sodium channels in the myocardium (11).

At high levels of exposure hydrocarbons may depress the sinus node activity and thereby cause sinus bradycardia and arrest. Hydrocarbons may also depress atrioventricular nodal conduction leading to varying degree of atrioventricular blocks (12). Brady arrhythmias may then predispose to escape ventricular arrhythmias. In case of more severe intoxication, it might result in asystole (12). The cardiac pathology in death cases is usually unremarkable, consistent with a sudden arrhythmia death (12). Although acute myocardial infarction secondary to hydrocarbon intoxication was also described in some occasions (12). We are reporting this case because of its rarity and possible long-term morbidity.

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CASE REPORT

Spontaneous vertebral artery dissection-Presented with severe ataxia and bilateral nystagmus

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Abstract :

In young and middle aged adults cervical artery dissection is an increasingly recognized etiology for stroke and here we are reporting a case of spontaneous vertebral artery dissection.29-year-old previously well healthy man presented with acute onset of vertigo, vomiting and gait ataxia following minor work at home garden. Examination revealed left side ptosis and bilateral cerebellar signs. Urgent non contrast CT brain revealed acute left cerebellar hemisphere infarction and Computed tomography angiography detected left side vertebral artery dissection.

The spontaneous vertebral artery dissection was diagnosed and treatment started with dual antiplatelet therapy. He had a remarkable resolution of symptoms with antiplatelet therapy and physiotherapy with balance training.This is a case of spontaneous vertebral artery dissection which we have to think as a cause for young stroke which is relatively uncommon.

Keywords : Spontaneous vertebral artery dissection, Wallenberg syndrome, anticoagulation.

Introduction

In young and middle-aged adults vertebral artery dissection is considered as an important etiology for posterior circulation strokes (1). This is increasingly recognized as a cause for wide variety of subtle neurological signs and symptoms (2). The underlying causes of these dissections are still unexplained even though combination of environmental and genetic factors may influence this scenario (2). The treatment of choice is anticoagulation by heparin and the warfarin but evidence are limited and incomplete (2). The vertebral artery dissections can be spontaneous or traumatic and if it is traumatic it will be associated with head, neck and cervical spinal injuries (3). The most common symptoms of spontaneous vertebral artery dissection are unilateral head ache and neck pain presented about 60% of patients. Around 23% to 43% of cases will be presented with symptoms resemble to Wallenberg syndrome (4). The CADISS randomized control study compared efficacy of anticoagulation and antiplatelet treatment and found there is no statistically significant different between these two treatment modalities (13, 15).

Case presentation

29-year-old man presented with acute onset vertigo and vomiting following about half an hour of minor work at the garden. He was picking weeds in the garden bending whole back and neck forward. He developed vertigo acutely and became severely ataxic so that he couldn't go back to home. He went to the bedroom with support of his father and laid down. Then he developed mild generalized headache and vomited several times. He didn't have clinical features suggestive of connective tissue disorders. His systemic review and family history were otherwise unremarkable.

On examination patient had left side partial ptosis with small size pupil and bilateral nystagmus with fast component to the left side. Pupillary reflexes were normal. There was loss of pain sensation in the left V1, 2, 3 of trigeminal nerve distribution. Temperature sensation was reduced in right upper limb. Coordination in upper limbs were normal. He was severely ataxic and couldn't walk without support. Heal-shin test was positive in both lower limbs. Bilateral knee jerks and ankle jerks were exaggerated but Babinski sign was negative. There were no bruits over carotid vessels. No evidence of trauma at neck. His systemic examination was otherwise unremarkable.

Urgent NCCT brain detected to have acute left cerebellar hemisphere infarction. Computed tomography angiography detected irregular luminal narrowing of the distal V1 segment of the left vertebral artery with near complete occlusion by the mural thrombus and diagnosed as left side vertebral artery dissection. The spontaneous vertebral artery dissection was diagnosed and he was started on dual antiplatelet therapy (aspirin 75 mg and clopidogrel 75 mg) with statins. He made a remarkable resolution of his symptoms with physiotherapy and balance training.

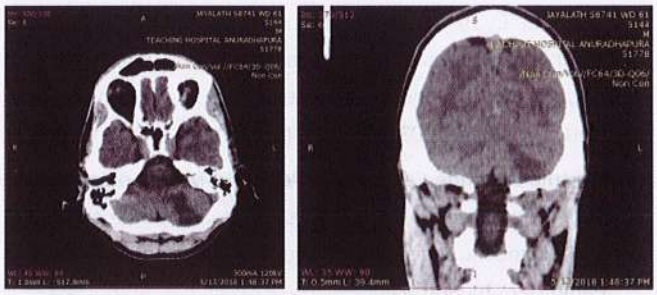

Figure1: Non contrast CT brain shows acute infarction in left cerebellar hemisphere

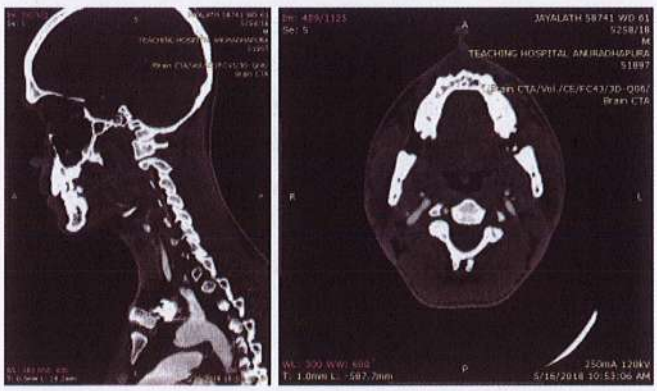

Figure2: CT angiogram shows irregular luminal narrowing of the distal V1 segment of the left vertebral artery with near complete occlusion by the mural thrombus.

