

The Galle Medical Journal

Journal of the Galle Medical Association

September 2013 Volume 18 Number 2 ISSN 1391-7072

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Galle Medical Association

72nd Annual Academic Sessions

27th - 28th September 2013

ABSTRACTS

ORAL & POSTER PRESENTATIONS

Oral Presentation – 01

Prevalence of normoalbuminuric renal insufficiency and associated clinical factors in adult onset diabetesLiyanage PLGC¹, Lekamwasam S², Weeraratna TP², Liyanage C³, Siriwardena HD¹*¹Department of Pharmacology, ²Department of Medicine, ³Nuclear Medicine Unit, Faculty of Medicine, University of Ruhuna, Sri Lanka.***Introduction**

Microalbuminuria signifies the onset of diabetic nephropathy, but normoalbuminuric patients with diabetes who have a low Glomerular Filtration Rate (GFR) are not uncommon. The purpose of the study was to estimate the prevalence of such patients and to assess the clinical correlates.

Methods

Cross-sectional study included patients with diabetes attending medical clinics at Teaching Hospital Galle. Diagnosis of albuminuria was made if urinary albumin excretion was >30 mg/g of creatinine in two out of three samples. Patients were stratified into chronic kidney disease stages according to the estimated GFR (eGFR) calculated by Modification of Diet in Renal Disease (MDRD).

Results

Mean (SD) age and duration of the disease of 456 (348 females) patients with diabetes were 60 (12) years and 10 (4) years. Sixty (13.2%) patients had low eGFR and 26.7% of them had normoalbuminuria. In the total sample, the proportion of patients with low eGFR and normoalbuminuria was 16 (3.5%). Among the patients with normoalbuminuria and low eGFR, 12.5% had retinopathy and none had any form of neuropathy. When age, duration of disease, systolic and diastolic blood pressures, smoking, glycaemic control, presence of hypertension and ischaemic heart disease were included in binary logistic regression model, only age was found to be significantly different (OR=1.1, P=0.03).

Conclusion

A considerable proportion of adult diabetics are normoalbuminuric despite low eGFR. This limits the role of microalbuminuria as a screening tool to detect the onset of diabetic nephropathy. These patients do not exhibit distinct clinical features that facilitate identification of them using clinical information. .

Oral Presentation – 02

Comparison of Cockcroft-Gault and Modification of Diet in Renal Disease Study equations in estimating glomerular filtration rate among patients with diabetes

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Introduction

The objective of this study was to estimate the prevalence of low-GFR and compare Cockcroft-Gault and Modification of Diet in Renal Disease Study (MDRD) equations in estimating GFR among patients with diabetes.

Method

Cross-sectional study included patients with diabetes attending medical clinics at Teaching Hospital Galle. GFR was estimated by the Cockcroft-Gault and MDRD. A GFR of <60 mL/min was taken as the cut-off for defining low-GFR. National Kidney Foundation (NKF) classification of renal disease was used to classify subjects based on their GFR.

Results

MDRD generated higher GFR values when compared with Cockcroft-Gault (median difference of 18.4 and IQR 8.3-31). GFR values of the two methods showed a moderate correlation ($r=0.4$, $P<0.01$). When subjects were classified according to the NKF guidelines, the agreement between the two methods was poor ($\kappa=0.13$).

Among 392 patients with diabetes low-GFR was more prevalent when applying Cockcroft-Gault equation (41.3%, 95% CI; 36.5 to 46.2) than the MDRD (12.24%, 95% CI; 9 to 15.5); $Z=9.3$, $P=<0.001$. This difference was seen among genders (In males: by Cockcroft-Gault 37.8% and MDRD 15.3% and corresponding values in females were 42.5% and 11.2%) and those above 55ys old were 53% and 15%. The difference was less pronounced among those <55ys (11.7 and 5.4%, $P=0.14$.)

Conclusion

The Cockcroft-Gault equation produced a lower estimate of GFR than MDRD equation and classified many people having impaired renal functions. The discrepancy was seen in both genders and those above 55 yrs. Studies should be done to compare these methods against a reference standard of measuring GFR to ascertain the most suitable method for clinical use.

Oral Presentation – 03

Ameliorative potential of *Coccinia grandis* on hepatic antioxidant status in STZ-diabetic ratsAttanayake AP¹, Jayatilake KAPW¹, Pathirana C¹, Mudduwa LKB²¹Department of Biochemistry, ²Department of Pathology, Faculty of Medicine, University of Ruhuna, Sri Lanka**Introduction**

The antihyperglycaemic activity of *Coccinia grandis* in streptozotocin induced (STZ) diabetic rats was scientifically proven by our group. However, the consideration of antihyperglycaemic activity of plant extract solely is not sufficient in retarding the full spectrum of associated cellular injuries. The present study is aimed to investigate the effect of aqueous leaf extract of *C. grandis* on liver enzymes, hepatic oxidative stress markers in STZ-diabetic rats.

Methods

Wistar rats were divided into four groups (n=6/group); healthy untreated rats, STZ - diabetic untreated rats, diabetic rats receiving the aqueous leaf extract of *C. grandis* (0.75 g/kg) and diabetic rats receiving glibenclamide (0.50 mg/kg). The treatment continued for 30 days. Serum activities of liver enzymes, concentration of hepatic total protein, reduced glutathione (GSH), activities of glutathione reductase (GR), glutathione peroxidase (GPx) and glutathione -S- transferase (GST) were estimated on the 30th day. Histopathological assessment of liver tissue was done on haematoxylin and eosin stained sections.

Results

The extract decreased the activities of liver enzymes; alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase by 47%, 12%, and 12% respectively (p=0.015). The liver GSH, activities of GR, GPx and GST of plant extract treated diabetic rats increased to, 591.40 ± 12.62 $\mu\text{g/g}$ liver tissue, 7.92 ± 0.75 , 7.76 ± 1.21 , 7.45 ± 1.67 nmol/min/mg protein respectively (p=0.020). Histopathological assessment corroborated the biochemical data.

Conclusion

The results revealed that administration of aqueous leaf extract of *C. grandis* markedly improves hepatic antioxidant status in (STZ) - diabetic rats.

Oral Presentation – 04

Effect of antioxidants (vitamin c and n-acetylcysteine) on the outcome of acute paraquat poisoning

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Introduction

The major mechanism of toxicity in paraquat (PQ) poisoning is production of free radicals. We conducted a trial on antioxidant strategies to combat oxidant-induced cellular damage in acute PQ poisoning.

Methods

Forty individuals following acute PQ ingestion were randomized. All patients received intravenous vitamin C (IV vit-C) 100mg, 500mg, 1000mg, 3000mg/day and 3000mg/8h for five-consecutive days. One arm received N-acetylcysteine (NAC) 20mg/kg in 200mL of 5%-dextrose over 15-minutes followed by 50mg/kg in 500mL over 12-hours twice per day for three days. The other arm received 5%-dextrose. These were compared to 24-historical and 80-parallel controls. The survival was compared by Mantel-Cox and Tarone-Ware test.

Results

The mean (SD) ages of the test, historical and parallel controls were 33 (17), 32 (18) and 34 (15) years.

The median survival time of the patients who received antioxidants and historical controls were eight (95%CI;1.8-14.2) vs one (95%CI;0.53-1.47) day (Mantel-Cox; P=0.03 and Tarone-Ware; P=0.01). The absolute risk reduction is 18.33% (95%CI;-2.66% to 39.33%, Number-Needed to Treat was six). The median survival time of parallel controls were seven days. There was no statistically significant survival difference between the individuals who received IV vit-C + placebo vs IV vit-C+NAC and tests vs parallel controls.

Stratified Cox Proportional Hazard model was done as variable sex violated the Proportional Hazard assumption ($X^2=66.6$, $p<0.01$). The median survival time of females and males in the test group were 10 and 6 days respectively.

Conclusions

IV vit-C±NAC has not shown improvement of survival following acute PQ poisoning. Stratified randomization by gender may be important.

Oral Presentation – 05**Neuro-muscular junction dysfunction in paraquat survivors****Jayasinghe SS^{1,2}, Pathirana KD³**¹*Department of Pharmacology, Faculty of Medicine, University of Ruhuna, Sri Lanka*²*South Asian Clinical Toxicology Research Collaboration, Faculty of Medicine, University of Peradeniya, Sri Lanka*³*Department of Medicine, Faculty of Medicine, University of Ruhuna, Sri Lanka***Introduction**

Evidence of neurotoxic effects of paraquat in humans is scant. We aimed to study the effects of paraquat on the neuro-muscular junction (NMJ) in survivors of paraquat poisoning.

Methods

A study was conducted recruiting a cohort of patients with acute paraquat poisoning. NMJ function was assessed by exercise modified slow repetitive stimulation (RNS) of the median nerve at rest (A) and 30-seconds (B) and two-minutes (C) after exercise of the thumb. The decrement response (DR) was calculated to the second, fourth and fifth stimuli at A, B and C. Post-exercise facilitation (B1/A1) and post-exercise exhaustion (C1/A1) were calculated.

Patients were assessed one and six weeks after the exposure. Results were compared with matched controls.

Data were analyzed with Mann-Whitney U and Wilcoxon Signed Ranks test.

Results

There were 28 (21 males) patients and 56 controls.

The median (IQR) DR at the second, fourth and fifth stimuli after exercise (B) at one week from exposure, of the patients and the controls were 1.7 (0.2 to 2.8) vs 0.3 (-0.7 to 1.4); P=0.02, 2 (1.2 to 4.7) vs 0.7 (-2.7 to 1.5); P=0.002 and 1.7 (0.6 to 4.6) vs 0.7 (-1.5 to 1.2); P=0.008 respectively. Significant improvement of median (IQR) DR was seen at the second stimuli after exercise (B) at six week from exposure, of the patients; 1.7 (0.2 to 2.8) to 0.3 (-0.8 to 1.0); P=0.04. No significant DR was found at A & C, post exercise facilitation and exhaustion in the patients compared to the controls.

Conclusions

Paraquat appears to produce NMJ dysfunction that can be demonstrated by slow RNS after exercise. Exposure to paraquat may be an important fact to exclude in a patient with idiopathic muscle weakness.

Oral Presentation – 06**Do the new guidelines for the management of urinary tract infection lead to misdiagnosis of clinically significant vesicoureteric reflux in infants?**Jayantha UK¹, Wijayasiri WAA², Danthanarayana M³¹*Department of Paediatrics, Faculty of Medicine, University of Ruhuna, Sri Lanka*²*Department of Community Medicine, Faculty of Medical Sciences, Sri Jayawardanapura, Sri Lanka*³*Medical Officer of Health, Bope Poddala, Sri Lanka***Introduction**

Urinary tract infection is a common bacterial infection representing 8% of children presenting with fever. There is no worldwide consensus in the management. Recent United Kingdom guidelines from National Institute of Health and Clinical Excellence (NICE) and guidelines from American Academy of Paediatrics (AAP) have recommend a drastic reduction of the use of imaging studies where renal ultrasound after first attack of UTI is limited to those who are younger than 6 months of age and MCUG is only indicated when there is ultrasound abnormality or atypical UTI.

Objectives

To find out the extent of misdiagnosis of vesicoureteric reflux by adhering to the NICE and AAP protocols.