Discussion

Epidemiologically 25 % of strokes in patients who are less than 45-year- old are due to spontaneous cervical artery dissection and the annual incidence is estimated to be 2.6 to 5 per 100000(12). Internal carotid artery dissection is two time higher than the vertebral artery dissections and there is no gender predominance. (12)

Digital subtraction angiography is the gold standard for cervical artery dissections even though magnetic resonance angiography and CT angiography has been shown noninvasive methods for diagnosis and follow up with acceptable sensitivity and specificity. (12)

The typical MRI findings will be an intraluminal thrombus and intimal flap which are characteristic of the vertebral artery dissections. Another pathognomonic feature is T1- weighted axial images showing hyper intensity of the vessel wall (4, 5 and 6).

The hemorrhage usually involves an intimal tear or bleeding of the vasa vasorum resulting in luminal narrowing leading to partial or complete obstruction in arterial dissections. This in turn led to subsequent ischemia distal to this part. (7) Thrombotic and embolic complications may follow the event. (7) Varying degrees of head trauma, unusual sleep postures, and other manipulations of the head and neck that may stretch the arteries." "Trivial" trauma, such as coughing and nose blowing may be the possible causative factors of cervical arterial dissection but the exact mechanism is not understood(7). Further associations have been made between dissection and Marfan's syndrome, cystic medial degeneration, and fibro muscular dysplasia (9).

A history of a delay between the onset of headache or posterior neck pain and subsequent neurological deficits should raise the suspicion of vertebral artery dissection. Delays as long as 6 weeks from the onset of pain to ischemic symptoms have been reported, although typically the delay is less than 24 hours. (10). Sub arachnoid hemorrhage will be a complication in these patients (3)

Vertebral arteries are more susceptible to traumatic dissection because of their anatomical structure and more prone to get stretch injuries at C5 C6 level (10, 11). The extra cranial course of the vertebral artery at its origin anchored to subclavian artery (V1 segment) and travelling through the spine within the intervertebral foramina (V2 segment).V1 segment is more vulnerable to dissection usually beginning above the origin. (11, 12). Posterior inferior cerebellar artery is originating from the vertebral artery and occlusion of either of these arteries give rise to features of lateral medullary syndrome of same side as in our patient who developed meiosis, and partial ptosis due to damage of ipsilateral sympathetic pathway results in Horner's syndrome(16, 17). And he showed some other features of Wallenberg syndrome such as nystagmus due to ipsilateral vestibular nucleus lesion and sensory impairment in the left trigeminal distribution due to ipsilateral fifth cranial nerve nuclear lesion. Posterior inferior cerebellar artery supplies to inferior part of cerebellar vermis and cerebellar nuclei (17).Inferior part of the cerebellar vermis also can get affected and may be the reason for his bilaterally positive heal shin test.

Anticoagulation or antiplatelet therapy alone are treatment options in these patients even though the evidence is incomplete, as demonstrable emboli are the most common cause for stroke in these patients and supportive to this treatment strategy (2,13) The CADISS randomized control study compared the efficacy between anticoagulation and antiplatelet treatment and concluded as no difference in efficacy (13). Another study based on systematic review with Bayesian meta-analysis compared the effects of antiplatelet drugs and anticoagulants and suggested antiplatelet should be given precedence over anticoagulants as a first line treatment in patients with cervical artery dissection unless results of an adequately powered randomized trial suggest the opposite (14). Univariate and multivariate analyses were conducted to analyze the association between treatment and new or recurrent events and clinical outcome in 370 patients and found it is similar with antiplatelet and anticoagulation treatment in treating intracranial and extra cranial carotid and vertebral artery

dissection (15).The rapidly increasing interest in endovascular techniques has resulted in many patients being treated with percutaneous angioplasty and stent deployment (2). These treatments generally well tolerated and radio graphically giving impressive results and the aneurysms associated with these dissections will never rupture and rarely end up in delayed ischemic symptoms (2). Persistent symptoms with optimal medical management will be referred for surgical interventions consisting of an in situ interposition graft or extra cranial-intracranial bypass (2)

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CASE REPORT

Anti-Myelin Oligodendrocyte Glycoprotein (MOG) antibody seropositivity in a patient with multiple sclerosis

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Abstract

Neuro myelitis optica spectrum disorders (NMOSD) are antibody mediated demyelinating disorders which can be presented as a seizure disorder. It is difficult to differentiate from Multiple sclerosis. Attending physician should be vigilant on the various presentations of NMOSDs because not only early diagnosis may impact on the prognosis, but incorrect diagnosis and treatment with drugs like interferon can completely harm the patient.

Background

Neuro myelitis optica spectrum disorders (NMOSD) are antibody mediated inflammatory diseases resulting in demyelination of the central nerve system. Initially it was considered as a variant of multiple sclerosis but later it was differentiated from multiple sclerosis since NMOSD patients found to be positive for serum NMO-IgG antibodies or aquaporin-4 (AQP4) antibody [1].

Myelin oligodendrocyte glycoprotein (MOG) is produced by oligodendrocytes and is a well known auto-antigen in NMOSD and acute disseminated encephalomyelitis (ADEM). [5] Aquaporin-4 (AQP4) antibodies are positive in 70% of NMOSD. [2, 3] Myelin oligodendrocyte glycoprotein (MOG) antibodies are identified in NMOSD patients who are negative for aquaporin-4 (AQP4) antibodies. [4] At the same time a small proportion of NMOSDs (1.1%) may show positivity for both antibodies [4]. It was also observed that most of the patients with positive MOG-abs were significantly younger than patient withAQP4-ab (median: 27 vs. 40.5 years) [4]. Additionally, it was also observed that anti MOG antibody associated NMOSDs have better outcomes than aquaporin-4 (AQP4) antibody associated NMOSDs [4]. We report a case of 28 year old male patient with NMOSD positive for MOG antibodies unfortunately could not be diagnosed and initially treated as Multiple Sclerosis for six years.

Case

A 28 year old father of one child presented with episodic incidences of epilepsy, blurring of vision and difficulty in walking for 6 years.

Six years ago, he was in Kuwait, had developed a left sided tonic-clonic fit with secondary generalization with bladder and bowel incontinence, rolling up of the eyes and a bitten tongue. It has been lasted for 10 minutes and spontaneously recovered. Following day, he developed a blurring of vision and difficulty in walking. Blurring of vision was gradually worsened but not progressed to blindness. Difficulty of walking was mainly due to the spasticity of legs more in left side but he recovered totally in one month without any residual weakness. Three years later from the initial event, he developed a right sided focal fit lasted for five minutes and difficulty in walking lasted for one month. He also had spasticity in right side without blurring of vision and recovered fully.

He presented to us three years after the second event with a sudden onset of right hand numbness and a focal fit. It was associated with muscle twitching, fatigability, blurring of vision, difficulty in walking and felt spasticity in right side of the body and a headache. There were no associated skin rashes, arthritis, mouth ulcers or psychotic features. He had no preceding infections and

vaccinations. On examination, visual acuity was 6/24 with optic atrophy in both eyes and asymmetric upper motor neuron type weakness of both lower limb (right>left) without sensory loss. Rest of nervous system and other systemic clinical examination were normal except low mood.

Magnatic Resonance Imaging of the brain showed large bilateral hazy, partly Gadolinum-enhancing lesions in the deep white matter and peri-ventricular areas. Cerebrospinal Fluid analysis demonstrated elevated proteins (100 mg/dL) without pleocytosis. Serum confirmed anti MOG-antibodies and it was negative for aquaporin-4 antibodies (AQP4).

Discussion

Neuromylitis optica spectrum disorder (NMOSD) is an inflammatory disorder in central nervous system which can mimic multiple sclerosis. Accurate diagnosis is important because some drugs such as interferon treatment can worsen NMOSDs. New diagnostic criteria are one of core clinical characteristics of NMOSD with positive antibodies. Core characteristic features are optic neuritis, acute myelitis, area-postrema syndrome (unexplained hiccups or nausea and vomiting), acute brainstem syndrome, symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions, symptomatic cerebral syndrome with NMOSD-typical brain lesions. If antibody is negative, the patient must have at least two core clinical characteristics (one of which must be optic neuritis, acute myelitis with longitudinally extensive transverse myelitis lesions, or area postrema syndrome) and must have additional MRI requirements. The additional MRI requirements are as follows: Acute optic neuritis: requires brain MRI showing (1) normal findings or only nonspecific white matter lesions or (2) optic nerve MRI with T2-hyperintense lesion or T1-weighted gadolinium enhancing lesion extending over 1/2 optic nerve length or involving optic chiasm. Acute myelitis: requires associated intramedullary MRI lesion extending over three contiguous segments or at least three contiguous segments of focal spinal cord atrophy in patients with history compatible with acute myelitis. Areapostrema syndrome: requires associated dorsal medulla/area postrema lesions. Acute brainstem syndrome: requires associated periependymal brainstem lesions [7]. Our patient had optic neuritis with anti-MOG antibody positivity fulfilling the criteria for anti- MOG syndrome.

Conclusion

NMOSD and MS are clinically similar condition but these two conditions have different management. Clinician should consider antibody and neuro imaging.

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CASE REPORT

Early Diagnosis of Acute Respiratory Distress Syndrome in Emergency Department

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Abstract :

Acute Respiratory Distress Syndrome (ARDS) is an inflammatory lung injury which claims high mortality and morbidity. Detection of ARDS at the first contact in Emergency Department is important to guide the management. There are several criteria to detect ARDS. This is a case report which describes early detection of ARDS at the Emergency Department and it's management.

Introduction

Acute Respiratory Distress Syndrome (ARDS) is an inflammatory lung injury due to various causes mainly infection in which increased lung microvascular permeability resulting in hypoxemic respiratory failure (1). It has high mortality with the average rate of 50% (2). It leads to high cost of management, prolong ICU stay & hospital stay and residual lung damage to individuals (3). Patients with Sepsis in ICU, around 40% will end up in ARDS (4). Even though there are several causes were identified for ARDS, severe pneumonia remains the leading cause for pulmonary originated ARDS. The differentiation of both of these and diagnose ARDS is a challenge to first contact clinician especially in the emergency department because of similar presentation (6). This is a case to describe the early detection of ARDS at the first contact mainly in the Emergency Department.

Case Presentation

A 40-year-old manual worker admitted to Preliminary Care Unit of Teaching Hospital of Peradeniya with the complain of fever, cough for one week and sortness of breath for two days. He is a known patient with bronchial asthma which is mild intermittent in nature and not on prophylactic inhaler. On further elaborating he was found to have with fever, dry cough with scanty sputum sortness of breath, pleuritic type chest pain which all fit into a classical symptoms of pneumonia. In addition, he is systemically unwell as he is having arthralgia, myalgia, headache and on & off abdominal cramps. He is with a stable cardiovascular state and he was not diagnosed to have with ischemic heart disease or heart failure in the past. He did not undergo any major surgical intervention in the recent past. Rest of his symptoms analysis and history were uneventful.

On examination he was ill looking, afebrile to touch, not pale or cyanosed. His hydration was inadequate. Respiratory system reveals that his respiratory rate was 30 with bilateral lower zone crepitation on auscultation. He is maintaining the saturation of 95% with room air. He is with stable cardiovascular examination with a heart rate of 80 and blood pressure of 130/80 mmHg without any failure features.