Methods

Infants with culture positive febrile urinary tract infections presented to renal clinic from 1997 to 2010 were included. All the patients underwent renal ultrasound scanning and micturating cystourethrogram (MCUG).

Results

Of the 280 infants with UTI, 104 presented at ≤ 6 months of age and for the rest (176) the age at presentation was > 6 months. *Escherichia coli* was isolated in urine of 250 patients. In age groups ≤ 6 and > 6 months, ultrasound examination of the urinary tract was normal in 72 and 143 infants respectively. In ≤ 6 months age group, vesicoureteric reflux of any grade was found in 17 and that of high grade in 4 infants with normal ultrasound findings. In the same age group with abnormal ultrasound findings, the corresponding figures were 4 ($p > 0.05$) and 4 ($p > 0.05$) respectively. In > 6 months age group, corresponding numbers were 29 and 14 respectively in the normal ultrasound group and 14 ($p < 0.01$) and 10 ($p < 0.01$) respectively in the abnormal ultrasound group. Further, while the ultrasound is normal, abnormal MCUG was present in 4 infants in ≥ 6 months age group and 7 infants in > 6 months age group occurring due to abnormalities such as posterior urethral valve and bladder diverticula.

Discussion and Conclusion

Almost every low grade VUR and around 50% high grade VUR have normal renal ultrasound. So the results show that avoiding MCUG in infants with UTI could lead to grave consequences. Some abnormalities in the urinary tract would have been totally missed if only confined to ultrasound. Hence, MCUG is an essential investigation in UTI in infants.

Oral Presentation – 07**Effect of the glycaemic load of Sri Lankan meals on glycaemic abnormalities detected in glucose tolerance****Herath HMM, De Silva CM***Department of Medicine, Faculty of Medicine, University of Ruhuna, Sri Lanka***Introduction**

South Asians including Sri Lankans are at higher risk for Type 2 diabetes (DM). Even though, this is likely to be multi-factorial, diet with high glycaemic load (GL) may be a contributing factor. However, the possibility that meals with high GL may increase the risk of type 2 diabetes has been a long-standing controversy.

Objective

The objective was to study the effect of intake of glycaemic load on glucose tolerance in previously healthy subjects.

Methods

A total of 132 healthy subjects from Bope-Poddala area were randomly recruited for the study. Selected subjects completed a detailed dietary questionnaire from which GL was calculated. Glucose tolerance test (GTT) was performed to identify the subjects with abnormal glucose tolerance.

Results

There were 79 (59.3%) female in the study sample with mean age of 49.1. The mean GL was 2296.2 Kcal/day. Glycaemic abnormalities were detected in 37 (28.0%) subjects out of whom 21 (15.9%) had impaired glucose tolerance (IGT) and 16 (12.1%) had DM. Subjects were divided into 04 groups (low, intermediate, high, very high) depend on intake of GL. There was no statistically significant difference between groups as determined by one-way ANOVA ($F(3,119) = 1.046, p = 0.375$). There was no significant correlation between the GL with two hour value of GTT ($r=0.066, P=0.233$).

Conclusion

Intake of meals with higher GL is not shown to be associated with higher prevalence of glycaemic abnormalities in this study. Further studies are needed to look for other contributing factors for the higher prevalence of DM and IGT in this population.

Oral Presentation – 08

Prevalence of modifiable cardiovascular risk factors in a semi-urban community in Sri Lanka

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Introduction

Major cardiovascular diseases (CVD) are leading causes of mortality among Sri Lankans. Risk factors contributing to CVD are ever changing. Comprehensive data are limited regarding the current prevalence of CVD risk factors in semi urban population in Sri Lanka.

Objectives

To evaluate the prevalence of major modifiable CVD risk factors in a semi urban population.

Methods

This cross sectional study was carried out in Boppe-Poddala area of Galle district. Two hundred and five adults between 20-80 years of age were recruited through a multi-stage cluster sampling technique. Selected subjects were evaluated using a pre-designed questionnaire for major CVD risk factors (smoking, obesity, physical inactivity, hypertension, dyslipidaemia and diabetes). Detailed examination was carried out followed by blood testing for fasting glucose, glucose tolerance test, HbA1C% and lipid profile.

Results

The mean age and BMI of the participants were 50.8 ± 13.3 years and 23.62 ± 4.44 Kg/m² respectively. The most prevalent modifiable CVD risk factor was dyslipidemia (62.8%) followed by obesity (37.1 %). The prevalence of smoking, physical inactivity and hypertension were 8.8%, 19.5%, and 18.1% respectively. There is alarming high prevalence of diabetes mellitus (20.49 %) and pre-diabetic state (24.5%) in this population. The Odds Ratio for the presence of diabetes/pre-diabetes among the obese persons compared with normal weight was 2.04.

Conclusion

There is a high prevalence of CVD risk factors in the study population. Dyslipidemia and obesity sequentially were the most prevalent cardiovascular risk factors. Close to 50% of the population suffer from either pre-diabetes or diabetes in this semi-urban population which is much higher than the national figure.

Oral Presentation – 09

A study on hospital acquired infections (HAI) among ICU patients at a tertiary care hospital in Southern province of Sri LankaLewkebandara RH¹, Vidanagama D¹, Nagahawatta A²¹Department of Microbiology, Teaching Hospital Karapitiya, Galle, Sri Lanka²Department of Microbiology, Faculty of Medicine, University of Ruhuna, Sri Lanka**Introduction**

A study was conducted among patients admitted to the general ICU at Teaching Hospital, Karapitiya with the aims of determining the incidence of different types of hospital acquired infections (HAIs), device utilization ratio, antibiotic sensitivity pattern of the bacterial isolates and the rate of colonization with multi-resistant organisms.

Methods

All patients staying for more than 48 hours in the general ICU from January to March 2010 were followed up. Infections were diagnosed using clinical parameters and microbiological and other investigations.

Results

We observed 655 'patient days in the ICU', 616 mechanical ventilator days, 644 urinary catheter (UC) days and 396 central venous catheter (CVC) days. Twelve device associated infections (DAI) and 14 HAIs were detected with DAI and HAI rates of 15.78% and 18.42% respectively among 76 patients.

Ten (13.15%) patients developed ventilator associated pneumonia (VAP). Two patients (2.63%) developed catheter associated urinary tract infections (CAUTI) and 2.63% (2/76) developed non CVC related blood stream infections (BSI). VAP and CAUTI rates per 1000 device days were 16.23 and 3.1 respectively.

Mechanical ventilator utilization ratio was 0.94 and urinary catheter utilization ratio was 0.98 but CVC utilization ratio was 0.6.

Carbapenem resistance was noted in 72% of *Acinetobacter* species and 39% of these isolates were also pan drug resistant.

Colonization with nosocomial micro-organisms was noted among 65% patients at the end of the second week.

Conclusions

HAI and DAI were significant problems in this ICU. Carbapenem resistance was the worst problem related to antibiotic resistance. Risk of respiratory tract colonization with drug resistant *Acinetobacter* species, Coliform species and *Staphylococcus aureus* increased with the duration of the ICU stay.

Oral Presentation – 10**Interaction between RyR2 and GSTM2 C terminal domain is confirmed by the tryptophan fluorescence spectroscopy**Hewawasam RP¹, Liu D²¹*Department of Biochemistry, Faculty of Medicine, University of Ruhuna, Sri Lanka*²*John Curtin School of Medical Research, The Australian National University, Canberra, Australia***Introduction**

Ryanodine receptor is essential for the Ca²⁺ release from the sarcoplasmic reticulum and subsequent contraction of the striated muscle. Glutathione S-transferase Mu-2 C terminal domain (GSTM2C) showed specific inhibitory effects on the cardiac ryanodine receptor (RyR2) but not on skeletal ryanodine receptor (RyR1). Thus, it was assumed that GSTM2C may bind to different sites on RyR1 and RyR2. The fragment RyRD3-1, which binds to GSTM2C, includes most of the Divergent Region 3 (Dr3).

Methods

In order to define the binding site precisely, deletion constructs of the identified region (RyRD3-1) were made. Deletion construct AD-RyR2D3-2 supported the growth of yeast colonies and grew faster than AD-RyR2D3-1 in yeast two-hybrid experiments, indicating stronger binding. Protein binding was determined from the reduction of the intrinsic tryptophan fluorescence of helix 5678 of GSTM2C by AD-RyR2D3-2 or the synthesized peptides, RyR2D3, RyR2D3 mutant corresponding to ARVC (Arrhythmogenic Right Ventricular Cardiomyopathy) and RyR2D3 short which overlaps with the DR3 region. The dissociation constant (K_d) was calculated for each experiment.

Results

Results showed that binding affinities of RyRD3 and RyR2D3 short peptide to H5678 were significantly different (P<0.01) from the binding affinity between AD-RyR2D3-2 and H5678. They also suggested that the double mutation associated with ARVC in the DR3 region of RyR2 increased the binding affinity of GSTM2C for RyR2.

Conclusion

In conclusion, results confirmed that GSTM2C binds to the DR3 region of RyR2. If GSTM2C binds to the DR3 region of RyR2 with a higher affinity in patients suffering from ARVC related ventricular arrhythmias, there is a possibility of reducing the excessive release of Ca²⁺ from cardiac SR during diastole in the presence of GSTM2C. This further improves the therapeutic potential of GSTM2C.

Oral Presentation – 11**Presence of general learning disability in children and adolescents referred for neurodevelopmental assessments****Senadheera C¹, de Silva MLK², Samaratunga SAVPB³***¹Department of Psychiatry, ²Research Project-Validation of Neuropsychological test battery, ³English Language Laboratory, Faculty of Medicine, University of Ruhuna, Sri Lanka***Background**

General learning disability (GLD) or mental retardation causes life-long disability affecting the quality of life of the individual and the family. Literature highlights the importance of establishing programmes for early recognition and intervention in order to minimise the personal and socio economic impact of GLD. Neuropsychological tests are administered to detect GLD.

Objective

We analyzed data of assessments carried out between 2007-2012 to find the detection of GLD in children and adolescents referred for neurodevelopmental assessments to the Department of Psychiatry, Faculty of Medicine, Galle.

Results

A total of 263 individuals have been assessed during the above period and **62%** (n=161) were males. Fifty four percent of the referrals (n=143) were made from the child psychiatry clinic. The age ranged from 3.7 to 18 years (mean=10.9 years). The majority (86%) were accompanied by a parent. Many (92%) presented with significant behavioural issues. A substantial proportion had a history of delay in motor development (36%) and speech development (48%). Two hundred and twenty four (85%) were attending school (mainstream), only two were preschoolers.

Neurodevelopmental assessments indicated that 61% (n=161) met the criteria for GLD. Out of them, 60% (n=96) were males. The mean age was 11.5 years (males - 11.2 and females - 11.8 years). Many (93%) of them had on-going behavioural problems.

Conclusion

The delay in the detection of GLD may deprive the individual of benefits of remedial interventions. These findings indicate the need of awareness raising in the community about issues on child development and available services of assessments and interventions.

Oral Presentation – 12

Therapeutic efficacy of imatinib mesylate in the management of philadelphia positive Chronic Myeloid Leukaemia (CML)

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Introduction

Chronic myeloid leukaemia is a disease entity with specific haematological, cytogenetic and molecular genetic features. In 95% of patients, the disease is characterized by the presence of the Philadelphia (Ph) chromosome. This has provided a rational and novel therapeutic approach of oral tyrosine kinase inhibitor Imatinib for the treatment of CML.