He was cannulated, blood was sent for necessary investigations and blood cultures. He was started with Intravenous Co Amoxyclav 1.2 g and Clarithromycin 500 mg oral. His initial arterial blood gas (ABG) shows pH: 7.48, pCO2: 28 mmHg, pO2: 57 mmHg, HCO3-: 20.8 in room air. His P: F ratio based on this ABG was 271 mmHg. Chest X ray was reported as normal initially (which was on day three of illness) (Figure 1) but repeated one confirmed evidence of pulmonary oedema

Figure 1

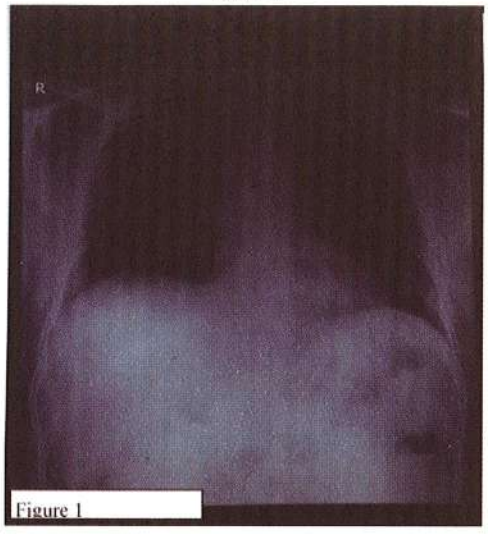

Figure 1

(Figure 2)

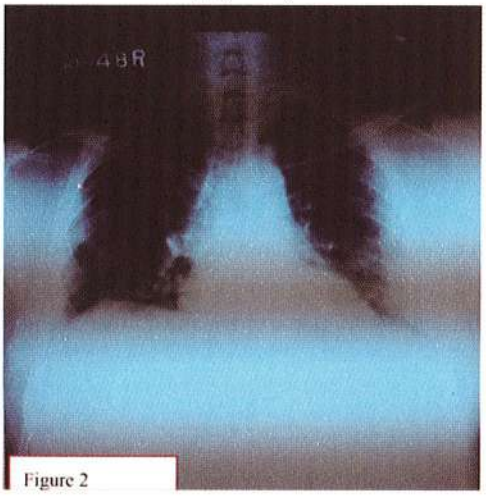

Figure 2

There was a strong clinical suspicion of Acute Respiratory Distress Syndrome (ARDS) based on this clinical picture and investigations findings. Patient was admitted to medical High Dependency Unit (HDU) for close observation and further management. He deteriorated on the following day and his ABG became pH: 7.46, pCO2: 30 mmHg, pO2: 59 mmHg, HCO3-: 21.3 with the oxygen support via face mask (FiO2 of 40%). His P: F ratio based on this ABG was 147 mmHg.

As he met the clinical criteria of ARDS, he was intubated and sent to Intensive Care Unit (ICU) for mechanical ventilation and further care. He was managed in the ICU for 14 days and discharged to home after 20 days of hospital stay. He was managed with lung protective ventilation during ICU stay.

Case Discussion

There are several diagnostic criteria to diagnose ARDS (5). Currently, there are two diagnostic criteria named as Berlin Criteria and American European Consensus Conference (AECC) criteria used to diagnose ARDS but the Berlin criteria is considered as more beneficial in poor resource settings (7). The early diagnosis in a patient with high index suspicious of ARDS is important to reduce the adverse outcome (5).

For the early detection, the pathogenesis based approach is an appropriate approach. The exact pathogenesis behind the ARDS is believed as 'non cardiogenic pulmonary oedema' (5). Non cardiogenic pulmonary oedema is detected by Extravascular Lung Water Index (8). V.A.Negovsky Scientific Research Institute for General Reanimatology has developed set criteria to diagnose ARDS early (5). The criteria include the following.

- Acute onset
- Extravascular Lung Water Index > 7 mmHg
- Oxygen index < 300 mmHg
- No Left ventricular dysfunction
- No signs of ARDS in direct Chest X- ray

These criteria will guide to diagnose ARDS early and initiate management early to overcome the high mortality and morbidity (5). The patient discussed in this case report we could not measure the Extravascular Lung Water Index but other the criterion fit into come to an early diagnosis of ARDS.

Conclusion

The early diagnosis of ARDS is important as well as management in Emergency department and other clinical settings. It will help to improve the outcome, reduce the cost, ICU & Hospital stay and reduce the mortality and morbidity.

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CASE REPORT

Pancreatic neoplasm presented with bile cast nephropathy

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Abstract :

Bile cast nephropathy has been a presenting feature of many billiary pathologies. Mechanism involved bile salts causing toxicity to tubules especially to proximal tubules. Etiology should be sought quickly not only to reverse the acute renal damage but also to eradicate the possible etiology.

Introduction

Bile cast nephropathy is a well known and commonly encountered phenomenon. It is also an entity which has been forgotton by modern literature. Patient with jaundice and renal failure should be worked out keeping the choelim nephropathy in mind because clinicians always think of hepato-renal syndrome and infections concomitantly affecting liver and kidney. Bile cast nephropathy has its own history of evolvement for more nearly 130 years. Many clinical reasons leading to direct hyperbilirubinemia can lead to the tubular damage which is reversible. Unfortunately some causes of bile cast nephropathy cannot be cured even we can reverse the tubular damage temporarily. Here we report a case of pancreatic head neoplasm obstructing the billiary tree presented with bile cast nephropathy.

Case history

A 45 year old welder presented with reduced urinary output for 3 days. He had a good urinary output in the past and gradually reduced urinary output over three days with dark colored urine. It was associated with pruritus, on and off fever with chills and rigors. He also had epigastric pain for 5 days duration. Relevant negative findings were, no recent history of diarrhea or vomiting, trauma or surgery but nausea is present but no dysuria, frequency, hematuria or loin to groin pains or history of renal stones. No recent hemorrhage or burns and no recent polyuric episodes. No history of periorbital swellings or frothy urine. Patient has not taken antibiotics, analgesics, diuretics or drugs for joint pains rather than Metformin for diabetes for 5 years. No history of muscle trauma or epilepsy. No history of blood disorders. No hiccups or mental state changes. Had treated at hospital for two episodes of epigastric pains needing more than three days admission where he was kept on liquid diets and intravenous drugs. Blood sugars were not more than 200mg/dl. Non smoker, but consume alcohol for 10 years, ½ a bottle arrack a day for last three years.

He was febrile and deeply icteric, not pale, mild hepatomegaly and splenomegaly and had non tender palpable gall bladder, no loin tenderness. Temperature 99 F, No clubbing, not cyanosed, No lymphadenoathy, Blood pressure 120/80mmHg, Pulse rate – 104/min, regular, JVP- normal, Heart sounds – normal, No added sounds (Muffled), Respiratory rate 16/min, Vesicular breathing , no added sounds, No effsusions , Abdomen Examination, Tender epigastrium, non tender gall bladder was palpable, No ascites, No loin tenderness. Hb 12.6, Platlet count 180000, WBC 15270, n 12690. Albumin +, Red cells 10-15, Pus cells 2-3,No casts, no sediments. 74 u/l, 50 u/l (22-60). Glucose 15.4 mmol/l. ALT 108, AST 95, ALP 509, GGT 256, Total protein 5.4, Albumin 3.3, Globulin 2.1, Total Billurubin 141 umol/l, direct 111. Serum sodium 135, potassium 4.5, chloride 138. His serum creatinine 3.4 then rose to 5.1.

Urine osmolarity was 288 mOsm/kg, urine sodium was 45mmol/d, fractional excretion of Na was 3%. Urine microscopy showed bile casts and renal biopsy was not carried out. USS abdomen, Evidence of CBD dialatation (1.69cm) and intrahepatic duct dialatation , Evidence of hyperechoic area seen in the head of pancreas, minimal free fluid seen in Morrison's pouch, Bilateral kidneys are swollen and more hypoechoic than normal, and B/L acute renal parenchymal disease. ESR 63, CRP 69. Blood picture no evidence of hemolysis. Endoscopic retrograde cholangiopancreatography (ERCP) visualized a distal stenosis of the CBD. Biopsy and brush of the CBD revealed an adenocarcinoma. Obstruction was relieved with endoscopic

stenting and nephropathy was reversed. Patient was offered surgery at a specialized center.

Discussion

Bile cast nephropathy was first described by Qunicke in 1899, from autopsies in patients with acute onset jaundice and renal failure showing deposition of bile pigments in the renal glomeruli and by Hessler in 1922 by demonstrating presence of marked granulated cells with free bilirubin in the caine and human urine. Therefore it was suggested that accumulation of bile in the renal cortex was nephrotoxic.[1] Further in 1937 it was again observed there was a reversible acute renal impairment which aggravated by hyperbillirubinemia and resolved when serum billirubin coming down. [2] It was given so many names later on such as cholemic nephropathy and later called as "jaundice-related nephropathy" and finally in 2013 as bile cast nephropathy as its disease range coming from proximal tubular dysfunction to renal failure bile and bile salts deposition in the tubules.[3,4]

Even though its exact etiology is unknown, any intrahepatic or extrahepatic insult leading to hiper bilirubinemia (whether hepatic or extra hepatic) can progress to this condition. It was observed that rats receiving bile salt infusions after renal ischemia developed renal failure irrespective of hydration status in 1968 suggesting a "two hit" hypothesis and further confirmed later as nephropathy was reversed with treatment for billirubinemia. [5,3] Negative chronotropic and inotropic effects due to high bile salt reducing renal perfusion also contributes to the pathology.

Alcoholic cirrhosis, dehydration, cholangiocar cinoma, infectious mononucleosis and steroid use are associated with bile cast nephropathy although hepatitis C or other causes of indirect hyperbillirubinemia is not.[6,7,8] Various mechanisms has been suggested in pathophysiology ranging from oxidative tubular cell damage in attempting for bile export out of cell [9,10]. Na+-H+, Na+-K+, Na+-Cl- pumps inhibition by sulfated bile salts at renal tubules due to pH changes enhances bile cast deposition, tubular injury.

The diagnosis is with the renal biopsy demonstrating bile casts in renal tubules. But bile casts in renal tubules in a patient with clinically proven tubular injury also can be given same weight as renal biopsy where the clinical status of the patient is not allowing renal biopsy.[11] There are currently no accepted treatment guidelines. But Interventions to reduce bilirubin to reduce billirubin load with relief of biliary obstruction via ERCP with stent placement and hemodialysis, have been found to have favorable outcomes. Even though, this appears to be an effective strategy initial stages of the disease course, its efficacy in established disease is not clear. Therefore Plasmapheresis may additionally be of utility.

Extracorporeal treatment options aimed at reduction of inflammatory cytokines and reduction of bilirubin including the molecular adsorbents recycling system (MARS), coupled plasma filtration adsorption (CPFA), and plasma filtration adsorption dialysis. [12] These methods of blood and/or plasma filtration have served utility in patients with sepsis, acute liver failure and acute on chronic liver failure via the filtration of inflammatory cytokines, bilirubin and bile acids, among other compounds such as amino acids and free fatty acids. MARS has shown improved survival rates in patients with acute on chronic liver failure in the setting of sepsis. [13,14]

In this patient since he is an alcoholic presented with jaundice and renal insufficiency the challenges may be not deviate to cirrhosis and liver injury related to alcohol and hepato-renal failure. He is a diabetic patient too. So weather his diabetes got worse with acute clinical condition or due to pancreatic pathology also should be worth to consider. On the other hand bile cast nephropathy being a tubular pathology reduced urinary output can be explained due to dehydration as his urinary osmolarity studies and urinary sodium excretion were for acute tubular necrosis as his urine output was improved with adequate hydration.

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CASE REPORT

Anaphylactic shock following administration of Lignocaine local anaesthesia

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Abstract :

Anaphylactic shock or hypersensitive reaction is an immune mediated manifestation. It can occur following exposure to any substance. Drug induced allergic reactions are reported in clinical practice. Lignocaine is one of the local anaesthetic agent commonly used in surgical and emergency medicine practice. Allergic reaction or anaphylactic shock to Lignocaine is under reported. This is a case report which describes the allergic reactions to Lignocaine, how to detect it, investigate it and manage it.

Keywords: Lignocine, Anaphylactic shock, allergic reactions

Introduction

Anaphylaxis is a life threatening disease. It is an acute event involving multiple systems and rapidly deteriorate the hemodynamic status to shock. Anaphylactic shock is an immune mediated, acute event with or without cutaneous manifestation. It commonly occurs following Type 1 hypersensitivity reaction (1,2). Several allergens are there to cause allergic and anaphylactic reaction (1). Common causes are foods, drugs, insect bite and immunotheraphy agent (3). Allergic leading to anaphylactic shock following exposure to Lignocaine is noted in clinical practice but under reported in literatures. Lignocaine is a commonly used local anaesthetic agent in clinical practice. This is a case report about anaphylactic shock following administration of Local anaesthetic lignocaine.