Aim

This study was conducted to evaluate the therapeutic efficacy of Imatinib mesylate, on Ph positive CML among the cohort of patients attending the Cancer Institute, Teaching Hospital, Karapitiya.

Materials and Methods

There were 37 patients with Philadelphia chromosome (Ph)-positive chronic-phase CML on oral Imatinib mesylate at daily doses of 400mg for more than one year duration. Haematological and molecular response for the treatment was evaluated overall and in relation to age and sex. Available clinic records used to identify patient characteristics at presentation.

Results

Out of 37 (67.5% males and 32.5% females) patients included in the study, 81.01% had Complete Haematological Response (CHR) and 35.14% had 'undetectable transcripts'/Molecular Response (MR). Among the patients who achieved CHR, 70% were male and 30% were females. Of the patients, 36.7% were less than 40 years and 63.3% were more than 40 years of age. There is no statistically significant difference between gender and CHR or age and CHR (p values 0.83, 0.14 respectively) and gender and MR or age and MR (p values 0.76, 0.53 respectively).

Conclusion

Imatinib mesylate was active against Ph-positive, chronic phase CML with a CHR rate of 81.01% and MR rate of 34.14% in the study cohort.

Oral Presentation – 13

The association of myocardial infarction and its severity with high sensitivity C-reactive proteinWickramatilake CM¹, Mohideen MR², Pathirana C¹¹Department of Biochemistry, ²Department of Medicine, Faculty of Medicine, University of Ruhuna, Sri Lanka**Introduction**

Atherothrombosis of the coronary vessels is understood as a disorder of inflammation. High-sensitivity C-reactive protein (hs-CRP) proposed as a new coronary risk marker may reflect either an acute phase reaction or the level of chronic inflammation. There is insufficient evidence on the association of hs-CRP with the severity of myocardial infarction (MI). This study aimed to examine if serum hs-CRP differs between men with and without MI and to find out if serum hs-CRP level is associated with severity of MI.

Methods

Two hundred and six male subjects (103 patients with ST-elevation myocardial infarction and 103 controls) were recruited. Serum lipids, hs-CRP and plasma glucose were estimated. The clinical risk scores; TIMI (Thrombolysis In Myocardial Infarction) and GRACE (Global Registry of Acute Coronary Events) scores were calculated during the acute phase. Modified QRS electrocardiographic score was calculated.

Results

Mean baseline hs-CRP concentration in STEMI patients was significantly higher compared to controls (3.7 ± 0.84 vs. 1.7 ± 0.6 mg/L, $p = 0.001$). Following adjustments for age, BMI, smoking, diabetes mellitus, statin and aspirin use it remained statistically significant (hs-CRP, 3.7 ± 0.16 vs. 1.71 ± 0.37 mg/L, $p = 0.001$). Severity of myocardial infarction graded by clinical risk scores significantly correlated with hs-CRP [TIMI ($r = 0.226$, $p = 0.022$), GRACE ($r = 0.361$, $p = 0.001$) and QRS score ($r = 0.314$, $p = 0.001$)]. Mean values of hs-CRP in different quartile ranges in each score were significantly different [TIMI ($p = 0.017$), GRACE ($p = 0.002$), QRS score ($p = 0.044$)].

Conclusion

Mean baseline hs-CRP level was high in acute STEMI compared to controls. Severity of myocardial infarction graded by clinical risk scores and QRS score was correlated with hs-CRP.

Oral Presentation – 14

Detecting bacterial pathogens causing infections in neonates admitted to the Neonatal Intensive Care Unit (NICU) at a tertiary care hospital in southern province of Sri Lanka

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Introduction and Objectives

A prospective study, carried out in the Neonatal Intensive Care Unit (NICU), Teaching Hospital Karapitiya from January to April 2011.

To find incidence of culture proven episodes of infections, to identify bacterial pathogens and sensitivity patterns, to determine most appropriate empirical antibiotics for current use in NICU, to find the rate of colonization with possible pathogens among neonates on admission and to assess usefulness of screening tests in predicting causative organisms of sepsis.

Methods

50 neonates were screened on admission and weekly to detect colonizing bacteria. On clinical suspicion of sepsis, specimens were cultured. Antibiotic sensitivity assessed.

Results

From 55 clinically suspected sepsis episodes, 17 (1/3) became culture positive. That is 340/1000 admissions. Rates of early and late onset sepsis (LOS) were 4% and 30% respectively.

Nosocomial infection rate (clinically suspected cases) = 50 episodes/ 1000 patient days. That of culture proven rate = 13.61 episodes/ 1000 patient days.

Thirteen (76%) isolates were coliforms. Of them, 11 (84.61%) produced extended spectrum beta-lactamase (ESBL). Imipenem, meropenem, amikacin and netilmicin were appropriate antibiotics for empirical treatment of LOS here.

On admission 35 (70%) were colonized, the commonest was coagulase negative Staphylococcus (50%). Twenty (40%) had coliforms including 8% ESBL producers.

Among culture positive episodes, 7 (41%) had same organism in surveillance samples.

Conclusions

Clinical suspicion of sepsis was high among neonates. Only 1/3 of them was proven by cultures. Predominating pathogens were coliforms and were resistant to commonly used antibiotics. Carbapenems and aminoglycosides were most appropriate empirical antibiotics for LOS in this NICU. Presence of multidrug resistant isolates on admission was a problem.

Oral Presentation – 15**Assessment of the age range, where juvenile T inversion pattern in right precordial leads of an ECG changes to the adult upright T wave pattern**

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Objective

To determine the age range, where juvenile T inversion pattern in right precordial leads (V1 to V4) in an ECG changes to the adult upright T wave pattern.

Method

A descriptive cross-sectional study was done in children aged 5 years and above referred to the Paediatric Cardiology clinic, Teaching Hospital Karapitiya from January 2012 to April 2013. Inclusion criteria were: children with no cardiac lesion or a haemodynamically insignificant cardiac lesion after a full cardiac evaluation. The cohort was divided into six age groups and the presence of juvenile and adult ECG patterns were evaluated.

Results

A total number of 1039 children were enrolled. At the age of 13 years 50% depicted both juvenile the adult ECG patterns. At the age range of 13-15 years 78 (60%) of a total of 130 showed the adult ECG pattern compared to 99 (44.4%) of a total of 223 at 11-13 years ($X^2 = 8.0$; $p = 0.005$). Even after 13 years of age the juvenile ECG pattern persisted in 30-40% of children.

Conclusions

Transition of the juvenile T inversion pattern in right precordial leads in an ECG to the adult upright T wave pattern occurs predominantly at the age range of 13-15 years. Presence of juvenile T inversion pattern in an ECG after 13-15 years can be a normal finding as well as may be a presymptomatic diagnosis of a cardiomyopathy. Although it is normal to have a juvenile ECG pattern above 13 years it is advisable to perform an echocardiographic evaluation on children above 13 years with juvenile T inversion pattern which may lead to early diagnosis of cardiomyopathy.

Oral Presentation – 16

Assessment of Frontal lobe functions in a community dwelling sample of Sri Lankan older adults

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Background

The prefrontal cortex plays a central role in a group of cognitive abilities called 'executive functions' (EF). Since the prefrontal cortex is vulnerable to neurological illnesses including dementia, assessment of EF is important for making clinical diagnoses. Modified Wisconsin Card Sorting test (MWCST) is a widely used neuropsychological measure of EF of older patients with cognitive impairment. There are no validated tests of EF available in Sri Lanka.

Objectives

To validate MWCST for a sample of older adult population in Sri Lanka. An age-related decline in the performance of the MWST was expected.

Methods

MWCST was administered to a sample of healthy volunteers living in Galle. In MWCST, cards varying on 3 basic features must be sorted according to each feature in turn and the test is continued until the participant completes 6 categories or sorts 48 cards. The number of sorted categories (SC) and preservative errors (PE) were compared in different age groups and education groups.

A total of 209 (74 males, 135 females), ranging in age from 50 to 80 years (mean=63 years) completed the test.

Results

The number of SC score for the age groups (50 - 59, 60 - 69 and above 70 years) were 4.4, 4.1 and 3.7 respectively ($p=0.075$), while respective numbers of PE were 6.8, 7.3, 8.7 ($p=0.25$). Low, middle and high education groups differed in terms of SC (means 2.9, 3.9 and 5 respectively, $p<0.001$). Those who had more years of education made less number of preservative errors ($p<0.001$). Effect of gender on MWCST performance was not significant.

Conclusions

The MWCST may be valid in the assessment of Sri Lankan older adults with high education.

Oral Presentation – 17**Use of retained patient samples in verification of precision of Full Blood Count test results in a private sector laboratory****Wickramaratne KAC***Department of Pathology, Faculty of Medicine, University of Ruhuna, Sri Lanka***Introduction**

Quality results are mandatory to assure effective patient care. High degree of precision and accuracy ensure quality of test results. To assure precision, internal quality control (IQC) is used. Commercial IQC material in haematology is costly and less stable. Use of patient samples can be a better alternative in IQC.

Objectives

To assess the possibility of use of retained patient samples in monitoring internal quality control in automated full blood count testing (FBC).

Methods

Study was carried out in a private sector laboratory. Randomly selected 200 patient samples received for FBC were retained from every session with copies of the initial reports. Tests (haemoglobin, red cell count, MCV, PCV, MCH, white cell count and platelet count) were repeated in the next session and the results were compared.

Results

Mean of the differences and Standard deviation of differences were well within the laboratory quality assurance criteria. Means(SDs) of the difference were 0.14(0.23), -0.01(0.06), 0.04(0.08), 0.63(1.2), -1.15(2.7), 0.2(0.43), -0.28(12) for white cell count, red cell count, haemoglobin, PCV, MCV, MCH and platelets respectively.

Conclusion

Retained patient samples can be used to assure precision of FBC results but including labile components like platelets in spite of differences in disease, blood collection and method of transportation.

Relatively high SD observed for MCV could be related to cell swelling during storage.

Oral Presentation – 18

Aetiological agents and antibiotic sensitivity in chronic suppurative otitis media in teaching hospital, Karapitiya

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Introduction

Chronic suppurative otitis media (CSOM) is chronic inflammation of the middle ear and mastoid cavity, presenting with recurrent ear discharges through a tympanic perforation. CSOM leads to serious complications and probably the commonest cause of deafness in children. Identification of the aetiological organisms causing CSOM aids in its management. Identifying antibiotic sensitivity of these organisms aids in prescribing antibiotics empirically.

Objective

To identify the aetiological microbiological organisms in patients presented with CSOM, with their antibiotic sensitivity and the effect of demographic factors in the causation.

Methodology

Cross sectional descriptive study was conducted including all the CSOM diagnosed patients presented until the sample size was met. Demographic factors, duration of ear discharge, unilateral or bilateral disease, results of the culture, antibiotic sensitivity of the organisms were collected.