Case History

A 53-year-old female patient with ASA 1 admitted to the surgical ward with pain at the surgical scar in the anterior abdominal wall. She denies other symptoms and her clinical examination was uneventful except scar tenderness over the surgical scar in anterior abdominal wall. She is not aware of her allergic history.

Pain does not respond to any analgesic and surgical team decided to inject Local anaesthesia of Lignocaine to surgical scar to exclude entrapped nerve and neuropathy. Lignocaine 5ml was injected into the surgical scar, patient developed itching, nausea, vomiting and generalized rash within 3 minutes of administration. Her blood pressure and respiratory effort also compromised. She was managed in ABCDE approach with IM Adrenalin 0.5ml (1:1000) with 1ml of Adrenalin IV (1: 10,000) and Phenagan 25mg with Hydrocortisone 200mg intravenously. Normal saline 1l was given intravenously. She recovered with all above measures.

Discussion

Local anaesthesia are widely used in clinical practice (4,5) especially in surgical, anesthetic, emergency department procedures. The agents used in local anaesthesia are two types based on their chemical structures. They are amino ester compounds (benzocaine, procaine) and amide compounds (lidocaine, bupivacaine, prilocaine) (6). It pharmacokinetic actions were described as blockage of voltage gated sodium channel and interrupt the pain stimulation (6).

Local anaesthesia induced allergic reactions are reported in several cases but true IgE mediated reactions are rare (6). Clinician need to be aware of it.

Pharmacological compounds particularly the ester compounds in the allergen which breakdown into Para Amino Benzoic Acid (PABA) cause this reaction. Local anaesthetics Lignocaine compounds also has similar chemical property (6).

Symptoms and Signs

Lidocaine related allergic reactions are manifested in a spectrum of symptoms from mild form of pruritus, hives to severe form of anaphylactic shock, heart failure and death (4,7). Clinician must be aware of IgE mediated symptoms such as pruritus, erythema, localized swelling, dyspnea, wheezing, bronchospasm, hypotension, shock and non-mediated such as contact dermatitis

Testing

There is no specific investigation to support or confirm the Local anaesthesia allergic reactions as there is no definitive hypothesis (6,8). Theories of Hapten/hapten protein and IgE mediated are still in the laboratory phase (8). However, BSACI recommends to do serial measurement of Serum Mast Cell tryptase (9). At the same time recent studies suggest some set of investigation.

Skin Prick Test: Skin prick test are easily done with safety in suspected individuals. It has 97% negative predictive value (10). Intradermal test: It is a painful procedure with high false positive rate (6)

Subcutaneous challenge test: It is considered to be the gold standard for IgE mediated allergic reactions but it is costly and need of emergency care management facilities. So this is still in controversial due to high cost, need of emergency facilities, and ethical principles issue (6). Eventhough it has drawbacks; the positive results should be considered seriously in clinical practice to decide alternatives for Local anaesthesia Lidocaine (6)

Management

Management of Lidocaine allergic reactions is similar to other allergic manifestations according to clinical severity. Key features of acute management include stop suspected drugs, treat the reactions, identify and avoid potential cross reacting drug, record precise details of the reactions and its treatment, identify a safe alternative, if necessary consider desensitization (9).

Conclusion

Hypersensitive reactions and anaphylactic shock following exposure of local anesthetia Lignocaine are more often but underreported. Detailed allergic history is vital. If positive allergic history, consider skin prick test of Lignocaine. Documentation of the event is important as well as treating to prevent future reactions.

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CASE REPORT

Efficacy of pulse Cyclophosphamide theraphy in scleroderma related interstitial lung disease and skin fibrosis

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Abstract :

Scleroderma related interstitial lung disease is a pulmonary fibrosing disorder characterized by systemic inflammation and progressive scarring of the lungs that leads to respiratory failure. Although certain immunosuppressive therapies may slow disease progression, current treatment strategies are not curative; consequently, SS-ILD continues to be a major cause of morbidity and mortality. We present case report describing effectiveness of cyclophosphamide pulse therapy improving lung function and radiological improvement in pulmonary fibrosis in Scleroderma related interstitial lung disease. The early screening and detection, close follow-up and aggressive management improving patient lifespan.

Introduction

Systemic sclerosis is a connective tissue disorder characterized by skin thickening, which may be accompanied by involvement of internal organs. SSc may affect the lungs by fibrosing alveolitis; pulmonary hypertension; lung cancer; pleural disease; aspiration pneumonitis; extra thoracic restriction through a"cuirasse effect"; diffuse alveolar damage and pulmonary haemorrhge.

Pulmonary hypertension and interstitial lung disease are most widely reported pulmonary complications that arise in scleroderma patients with a third of patients having pulmonary fibrosis. The 5-year mortality for patients having progressive systemic sclerosis and ILD have a survival of 82-90%. Successful treatment of scleroderma renal crisis has rendered pulmonary complications. Severe restrictive lung disease being present in 13% of patient SSc.

Case report

A 50 year old male patient carrying a diagnosis of scleroderma since 2017, Initially he was presented in 2012 to the dermatology unit with the symptoms of Skin thickening of arms, forearms and digits, freckling of skin around mouth and Reynaud's phenomenon. He didn't havr any nail changes other than some skin discoloration around nail folds. He did not had GI or respiratory manifestations. He was assessed at the Dermatology unit but defaulted follow up

2017 June he was presented to Central Chest Clinic, Colombo with the symptoms of exertional Shortness of breath x 3/12, mMRC grading-iii, with intermittent fever, orthopnea and paroxysmal nocturnal dyspnoea. On Examination he had dermatological manifestations of Systemic Sclerosis. He was plethoric, had bilateral ankle oedema and lungs bibasal end inspiratory fine crepitations. In further patient evaluation reveled 6MWT (six-minute walk test) positive, walking distance 150m, patient oxygen saturation different in pre and post-test significance. (Pre test SPO2 97%- Post test SPO2 72%), CXR and HRCT had evidence of interstitial lung disease, 2D-Echo reveled normal.