Results

Three hundred and eighty four patients were included in the study. There was no statistically significant difference in age or sex in the study group. One hundred and five (27%) has had the illness for more than 5 years and 60(15%) had bilateral disease. Two hundred and ninety six (77%) cultures yielded a growth of an organism out of which 193(59%) was *Pseudomonas sp.*, followed by Coliform 74(22%) and *Staphylococcus aureus* 53(16%). Sixty two (19%) were multidrug resistant. Two hundred and twenty eight (71%) of cultures were sensitive to Ciprofloxacin followed by Amikacin 213(66%), Ceftazidime 156(48%) and Gentamicin 51(16%).

Conclusions

The commonest microbiological agent identified in CSOM was *Pseudomonas sp.* Demographic agents did not seem to affect the disease manifestation. Most causative organisms were sensitive to Ciprofloxacin.

Poster Presentation – 01**Prevalence of the colour blindness and its impact on their education among undergraduates of University of Ruhuna**

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Background and Objectives

Previous studies have shown that colour blindness affects the education and carriers of professionals. This study was designed to elicit the prevalence of colour blindness and its impact on undergraduates.

Materials and Methods

Colour vision of the randomly selected 309 engineering and 91 medical students was tested by using Ishihara pseudo- isochromatic plates. Impact of the disease was assessed by self administered questionnaire given to the identified students.

Results

Ten male students out of 400 students were identified as red green colour blind. Prevalence of the disease was 2.5% in the study sample and it is 3.3% among male students. Sixty percent of the affected individuals were aware about their disease. Seventy percent of affected students face difficulties during their day today activities and 90% of the students found difficulties in academic activities due to the colour blindness.

Conclusion

Detection of the colour blindness at the entry to the university and counseling the affected individuals on their weakness before embarking on selected carrier will be appropriate.

Poster Presentation – 02

Colour preferences among patients with chronic pain

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Objectives

A difference in color preferences of patients in varying stages of health has been evaluated in previous studies. This study was designed to determine colour preferences among patient with chronic pain.

Materials and methods

Study sample consisted of 100 (51 males) non-colour blind patients with mean age (SD) of 38(9.1) years. The study was conducted in two phases. During Phase I, patients answered interviewer administered questionnaire given in hospital setting to obtain the patients' colour preferences for known objects. The colour preferences of each patients was assessed by using a standard colour palette and coloured objects in a controlled viewing setting in Phase II. Results were compared with age and sex matched healthy 100 volunteers with mean age (SD) of 40(8.7) years. Chi- square test was performed to analyze the results.

Results

Blue (n=27) and yellow (n= 25) are the most preferred as wardrobes colours. Patients have selected Green (n=22) and yellow (n=21) as most preferred colours for their bedrooms. Most of the patients (n=39) liked to see their doctor in white coloured attire. Patients have shown statistically significant results in selecting colours to their wardrobes, bedroom and doctor's attire.

Patients selected colors in yellow region (n = 33) of the master colour pallet as most preferred colour while most disliked colours were in yellow to red region (n=53) and it was statistically significant. White (n= 44) was selected as the most preferred colour for medicinal tablets and this was not statistically significant.

Colour preferences among male and female patients were not statistically significant.

Conclusion

There is a significant difference in colour preference of healthy individuals and patients with chronic pain.

Poster Presentation – 03**Clinical profile and outcome in a tertiary level Pediatric Intensive Care Unit****HMD Hewagegana, WCS Jayawardana, HPI Jayalath, UBL Liyanage***Paediatric Intensive Care Unit, Teaching Hospital Karapitiya, Sri Lanka***Introduction**

Pediatric Intensive Care is a relatively new specialty in Sri Lanka. Published data on clinical profile and outcomes for Sri Lankan PICUs are limited.

Objectives

The objectives of the study was to study the clinical profile and outcome of patients admitted to a tertiary level Pediatric Intensive Care Unit, to provide benchmark values for future studies and to highlight the areas that needs further studies.

Materials and Methods

Retrospective observational study of consecutive 100 admissions from July 2012. Factors studied include, demographic data, clinical profile, interventions and outcome.

Results

One hundred patients were admitted (78 emergency and 22 elective). Female to male ratio was 1.7:1 and 5-12y age group predominated in both sexes (33%). Main Diagnostic group was respiratory (33%). Twenty seven percent had underlying chronic conditions. These 27 patients contributed to 45% of total ventilator days and 40% of total ICU days. Mortality rate in this group was higher (29.6% vs. 13.6%).

Fifty two percent of patients received mechanical ventilation. Median duration of ventilation was 4 days (IQR 2-13). Thirty six percent received inotropes and 29% of patients had central lines. Fifty percent of patients received a blood product.

Twenty seven percent of all patients and 95% of non survivors had multi organ dysfunction.

Gross mortality rate was 18% (n=18) and PIM-11 adjusted standard mortality ratio was 1.7. Median ICU stay was 5 days (IQR=3-9.8).

Conclusion

Patients with chronic conditions contribute to significant portion of total ICU and ventilator days. Multi organ dysfunction syndrome remains a major cause of death. Our blood product transfusion rates are very high compared to other studies and an audit is required to find out reasons. Gross mortality rates are comparable to that in the region but there is room to improve in standard mortality rates.

Poster Presentation – 04

Audit on Deaths within 24 and 48 hours of admission to Medical Intensive Care Unit (MICU) at Lady Ridgeway Children's Hospital (LRH) in 2011

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Introduction

Deaths within the first 24 and 48 hours of admission to MICU occur partly due to poor pre-admission management and delayed admission. These are crucial factors determining the outcome. Poorly organized long-distance transfers and lack of proper inward care lead to deterioration of organ functions in already compromised patients. In developed countries, the MICU team is involved in management of critically-ill-patients in paediatric-wards and specially trained teams are available for transport.

Objectives

To identify the prevalence and correlates of deaths within 24 and 48 hours of admission to MICU, LRH.

Methodology

A clinical audit was performed during a 12 month period from January 2011 at MICU, LRH. The data on socio-demographic factors and nature of transfer to MICU were gathered from the medical audit forms used during the MICU admission. Data was analyzed using SPSS software.

Results

Total number of admissions to MICU during 2011 were 542. Mortality rate was 25.8% (n=140). Out of these deaths, 15% (n= 21) and 11% (n=16) had occurred during 24 hours of admission and 24 to 48 hours respectively. Therefore, a significant proportion (26%) out of all deaths at MICU had occurred within the 48 hours of admission. There was no significant association between the proportion of deaths within 48 hours in relation to whether the patient was admitted from LRH or outside hospitals (P>0.05).

Conclusion

Significant proportion of deaths at MICU had occurred during the first 48 hours. Therefore, we recommend further interventional studies to correlate the outcome of patients with and without prior involvement of MICU team in the management of inward critically ill patients.

Poster Presentation – 05**A study on the impact of urine culture results in the management of patients with urinary tract infections****Wickramasinghe D, Jayasekara GJVM, Vidanagama DS***Department of Microbiology, Teaching Hospital, Karapitiya, Sri Lanka***Introduction**

Current knowledge on antimicrobial susceptibility pattern of uropathogens is essential for appropriate therapy of urinary tract infections (UTI).

Objectives

To identify the bacteriological profile of patients with UTI and to determine the impact of culture report on patient management.

Materials and Methods

A prospective study was carried out from December 2012 to February 2013 in the Department of Microbiology, Teaching Hospital Karapitiya. All significant adult (>13 years) uropathogens and their susceptibility patterns were noted. Patients were followed up for modification of therapy and clinical impact.

Results

Of 2173 tested adult urine samples, 250 showed significant growth of pathogens and the commonest isolates were *coliforms* (76.4%) followed by *Pseudomonas* spp. (5.2%) and *Enterococci* (4.8%). Of the coliform isolates 33.6% produced extended spectrum β -lactamases (ESBL). From the positive cultures 52% were from females and the majority was from 39-64 year age group (40.6%). Among the coliforms high prevalence of resistance was observed against ampicillin (77.4%) and ciprofloxacin (74.3%). Majority (91.5%) of the patients' antibiotic treatment were started after culture and ABST. The percentage responding to empirical antibiotics was 65%. After receiving culture reports 35% of those with ESBL UTI and 24.3% of those with UTI caused by other organisms had changed antibiotics according to ABST results.

Conclusion

This study revealed that *coliforms* were the predominant bacterial pathogen and one third of them were resistant (ESBL producing) to first line antibiotics. Most empirical regimes are not effective against ESBL producing organisms which would never be detected without culture and ABST. Majority of the patients' (>90%) antibiotic treatment were started after culture and ABST. Therefore, culture and ABST is important in the management of urinary tract infection and detection of resistant strains as well as for the exclusion of the urinary tract infection.

Poster Presentation – 06

The frequency and effects of home therapeutic measures in acute poisoning: A cross-sectional study

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Introduction

Early medical interventions improve outcomes in acute poisoning. Community beliefs lead to the adoption of home therapeutic measures (HTM) prior to seeking hospital treatment. Objectives were to assess the frequency of HTM, the nature of interventions, potential dangerous practices, influence of HTM on delaying hospital treatment.

Method

A cross-sectional study was conducted at Teaching Hospital Karapitiya for three months from April 2013. Data was collected using semi structured interviews. Mann-Whiney-U test was used to compare times elapsed prior to hospital admission between groups with and without HTM.

Results

Out of the 321 patients admitted with poisoning 163 (50.7%) were males. Mean age was 25 ± 15 years. Ingestion of medicines (43.6%), plant-poisons (20.8%) and pesticides (19.9%) accounted for most. HTM were used in 19.9%. Induction of emesis was the commonest (84%). Ingestion of coconut milk (46%), salt water (11%), soap water (7%), clean water (4%), king-coconut water (2%), bananas (2%) and stimulation of pharynx with a finger (19%) were the methods adopted. Among those with induced emesis, 17 were following ingestion of petroleum products or corrosives. HTMs was used regardless of level of consciousness. Median (IQR) of door to needle time of the patients who did and did not receive HTM were 3(2-8) and 3(1.5-10) hours respectively (P=0.9).

Conclusion

Induction of emesis was the primary aim of HTM. Potentially dangerous practices such as induction of emesis following corrosive and petroleum product poisoning were noted. HTMs did not contribute to treatment delays. Public education on potential dangers and benefits of HTMs is a need.

Poster Presentation – 07**The incidence of third head of biceps brachii muscle; a cadaveric study****Samarawickrama MB, Nanayakkara BG, Munasinghe AMY, Deshan VGU***Department of Anatomy, Faculty of Medicine, University of Ruhuna, Sri Lanka***Introduction**

Wide variation of biceps brachii muscle in its number of heads has awakened the interest of clinicians, anatomists and researchers.

Aim

The aim of this study was to investigate the incidence of occurrence of third head of biceps brachii in a group of Sri Lankan subjects.

Methods

A total of 113 upper limbs in 58 formalin fixed cadavers were studied for the presence of third head of biceps brachii muscle. Details of such additional heads were noted and their attachments and morphology were studied in detail.

Results

The study sample consists of 36 males and 22 female cadavers. Out of 113 upper limbs, biceps brachii muscle with three heads was found in 11 limbs. Among those 9 (81.8%) were males and 2 (18.2%) were females. However, bilateral three heads were not found in any of the cadavers. Of the total eleven, nine (81.8%) of the third heads were originated from the shaft of the humerus closer to the insertion of the coracobrachialis muscle. In all the subjects, third heads were found to fuse distally with the common bellii of the biceps brachii muscle.

Discussion and Conclusion

The results of this study reveal that the incidence of third head of biceps brachii is 9.7% in the sample studied. The occurrence of third head of biceps is significant. Knowledge of occurrence of third head of bicep brachii is important for surgeons and anatomists.

Poster Presentation – 08

Variations of the course and division of the sciatic nerve - A cadaveric study

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Introduction

It is very important to know the exact course of the sciatic nerve in the gluteal region for prevention of iatrogenic injury during intramuscular injection to the gluteal muscles. Similarly the knowledge of the level of division of the nerve is helpful during above knee amputation surgery and reconstructive surgery of the lower limb.

Objective

To find out variations in the course of the sciatic nerve in the gluteal region and its division into tibial and common peroneal nerves.

Method

The exact entry point of the nerve to the gluteal region and its exit point from the gluteal region and the level of its division were studied using formalin fixed cadavers.

Results

Study sample included 27 cadavers with 21 males and 6 females. Five levels of nerve division were identified with the commonest level being at the lower 1/3 of the thigh. One sciatic nerve had divided in the pelvis. All the nerves passed inferior to the piriformis muscle except the one divided in the pelvis. In majority of the nerves studied, the entry and exit points of the nerve were not exactly at the point which described in text books.

Discussion and Conclusion

The variations of the entry and exit points of the nerve were -1.33cm and +0.32cm respectively from the described surface marking points. Knowledge of this variation is important for the anaesthetist during sciatic nerve block. Similarly the variation of the level of division is important in evaluating nerve injuries and identification of the nerve during amputations of the lower limb.

Poster Presentation – 09**Correlation between continuous assessment in anatomy and second MBBS results**

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Introduction

Continuous assessments as a system of evaluating medical students' performance have been in existence during their preclinical training. However, it has not been assessed to show the correlation between continuous assessment grades and second MBBS results.

Objective

To find out whether the grade obtained in continuous assessments in Anatomy by medical students reflect the second MBBS examination results.

Methods

The study was conducted to the 33rd batch of medical students. The second MBBS results were compared separately with the assessments grades taken for MCQs, gross anatomy spots, histology spots and neuroscience during the course.

Results

Considering results of third term assessment MCQ grading; those who have got higher grades (A&B) had obtained more classes (58%), than those who have got lower grades (D&E = 11%). On the other hand the failure rate was higher in lower grades (55%), than the higher grades (8%). Similar results were observed for the grades obtained for MCQs and Spots at other terms and second MBBS results. This was statistically significant ($p < 0.001$).

Discussion and Conclusion

This study highlights that the grades obtained at the Anatomy assessments significantly reflect the second MBBS results of the student. Therefore knowing the grades of assessments one can predict the failures and can make more attention on them. The knowledge of this study will be helpful to increase the awareness of the importance of the continuous assessments among preclinical students. We suggest further studies to compare the assessment grades obtained for Biochemistry and Physiology and the second MBBS results.

Poster Presentation – 10

A descriptive study on homicides in Galle, Sri Lanka

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Introduction

The intentional killing of a human being by another is the ultimate crime. Its indisputable physical consequences manifested in the form of a dead body also make it the most categorical and calculable.

Objective

To find out epidemiological, socio-economic and postmortem data on homicides and compare them with the findings of previous studies.

Materials and Methods

A retrospective study was carried out at the Teaching Hospital, Karapitiya during the year 2011. All the potential homicide cases referred during the study period were analyzed.

Results

Forty (34 males) homicides were studied. The majority (62.5%) was in the 21 - 40 age group and 85% of them were married. Most of the homicides were reported from the Meetiyyagoda (20%), Elpitiya (15%) and Karandeniya (15%). A sharp force was the commonest method ($n = 18$; 45%). The number of homicides by firearm and blunt force were 13 (30%) and 9 (25%) respectively. All assailant unknown (20%) cases were firearm deaths. Knife (50%) was the commonest weapon used in sharp force trauma followed by swords (44%). Chest remains the commonest site of injury in both sharp force (16) and firearm (entry wound 14, exit wound 09) deaths. In blunt force trauma, head and face remains the targeted sites (100%).

Discussion and Conclusions

Majority were young married males. Sharp cutting weapons have become more popular. Swords are being used as often as the knives. In studies done in the year 2006 and 2008, firearm was the commonest method used. There is a definite change in the method used for homicides in the war era and post-war era. Firearms are being used in cases where the assailant is unidentified.

Poster Presentation – 11**Knowledge and attitudes of nursing students in educational institutions in Galle District towards deliberate self harm****Samarawickrama NS***Allied Health Science Degree Programme, Faculty of Medicine, University of Ruhuna, Sri Lanka .***Introduction**

Attitudes of health care professionals towards patients with deliberate self-harm (DSH) are considered to be largely negative. The type and quality of care those patients receive will depend on the way they are viewed by the health care professionals including nurses.

Objectives

To assess knowledge on DSH and attitudes towards DSH patients in final year nursing students following two different programmes; Diploma course in Nurses Training School, Galle and Degree Programme in University of Ruhuna.

Method

A questionnaire including 12 items to assess knowledge on DSH and 13 items to assess attitudes towards DSH patients was given to 31 nursing undergraduates and 176 diploma students.

Results

Two hundred completed questionnaires were returned. Response rate was 96.62%. Thirty eight percent of participants were aware of all the details included in the definition of DSH. Only 5% knew common facts of DSH in Sri Lanka, while 14% knew the difference between suicide and DSH. The percentage of nursing undergraduates who had good knowledge on above mentioned three areas was 23% while that of diploma students was 3% ($p=0.001$).

Almost all (99%) were of the opinion that DSH patients should be treated as any other patient. All nursing undergraduates and 98% of diploma students agreed that DSH patients should be taken serious and listened to.

Conclusion

The results indicate that the final year nursing students have gaps in their knowledge on DSH. However, they have developed caring attitudes towards DSH patients irrespective of the training programme they follow.

Perigraft seroma following Right Modified Blalock Taussig shunt in a child with complex cyanotic heart disease

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Case report

A three and half year old boy with Tetralogy of Fallot and pulmonary atresia was admitted for cardiac catheterisation to assess suitability for the Rastelli procedure (Total correction of Tetralogy of Fallot with right ventricle to pulmonary artery conduit).

Palliative modified Blalock Taussig (BT shunt) was done in June 2011 as his pulmonary arteries were hypoplastic. A 5mm polytetrafluoroethylene (PTFE) expanded Gore-Tex graft was interposed between the right subclavian and right pulmonary artery through a right posterolateral thoracotomy. Heparin was given for 48 hrs followed by aspirin (3 - 5 mg/kg per day). Saturation was maintained at a satisfactory level. He did not have postoperative complications. The patient was discharged on the 10th day after the procedure and followed up regularly to assess the growth of branch pulmonary arteries and the shunt function.

Two years after the modified BT shunt, a chest radiograph was taken and it showed a large well demarcated right superior mediastinal mass with no marked tracheal displacement. The radiograph and ultrasonography were suggestive of a seroma around the right modified BT shunt (Figure 1). Cardiac catheterisation revealed a large seroma compressing the right lung with reduced lung arborization of the right upper zone. His right pulmonary artery was not adequately grown when compared to left pulmonary artery. There was no graft compression by the seroma (Figure 2).

The seroma was aspirated, completely, under ultrasound guidance using an 18G spinal needle (Figure 3A). Aspirate yielded 90 ml of amber coloured fluid (Figure 3B). Post aspiration chest radiograph revealed expanded right lung (Figure 4).

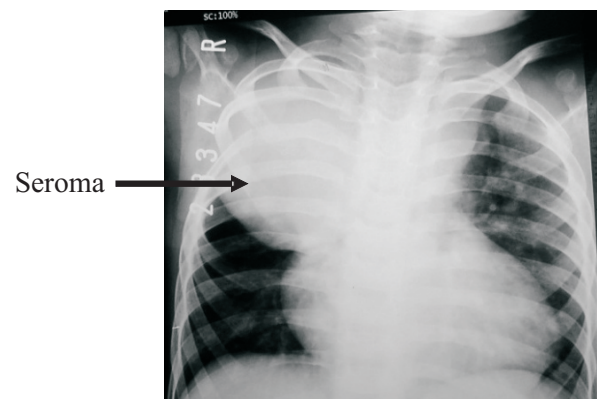


Figure 1: Chest X-ray two years after BT shunt

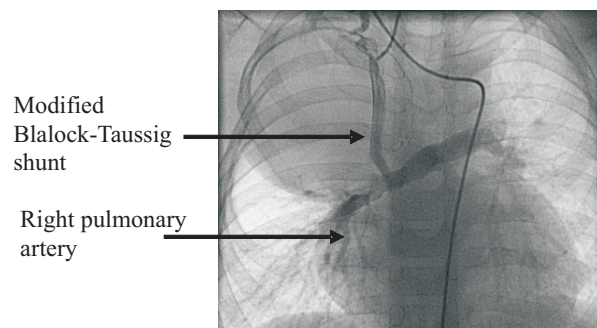


Figure 2: Seroma compressing the right lung with reduced lung arborization of the right upper zone

Discussion

The original procedure of BT shunt was an end-to-side anastomosis in which the subclavian artery was sacrificed (1,2). With the advent of artificial vessels made of materials such as Gore-Tex, a change in the procedure was introduced. In 1976, Gazzaniga et al, (3) were the first team to perform a modified Blalock-Taussig shunt, using a polytetrafluoroethylene graft (Gore-Tex; W.L. Gore) as an interposition between the subclavian and pulmonary arteries (Figure 5).

Several well-known complications of the modified BT shunt, such as shunt thrombosis, infection, haematoma, aneurysmal dilatation, mycotic pseudoaneurysm and perigraft seroma have been described. A perigraft seroma is defined as a sterile collection of fluid in a non-secretory wall surrounding the shunt. The cause of the formation of a perigraft seroma is still a matter of debate. One of the most widely accepted theories is that handling of the polytetrafluoroethylene graft causes leakage because of a change from a hydrophobic state into a hydrophilic one. The fluid collection thus contains graft ultrafiltration (transudate) (4).

Perigraft seroma development around a modified Blalock-Taussig shunt is a relatively rare but, nonetheless, well-known complication. In recent literature, the prevalence of this complication has been reported as ranging from 2.5% to 9.5%. Seroma formation normally takes place within first 2 months following surgery but our patient developed this complication after two years. This indicates the need of maintaining the vigilance and performing routine chest radiographs at regular intervals to detect this complication at pre-symptomatic stage. Cases presenting after 8 years also have been reported (5).

Patients with seroma may present with symptoms such as intermittent stridor, respiratory distress and or episodic desaturation within weeks of surgery. Most seromas reported to have encompassing the graft.

For the diagnosis, chest radiography shows the first sign of the seroma after modified BT shunt. Thoracic sonography also can demonstrate the perigraft seroma and the function of modified BT shunt. Thoracic computed tomography (CT) or magnetic resonance imaging (MRI) may be performed to study perigraft seromas in detail. When seroma is found in a critically ill patient, ultrasonography has an advantage over CT and MRI because of its portability and capability for bedside use.