The positive of anti- centromere (Scl70)antibodies and based on the skin biopsy, the diagnosis of systemic sclerosis with interstitial lung disease was made. Management started with oral cyclophospamide 300mg and azithioprine 15mg.Patient defaulted follow up after the extensive evaluation.

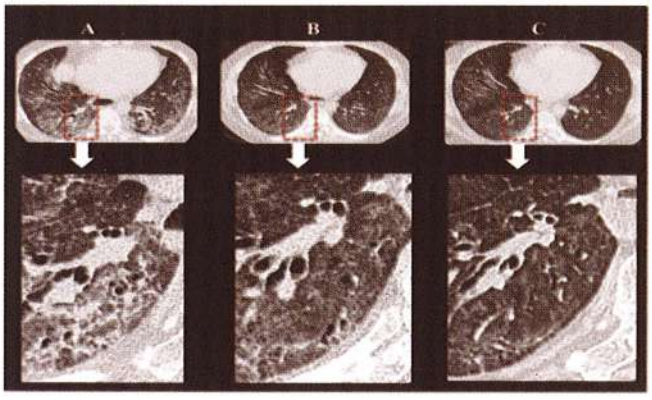
He admitted to teaching hospital Batticaloa in january 2018 with progressive difficulty in breathing end up with respiratory failure managed at medical intensive care unit. He was referred back to

respiratory clinic after acute management over because of a sub acute onset of nonproductive cough and shortness of breath on excertion for last few months. Symptoms were intermittent. Chest auscultation revealed fine bibasilar crackles and finger clubbing. Lung function showed a restrictive pattern (total lung capacity 75%, forced vital capacity 80%) and reduced diffusion capacity of carbon monoxide (Dlco) of 60% underwent high resolution chest computer tomogram that showed reticulation, ground glass opacification, and traction bronchiectasis with nonspecific interstitial pneumonitis. Given his symptoms and objective findings of lung involvement, he was started on pulse Cyclophosphamide therapy 5 cycles given monthly and followed closely to monitor the symptoms.

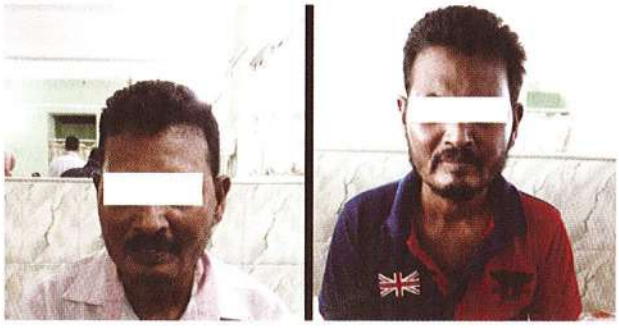
He showed improvement in his lung function assessment and repeat high resolution chest tomogram after 5 cycles of pulse Cyclophosphamide.

In addition to lung function he showed improvement of skin changes at the end of 5cycles of Cyclophospamide and completely resolved skin discoloration and fibrosis.

(figure-1).



Axial high-resolution chest CT Images from (A) show thickening of the interlobular and intralobular septae, ground glass opacification and traction bronchiolectasis. These changes were more severe in the lower lung zones. Subsequent imaging (B, C) showed successive improvement with only subtle residual interstitial reticulation and ground glass change evident on (C).



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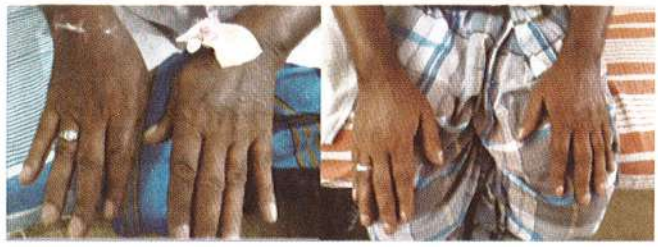

This images show improvement after cyclophospamide pulse five cycle appearance and skin thickness and colour.

Disscussion

SSc-ILD is a fibrosing lung disorder characterized by the activation of immune cells and hyperplasia of fibroblasts leading to increased production and turnover of collagen. This results in increasingly fibrotic lungs that are prone to respiratory failure. Almost 90% of subjects with scleroderma who lack symptoms of respiratory compromise show changes consistent with ILD on CT imaging, and 100% show histopathological changes in autopsy. Thus early detection if ILD in the setting of scleroderma is imperative since it has prognostic value and may prompt early treatment and frequent follow up.

Dyspnoea is a common symptom of fibrosing alveolitis in systemic sclerosis (FA-SSc), initially exertional but with disease progression the patient may become breathless at rest. Cough in FA-SSc may be dry or productive. Haemoptysis is uncommon in FA-SSc and should alert the clinician to the possibility of scar malignancy, which may occur in up to 3% of SSc patient and associated with the presence of FA-SSc. Haemoptysis can also occur from endobronchial telengiectasia.

The commonest physical finding in FA-SSc is bilateral basal crackles. Digital clubbing is uncommon, possibly as a result of impaired peripheral blood flow in SSc and skin tightening. Features of pulmonary hypertension may be present (raised jugular venous pressure, loud Pulmonary 2nd heart sound, pedal oedema and a right ventricular/ parasternal heave). Pulmonary arterial hypertension be hypoxaemia induced, due to disease severity, it may well be because of pulmonary vascular disease, particularly in ISSc and if the patient is anti-centromere antibody positive. The prevalence of isolated PAH in patients with dSSc is 2%.The prevalence of PAH appears to be no different in SSc patient with 18% and without 22% FA-SSc. The extent and severity of cutaneous and pulmonary involvement do not correlate very well but FA-SSc is more common in dSSc,and PHT in ISSc.