Treatment modalities includes aspiration using sterile technique with a large bore needle (14 - 18 Guage) or angiocatheter followed by application of pressure dressing that promotes the obliteration of seroma and eventual healing. Chronic seromas as in our case is difficult to obliterate with needle aspiration. It may need closed suction drains to prevent recurrences. In cases with blocked BT shunts, it may need balloon angioplasty or surgical refashioning of the shunt.



Figure 3: Aspiration of seroma under ultra sound guidance

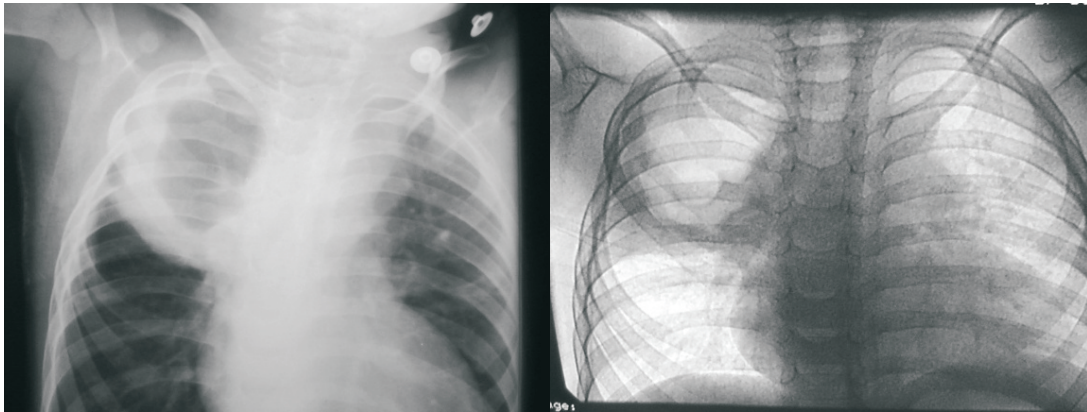


Figure 4: Post aspiration chest X-ray

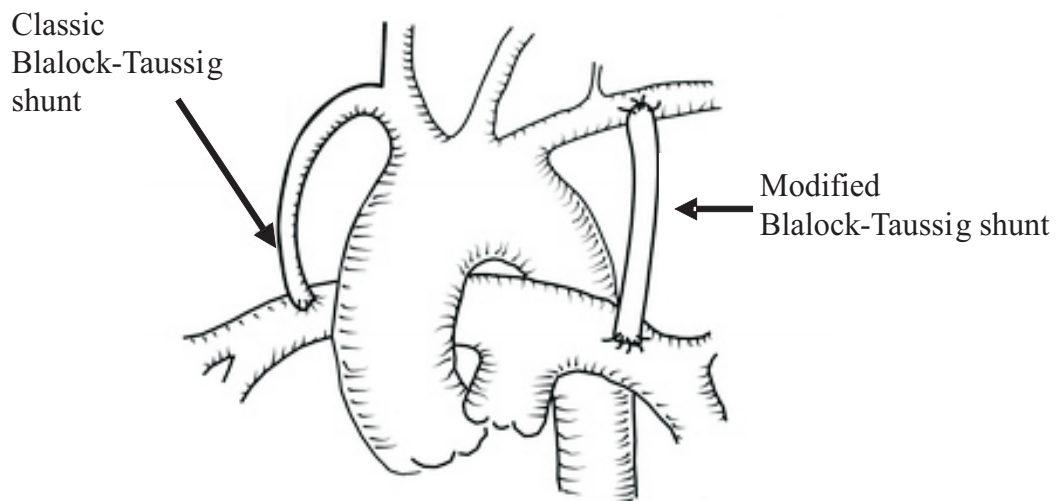


Figure 5: Modified BT shunt

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Hypokalaemia-induced rhabdomyolysis as the presenting feature of primary hyperaldosteronism

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Introduction

Primary hyperaldosteronism (PHA) is a well established cause of secondary hypertension. It is characterised by hypertension, hypokalaemia and metabolic alkalosis. In some extreme conditions, PHA can induce excessive potassium excretion resulting in profound hypokalaemia followed by rhabdomyolysis. Although muscle weakness is a well known manifestation of marked hypokalaemia, rhabdomyolysis is a rare presentation of hypokalaemia (1). Rhabdomyolysis presenting with severe hypokalaemia as the first manifestation of primary hyperaldosteronism is extremely rare (2). We report a 38-year-old female with arterial hypertension who presented to the Emergency Department with generalised muscle weakness associated with rhabdomyolysis as the presenting symptom of PHA.

Case report

A 38-year-old female with a history of hypertension for 8 years presented with acute onset rapidly progressive muscle weakness mainly affecting proximal girdle muscles for four days. On physical examination she had a lean body habitus with a BMI of 18 kg/m². She also had a multinodular goitre but was euthyroid, clinically. Her blood pressure was 170/90 mmHg, both supine and standing positions. Nervous system examination of both upper limbs and lower limbs revealed marked proximal muscle weakness. Deep tendon reflexes were normal while plantars were flexor, bilaterally. There was no sensory deficit.

Investigations revealed normal basic haematological parameters, severe hypokalaemia, increased renal

potassium loss and high creatine phosphokinase (CPK) level (Table). Based on these findings we established the diagnosis of rhabdomyolysis due to hypokalaemia. Intravenous potassium supplementation was initiated. Proximal muscle weakness completely recovered after correction of hypokalaemia and serum CPK levels normalized within one week.

Further investigations revealed elevated plasma aldosterone / renin ratio and CT scan of the abdomen revealed bilateral adrenal hyperplasia with a dominant nodule in the left side (Figure). Adrenal vein sampling was not done due to financial constraints.

The diagnosis of PHA due to bilateral adrenal hyperplasia was confirmed and she was started on spironolactone. Potassium supplements were gradually withdrawn. Blood pressure and serum potassium level remained normal and clinically there was no proximal muscle weakness during five months of follow up.

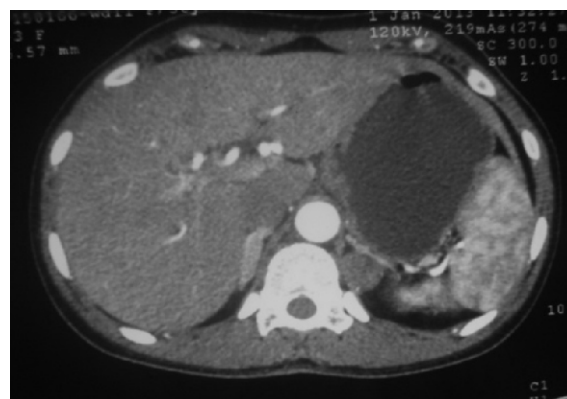


Figure: Contrast enhanced CT scan of the abdomen showing bilateral adrenal hyperplasia with a dominant nodule on the left side.

Table: Investigation results

Serum electrolytes: Na - 148 mmol/L, K - 1.9 mmol/L;

Spot urine electrolytes: Na 10 mmol/L, K 25 mmol/L

24 hour urinary excretion of electrolytes: Na - 55 mmol/L, K - 38 mmol/L

Creatine Phosphokinase: 2840 U/L (26 -192); Repeat test: 2499 U/L

Thyroid function tests

- TSH: 0.546 μ IU/mL (0.4 – 4.0)
- Free T4: 1.43 ng/dL (0.89 – 1.76)
- Free T3: 4.66pmol/L (4- 8.3)

Antithyroid peroxidase (microsomal) antibodies (TPO): 3.5 IU/ mL

ESR: 20 mm/1st hr

Arterial Blood Gas analysis

- pH - 7.638 (7.35 – 7.45)
- pCO₂ - 29.2 mmHg (35 – 46)
- pO₂ - 85.9 mmHg (75 – 100)
- HCO₃ - 31.6 mmol/L (22 – 26)

Plasma renin activity (PRA): 0.7 ng/ml/hr (0.1 – 3.1)

Aldosterone: 23.6 ng/dl (supine 30 min) (3 to 16 ng/dl)

Plasma Aldosterone/ renin ratio: 33.7 (< 20)

Overnight dexamethasone suppression test: 41.5 nmol/L (< 50 nmol/l)

Serum calcium: 2.4 mmol/l (2.1 – 2.5)

Serum Mg: 1.6 mg/dl (1.6 – 2.6)

Blood urea: 34 mg/dL

Serum creatinine: 98 μ mol/L

24 Hours Urinary VMA excretion: 5.1 mg/24 hrs (1 – 11)

USS abdomen: No suprarenal masses seen

Discussion

PHA is characterised by hypertension, hypokalemia, suppressed PRA, and increased aldosterone excretion (3). Bilateral adrenal hyperplasia and aldosterone producing adenoma are the most common subtypes of PHA(1).

Rhabdomyolysis is defined as a pathological condition of skeletal muscle cell damage leading to the release of toxic intracellular material into the blood circulation, such as creatine phosphokinase (2). The major causes of rhabdomyolysis include trauma, excessive muscle activity, and hereditary muscle enzyme defects, and a variety of medical causes, including drugs and toxins, muscle hypoxia,

metabolic and endocrine disorders, infections, and temperature alterations. Hypokalaemia is a recognised cause of rhabdomyolysis. When serum concentration falls below 3 mEq/L, malaise, muscular weakness, fatigability may occur. However, muscle enzyme elevation is usually not seen until potassium concentration falls below 2.5 mEq/L. Frank rhabdomyolysis is usually observed only when serum potassium values are below 2 mEq/L(4).

Rhabdomyolysis is not common in PHA although hypokalaemia induced myopathy is a well known association. In this case, rhabdomyolysis was the presenting symptom of PHA. Correction of hypokalaemia with intravenous potassium

supplements resolved rhabdomyolysis normalising creatine phosphokinase values, before hyper-aldosteronism was treated with spironolactone. This supports that the main cause of rhabdomyolysis was hypokalemia and not the direct effect of aldosterone (4).

In conclusion, hypokalaemia severe enough to cause rhabdomyolysis can be a rare presenting manifestation of PHA. Also when rhabdomyolysis, hypokalemia and metabolic alkalosis occur together in a hypertensive patient, PHA should be considered and further investigation for PHA should be initiated (4).

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Primary pulmonary alveolar proteinosis

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Introduction

Pulmonary alveolar proteinosis, a rare pulmonary disorder, was first described by Rosen *et al* in 1958 (1). It is characterised by abnormal accumulation of surfactant derived substances in the alveoli, due to a defect either in the production of surfactant or the clearance by alveolar macrophages, which explains the high association with malignancies and unusual infections. Those affected could have mild symptoms, spontaneous resolution or progressive disease with respiratory failure.

Case report

A 35-year-old female presented with progressively worsening exertional dyspnoea for six months. She also complained of chronic cough, low grade fever for two months, pleuritic-type chest pain, loss of appetite, fatigue, malaise and a marked weight loss (27 kg over 6 months). She gave a history of exposure to dust at her domestic employment of manufacturing bricks. She had never smoked but exposed to passive smoking at home. Screening for tuberculosis in the previous month had been negative. Despite the negative tests, she had been treated with specific anti-TB drugs owing to the nature of the symptoms and other findings.

On physical examination, she was afebrile, tachypnoeic, centrally cyanosed with a SaO₂ of 65% on air. There were few scattered crepitations bilaterally.

Arterial blood gas analysis revealed Type I respiratory failure with PCO₂ 29 mmHg and PO₂ 63mmHg. Lung function tests showed restrictive lung disease (Figure 1).



Figure 1: Chest radiograph showing bilateral interstitial and alveolar shadows

Sputum for gram stain and culture didn't show any pathogens and three sputum samples were negative for acid fast bacilli. There were no malignant cells in sputum cytology. Her lactate dehydrogenase was 397 U/L (85 - 234) and HIV I and II antibodies were negative. Other laboratory tests revealed normal haematological parameters with normal kidney and liver functions (Figure 2).

Her bronchoalveolar lavage fluid analysis showed numerous, round to irregular, hyaline periodic acid Schiff (PAS) positive casts. After evaluating her clinical, radiological and histological information the diagnosis of primary pulmonary alveolar proteinosis was made.

She was managed, initially, with high flow oxygen to maintain the SaO₂ 92% and subsequently whole lung lavage under anaesthesia. After two cycles of lavage therapy her functional capacity improved and oxygen saturation improved markedly (96% on air).



Figure 2: High resolution CT chest showing bilateral extensive ground glass opacities with associated diffuse small smooth intra lobar septal thickening (crazy paving) in both lungs fields

Discussion

Pulmonary alveolar proteinosis (PAP) is a rare disease with a prevalence of a 0.1 per 100,000 population. It occurs in all age groups and most common in men (male : female 4 : 1) and among people aged 20 to 50 years. The disease is commoner among smokers (3 times) than among non-smokers.

There are three clinically distinct forms of PAP. They include congenital (2%), primary (90%) and secondary (5-10%). Congenital PAP is due to a heterogeneous mutation of genes encoding surfactant proteins. (2,3). Primary PAP is considered an autoimmune condition with excess surfactant production caused by GM CSF neutralizing antibodies, receptor deficiency or gene deficiency / mutation, which lead to lack of macrophage stimulation. Immature alveolar macrophages are incapable of proper surfactant clearance. Secondary PAP develops in association with conditions like haematological malignancies, inhalation of toxic dust, fumes or gases, infections or pharmacologic immunosuppression and lysinuric protein intolerance.

PAP can be asymptomatic or it can be more chronic with dyspnoea and cough. Cough is usually dry, but sometimes accompanied by white, tenacious and sticky sputum. Fever and weight loss also can occur. Physical examination is typically nonspecific. Rarely cyanosis, clubbing, crepitations can be seen. Radiological findings are nonspecific with typical finding of bilateral central and symmetrical opacities in interstitial and alveolar spaces. High resolution CT

chest revealed bilateral extensive ground glass opacities with associated small smooth intra lobar septal thickening (crazy paving).

Elevated LDH levels are nonspecific in PAP. GM-CSF auto antibodies are elevated in primary PAP, but normal in secondary and congenital PAP. Pulmonary function tests reveal restrictive pattern of lung disease, decreased CO diffusion capacity, increased alveolar-arterial partial oxygen pressure gradient, hypoxaemia and elevated shunt fraction.

Open lung biopsy is the gold standard for the diagnosis of PAP. It shows characteristic milky fluid containing large amounts of granular acellular eosinophilic proteinaceous material with foamy macrophages engorged with PAS positive intracellular inclusions.

Treatment of PAP depends on the physiological impairment, rate of progression or remission and the underlying pathology. Whole lung lavage under general anaesthesia is the gold standard treatment for primary PAP. For congenital PAP supportive treatment and occasionally, lung transplantation is practiced, while conservative therapy and management of underlying condition is reserved for secondary PAP (4). In conclusion, the differential diagnosis of PAP should be considered in a patient who comes with chronic cough and dyspnoea in whom initial investigations negative for common causes. A common mistake is to treat them as pulmonary tuberculosis leading to delay in correct diagnosis and specific treatment. Although pulmonary tuberculosis is a common disease, the possibility of PAP should be considered when laboratory tests fail to confirm TB etiology and the expected therapeutic response with anti-TB drugs is not seen during the follow up.

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An unusual case of diaphragmatic hernia

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Case report

A 27-year-old man was admitted to the medical casualty with severe left sided chest pain and repeated vomiting. On admission, he was acutely ill and restless. Radial pulse was of low volume and fast at 100/min while blood pressure was 80/60 mmHg. The trachea had shifted to the right side and air entry to the left chest was markedly reduced. The opacity seen in the chest radiograph was initially considered to be a large left sided pleural effusion. A chest drain was inserted into the left pleural cavity, but there was only a little improvement of the patient's clinical picture (Figure 1). The patient was reviewed and the diagnosis of obstructed left diaphragmatic hernia was made. Abdominal radiographs were not of much help.

After resuscitation, a nasogastric tube was passed and the patient was given general anaesthesia. A midline upper abdominal incision was made and extended through the seventh intercostal space into the thorax due to the difficulty of delivering the contents of the hernial sac which included the spleen, left adrenal gland, most of the transverse colon, splenic flexure of the colon and the body of the stomach (Figure 2 A & B). The defect was found to be located posterolaterally in the peripheral part of the left hemidiaphragm and the peripheral muscular part of the diaphragm had to be divided to reduce the colon, spleen and the stomach back into the peritoneal cavity (Figure 3).

Discussion

Late presentation of congenital diaphragmatic hernia is reported to be 5-25% (1). Acute respiratory distress seems to be a more common presentation than acute intestinal obstruction. Causes of late presentation are either due to late rupture of the hernial sac that

contained the viscera or plugging of the hernial defect by solid organs such as the spleen prior to herniation of hollow viscera into the chest (2). The usual left sided hernia contain small bowel, spleen, stomach and colon whereas right sided herniae may contain liver and intestines (2). Small defects tend to present with obstruction / strangulation of viscera whilst large defects present with respiratory distress and compromised circulation (3). Misinterpretation of the chest radiograph as a pleural effusion is common in this condition and leads to insertion of chest drains and delay in life saving surgery as seen in our case (4). Obtaining a chest radiograph after insertion of a nasogastric tube is useful in arriving at a correct diagnosis.

The mass effect of the intrathoracic viscera causes mediastinal shift, kinks the vena cava and pulmonary veins resulting in reduced cardiac output. Emergency surgery is needed to reduce the contents of the hernia and to repair the diaphragmatic defect. Most hernias could be reduced abdominally but rarely thoracotomy is necessary. Non-absorbable suture is used to repair the defect together with chest drainage and manual inflation of the collapsed lung prior to closure of the chest.

Important anaesthetic considerations are fast fluid resuscitation via large bore intravenous access, passage of nasogastric tube and aspiration of gastric contents, antacid premedication, and rapid sequence induction with cricoid pressure to prevent / minimise aspiration pneumonitis. Difficult intubation may necessitate awake fiberoptic intubation or tracheostomy under local anaesthesia. Face mask ventilation and nitrous oxide should be avoided to prevent gastric insufflation and distension which would worsen thoracic mass effect / mediastinal shift. Re-expansion of the collapsed lung prior to thoracotomy too would exacerbate the mass effect.

Therefore a double lumen tube should be used to ventilate the normal lung alone initially with small tidal volumes and low pressures. Alternatively, a single lumen tube with a bronchial blocker may be used (4).



Figure 1: Erect Chest Radiograph after insertion of the intercostal tube

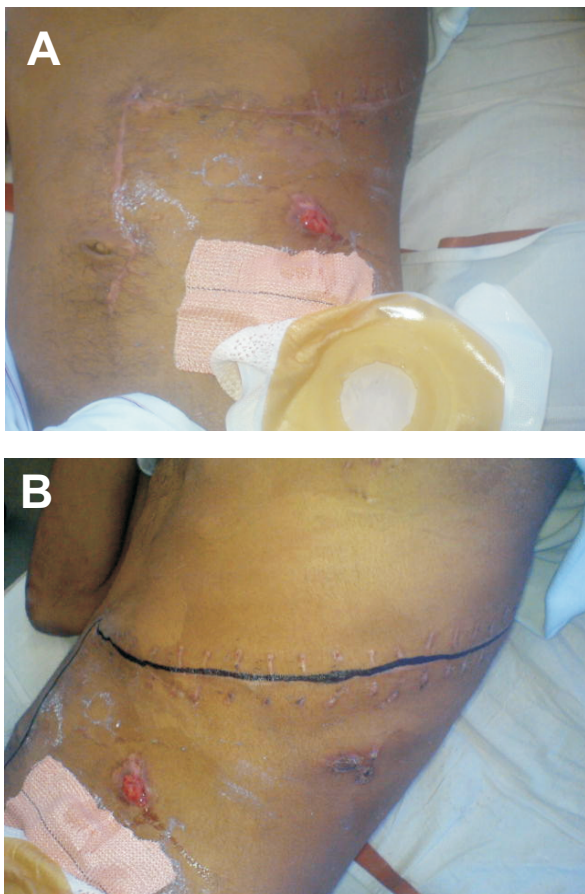


Figure 2: Healed thoraco-abdominal incision with the site of gastrostomy tube insertion

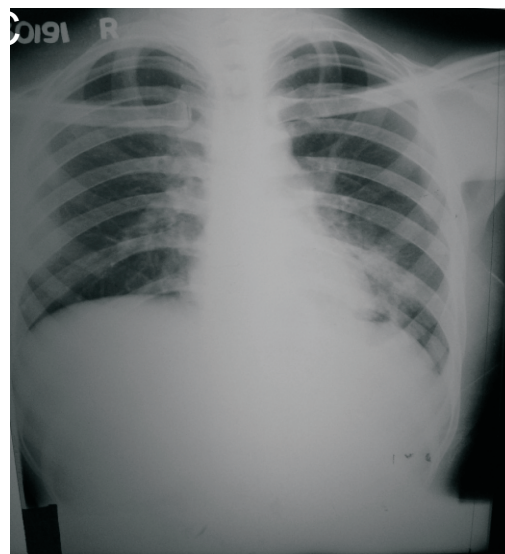


Figure 3: Postoperative chest radiograph after removal of the intercostal tube

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The Galle Medical Journal

Journal of the Galle Medical Association

September 2013 Volume 18 Number 2 ISSN 1391-7072

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The Galle Medical Journal

Journal of the Galle Medical Association

Volume 18: Number 2, September 2013

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From the Editors,

With great pleasure, we present the September 2013 issue of the Galle Medical Journal. Timely publication of the journal has helped to attract the attention of medical writers and the number of submissions has increased substantially during the recent past. Inevitably, this leads to a higher proportion of rejections.

Although the GMJ is freely accessible through the Sri Lankan Journals Online website, efforts are being made to make the contents of the journal more visible and accessible. Despite major advances in the IT front, communication barriers still exist.

The majority of submissions and inquiries we receive are in the fields of original research and case reports. We would encourage readers to submit manuscripts of other types such as pictures, comments, debates and view points. They can enhance the spectrum of the content and improve the outlook of the journal.

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Editors / GMJ

The Galle Medical Journal 2013 September
The Galle Medical Association
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ISSN 1391-7072

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GALLE MEDICAL JOURNAL; INSTRUCTIONS TO AUTHORS

The Galle Medical Journal is published by the Galle Medical Association. The *journal* is published biannually, March and September and the submissions are accepted throughout the year. The aims of the *Journal* are to foster co-operation among the medical fraternity and to be a forum to make literary contributions, share experiences encountered in medical practice, update their knowledge and have debates on topics related to all aspects of medicine. Also, we attempt to cater to the educational needs especially of the postgraduate trainees. The *Journal* publishes original articles, reviews, leading articles and case reports. When an article is reviewed for publication we expect that the work it reports has not been submitted simultaneously to another journal, has not been accepted for publication elsewhere or has not already been published. All manuscripts will be reviewed anonymously before acceptance.