Approximately half of patients with SSc carry an autoantibody, either anti-topoisomerase-I (26%) or anti-centromere antibody (ACA [22%]), with no patient carrying both autoantibodies. Anti topoisomerase-I is associated with diffuse cutaneous disease and FASSc. Whereas ACA is associated with limited cutaneous disease and pulmonary hypertension.

The classical PFT abnormalities seen in FASSc include a restrictive ventilatory defect associated with a depressed gas transfer (TLCO). Lung volumes may give an indication of fibrosis severity but with co-existent emphysema, they may be relatively normal because

of gas trapping. TLCO can be up to 20% less (on % predicted) than lung volumes but further, more disparate, loss of TLCO raises the possibility of co-existent pulmonary vascular disease (PVD).

Restrictive ventilatory defect is characterised by a reduction total lung capacity (TLC), forced expiratory volume in 1 s (FEV1) and forced vital capacity (FVC) with an elevated FEV1: FVC ratio.

A single PFT result gives a snapshot of disease extent but, in order to get a view of disease activity, serial testing is required as subtle downward trends may be revealed, which may reflect disease activity. Decreases of<10% may be reassessed at a 3-month interval to see if this is the start of a trend downwards.

The six minute walk test (6MWT) is highly reproducible in FA-SSc but its use in FA-SSc is limited by its weak correlation with % predicted FVC and Borg dyspnoea index and a non-correlation with % predicted gas transfer.

The chest radiograph (CXR) in FA-SSc is abnormal in up to 80% of cases (it can appear normal) and fibrosis on the CXR may predate the onset of scleroderma. Typical CXR features include a predominantly bibasal reticulonodular pattern. Cystic areas may form within fibrotic areas giving a "honeycomb" appearance. Fibrosis may result in elevation of the hemidiaphragms and decreased lung volumes. Pneumothoraces may result from rupture of subpleural cysts.

Oesophageal dilatation may be seen on CXR but is better visualized with HRCT and has been found in 80% of asymptomatic cases on HRCT.

HRCT is a major advance in the management of FASSc and may obviate the need for confirmatory histology. In SSc patients with a normal CXR, 29% of cases of SSc will have an abnormal thoracic HRCT. When CXR and HRCT are used in SSc to evaluate dyspnoea or abnormal pulmonary function tests, the CXR is abnormal in 59% cases whereas the HRCT is abnormal in 88% cases. Overall, HRCT can detect pulmonary abnormalities in 60–90% SSc patients.
Several HRCT abnormalities may be seen in FASSc: -

- Ground glass (GG) opacification
- Reticular pattern (fine through to honeycombing)
- Subpleural distribution (especially honeycombing)
- Traction bronchiolectasis
- Cysts of 1–3 cm diameter
- Various lines – septal, subpleural, and long (non-septal) parenchymal lines.
- Micronodulation (especially subpleural but also intralobular).

DTPA scanning in SSc patients may detect pulmonary involvement in SSc at an earlier stage, even in the presence of normal chest radiology (CXR and HRCT).

Open lung biopsy (OLB) has a greater yield than transbronchial biopsy (94% vs 72%) but is generally not repeatable, which makes its use as a measure of disease activity unacceptable. Video-assisted thoracoscopic surgery is now frequently used for surgical lung biopsy in diffuse lung diseases and has a similar safety and diagnostic efficacy but a reduced operative and hospital stay.

Regarding treatment of FA-SSc Studies have failed to show any convincing benefit when FASSc patients are treated with corticosteroids. Additionally, high dose corticosteroids (>20 mg/day prednisolone) are associated with renal crisis, independent of blood pressure. High dose corticosteroids are therefore not recommended unless there is accelerated disease, in which case the kidneys should be "protected" with Iloprost, which may ameliorate renal vasospasm.

Early studies of cyclophosphamide have shown variable benefits on pulmonary function and survival, although the consensus opinion is that cyclophosphamide is the best drug for FASSc. Intravenous cyclophosphamide can result in partial regression of FA-SSc, as judged by serial PFT or serial HRCT.

A beneficial effect of cyclophosphamide therapy was also supported by several statistically significant differences in the secondary end points, even though these differences were also small. Changes in scores for skin thickness favored cyclophosphamide, although the magnitude of the change in the scores was limited, as compared with the inherent variability of this outcome mea- sure. In addition, changes in the severity of dyspnea, as assessed according to the transitional dyspnea index, favored cyclophosphamide.

An important consideration when interpreting these limited therapeutic benefits of treatment with cyclophosphamide is the need for a thorough assessment of the risks of the drug, arguably the most toxic immunosuppressive agent currently used to treat autoimmune diseases. When cyclophosphamide is used as an immunosuppressive agent in the treatment of other rheumatologic diseases, the risks of cancer and gonadal failure increase with cumulative doses and are greater when the drug is administered daily, rather than as an intermittent monthly bolus.

Daily cyclophosphamide results in higher cumulative doses than do monthly boluses when both are administered for the same duration. For example, one year of oral cyclophosphamide at a daily dose of 2 mg per kilogram of body weight for scleroderma-related interstitial lung disease would expose a patient weighing 75 kg (165 lb) to a dose of 55 g, as compared with exposure to 9 g after six pulses of intermittent monthly boluses for lupus nephritis. Cumulative doses of 30 to 100 g of cyclophosphamide are associated with a substantially greater risk than are lower doses.

We acknowledge that although there appears to be a very striking temporal relationship to the improved symptoms, PFTs and HRCT changes with the administration of cyclophosphamide therapy for SSc-ILD, shown some continued improvement even after the drug was discontinued

In conclusion,

Our report demonstrates the efficacy of cyclophosphamide in a patient with rapidly progressive SSc who had Lung fibrosis. cyclophosphamide (one course-5cycle pulse for 6month) had a marked effect on lung involvement, leading to a dramatic clinical and radiological improvement. We suggest that cyclophosphamide appears to be worthy of consideration as an additional therapeutic modality for SSc patients with progressive lung involvement, where

disease is recalcitrant to traditional treatment. There is supportive evidence suggesting a better response rate when introduced earlier in the disease course. For management of SSc-associated lung disease.

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