Manuscripts must be submitted with the text type written in 12-point Times New Roman font double spaced. Text and all illustrative material should be submitted in two hard copies **and** the electronic version in Microsoft Word document format. In order to avoid delay we require authors to comply with the following requirements. All manuscripts should accompany a covering letter indicating the number of words in the manuscript, institution where ethical clearance was granted, conflicts of interest and contact details of the corresponding author.

Types of contributions:

Review articles and Leading articles: We encourage submission of review or leading articles which are less than 3000 words in length and address topics of current interest. They should be supported by no more than 20 references. Submissions may be subjected to external review before acceptance.

Original articles: Should normally be in the format of introduction, methods, results and discussion. Each manuscript must have a 200 word structured abstract. The text should be limited to 3000 words and maximum of 5 tables/figures taken together with no more than 15 references. Lengthy manuscripts are likely to be returned for shortening. The discussion in particular should be clear and concise and should be limited to matters arising directly from the results. Avoid discursive speculation.

Case Reports: These should not exceed 750 words and 5 references; no abstract is required. Case report should be informative and devoid of irrelevant details.

References:

These should conform to the Vancouver style. The reference in the text should be numbered consecutively in Arabic numerals in parentheses in the same line of the text in the order in which they appear. The first five authors should be listed and if there are more than five, then the first three should be listed followed by *et al.* Examples are given below:

1. Kumar A, Patton DJ, Friedrich MG. The emerging clinical role of cardiovascular magnetic resonance imaging. *Canadian Journal of Cardiology* 2010; **26**(6): 313-22.
2. Calenoff L, Rogers L. Esophageal complication of surgery and lifesaving procedures. In: Meyers M, Ghahremani G, eds. *Iatrogenic Gastrointestinal Complications*. New York: Springer, 1981: 23-63.

Units/Abbreviations

Authors should follow the SI system of units (except for blood pressure which will continue to be expressed in mmHg). Authors should use abbreviations sparingly and they should be used consistently throughout the text. Manuscripts that do not conform to these requirements will be returned to you for necessary modifications.

Manuscripts should be addressed to Editors, Galle Medical Association, Teaching Hospital, Karapitiya.

Chronic pain following Lichtenstein tension free inguinal hernia repair

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ABSTRACT

Introduction & Objective: Chronic pain following the repair of inguinal hernia has been a topic of interest in the past few decades, probably due to its significant adverse impacts on the quality of life of the patients who undergo the procedure. In this study we assessed the site, severity and incidence of chronic pain following Lichtenstein tension free inguinal hernia repair and its association with preoperative duration of hernia, presence of preoperative groin pain, presence of inguinoscrotal hernia, type of hernia and several preoperative risk factors for inguinal hernia.

Methods: Single unit prospective study conducted for a period of one year in Colombo South Teaching Hospital included patients who underwent standard Lichtenstein tension free inguinal hernia repair. Interviewer-administered pre-designed questionnaire was completed in the preoperative and post-operative stages. Postoperatively, patients were reviewed after 3 months to assess the presence of pain according to the International Association of the Study of Pain (ISAP) criteria. Severity of pain was evaluated with Wong-Baker FACES pain rating scale.

Results: Total of 98 patients underwent surgery but only 80 patients returned for the review. Twenty eight (35%) patients had pain and all were males. All of them had intermittent pain. Nature of the pain was aching in 71.4%, pricking in 14.3%, burning in 7.1% and constricting in 7.1%. Pain closer to the pubic tubercle was reported by 28% while 42% had pain closer to the mid inguinal point. Pain closer to the umbilicus was reported by 21% while 7% had pain over the scrotum. Only 14.3 % were on treatment for the pain, mostly simple oral analgesics. Moderately severe pain was reported by 14% and rest of them complained of mild pain only. Constipation had a significant association with the incidence of chronic pain following Lichtenstein repair but smoking, preoperative duration of hernia, presence of preoperative groin pain, presence of an inguinoscrotal hernia, type of hernia or the other preoperative risk factors for inguinal hernia, such as weight lifting, chronic cough, prostatism had no statistically significant associations with the incidence of chronic pain following Lichtenstein tension free inguinal hernia repair.

Conclusion: Nearly one third of patients reported varying degree of pain following Lichtenstein tension free inguinal hernia repair but it was a mild aching pain which was tolerable and did not require analgesics in the majority. In most cases, this pain was related to the mid-inguinal point or the pubic tubercle. Constipation showed significant associations with the incidence of pain following Lichtenstein tension free inguinal hernia repair.

Keywords: Post-operative pain, Lichtenstein tension free inguinal hernia repair, Inguinal herniorrhaphy

Introduction

Chronic pain following inguinal hernia repair has been a topic of interest in the past few decades, probably due to its significant adverse impact on the quality of life of the patient as shown in some previous studies (1). Until Cunningham's cooperative hernia study showed the significance of

the chronic pain following herniorrhaphy in 1996 (2), it was considered as an infrequent and insignificant complication after surgery (3). Since then many studies have reported significant prevalence of chronic pain following inguinal hernia repair and some studies have assessed the predisposing factors for chronic pain after inguinal hernia repair.

Material and Methods

This was a single unit prospective study conducted over a period of one year. Ninety eight consecutive patients operated for inguinal hernia over a period of one year were included in this analysis.

Operative technique: All patients underwent standard Lichtenstein tension free mesh repair. A 6×11 cm polypropylene mesh was trimmed to fit the space of the inguinal canal floor, with a slit cut laterally to accommodate the spermatic cord. A closed vacuum drain was used in all cases as a standard procedure to minimize the risk of post-surgical haematoma formation. Skin closure performed with Nylon 2/0 interrupted suture which was removed on the 10th postoperative day. Postoperatively, all patients were observed in the ward for 1-2 days or till the daily drainage was less than 30cc and discharged. Interviewer-administered pre-designed questionnaire was completed in two stages. In the first stage preoperative data of the hernia, were collected after assessment of the patient. In the second stage, presence of pain was assessed 3 months after the surgery during the clinic visit after a brief examination of the surgical site, the scrotum and the abdomen of the patient. Wong-Baker FACES pain rating scale was used to quantify the severity of the pain. In our study we classified the rating of the pain scale as, 1 - 3 (mild pain), 4 - 5 (moderate pain), 6 - 7 (moderately severe pain) and 8 - 10 (severe pain).

Informed written consent was obtained from all patients. SPSS 13 version was used for statistical analysis, and the statistically significant association was determined by applying the Chi-square test. P value < 0.05 was considered statistically significant.

Results

A total of 98 patients (95 men) with inguinal herniae were treated by Lichtenstein operation during the year. The mean (range) age of the patients was 54.6 years (22 - 80 years). Only 80 patients returned for the review after 3 months. Only 5 patients were operated under general anaesthesia. The remaining 93 patients underwent the operation under spinal anaesthesia. Twenty eight (35%) reported pain after 3 months of surgery and the average age of those patients was 51.8 ys and all of them were males.

Timing & Nature of pain

All the patients with pain complained of an intermittent pain rather than a continuous pain. Out of the patients with pain, 71% reported an aching type pain and 14% complained of a pricking type pain. Pain was of burning type in 7.1% while a similar proportion reported a constricting type pain (Table 1).

Table 1: Site & nature of chronic pain following Lichtenstein tension free mesh repair

Site of Pain	n (28)	%
A Over or closer to the pubic tubercle	8	28.6
B Over or closer to the level of deep inguinal ring	12	42.9
C Over or closer to the anterior superior iliac spine	0	0
D Scrotum	2	7.1
E Above the level of inguinal ligament and and/or closer to the umbilicus	6	21.4
Non specific /generalized	0	0
Nature of the pain	n (28)	%
Aching	20	71.4
Pricking	4	14.3
Burning	2	7.1
Constricting	2	7.1

Site of pain

Every patient with chronic pain was specific about the site of the pain and none of them mentioned about a non-specific or generalized pain. Nearly 43% of patients complained of a pain over or closer to the area of the deep inguinal ring (Site B) (Table 1).

Severity of pain

In the Wong-Baker FACES pain rating scale only the numbers 2, 3 and 4 were selected by the patients in quantifying the severity of their pain. Number 2 indicated ‘Hurts a little bit’ and 4 indicated ‘Hurts little more’. Number 3 was the severity in between the above two levels. Number 2 and 3 were selected by 42.9% (n=12) each and number 4 by 14.3% (n=4). None of them reported a severity beyond number 4. Only 14.3% (n=4) were receiving a treatment for the pain and in all cases this was limited to simple oral analgesics. None of them received native treatment or used any type of application or invasive treatment for the pain.

Predisposing factors for chronic pain

Forty eight (60%) patients has had preoperative groin pain and among patients with chronic pain, 71.4% (n=20) has had a preoperative groin pain

but there was no statistically significant association between the preoperative groin pain and the incidence of chronic pain following surgery. Forty four patients had direct inguinal herniae, 30 patients had indirect inguinal herniae and only 6 patients had both types. But the type of hernia and the incidence of chronic pain had no statistically significant association. Preoperative inguinoscrotal hernia did not show a significant association with the incidence of postoperative chronic pain. Out of preoperative risk factors, constipation was the only factor which demonstrated a statistically significant association with the incidence of chronic pain following surgery. Smoking was not significant at 5% level but significant at 10% level only. Weight lifting, prostatism or preoperative chronic cough had no statistically significant association with the incidence of chronic pain following Lichtenstein operation (Table 2). Neither the preoperative duration of hernia nor the presence of preoperative groin pain had a statistically significant association with the incidence of chronic pain following Lichtenstein tension free inguinal hernia repair. (Table 3 and Figure).

None of our patients developed mesh infection and / or recurrence during the follow-up period.

Table 2: Preoperative duration of the hernia, groin pain, presence of Inguinoscrotal hernia, type of hernia and incidence of chronic pain following Lichtenstein tension free mesh repair.

	Patients without chronic pain		Patients with chronic pain	
	(n=52)	%	(n=28)	%
Preoperative duration of hernia				
< 6 months	8	15.4	6	21.4
6 M – 1 year	22	42.3	8	28.6
1 - 5 years	18	34.6	6	21.4
> 5 years	4	7.7	8	28.6
Preoperative Inguinoscrotal hernia	18	34.6	6	21.4
Pre-op pain groin pain	28	53.9	20	71.4
Type of hernia				
Direct	28	53.9	16	57.1
Indirect	20	38.5	10	35.7
Direct & Indirect	4	7.7	2	7.1

Table 3 : Preoperative risk factors for chronic pain following Lichtenstein tension free mesh repair.

Preoperative risk factors for Hernia	Patients without chronic pain		Patients with chronic pain	
	(n=52)	%	(n=28)	%
Smoking	16	30.8	14	50.0
Wt lifting	28	53.9	20	71.4
Constipation	20	38.5	18	64.3
Prostatism	4	7.7	4	14.3
Chronic cough	14	26.9	8	28.6

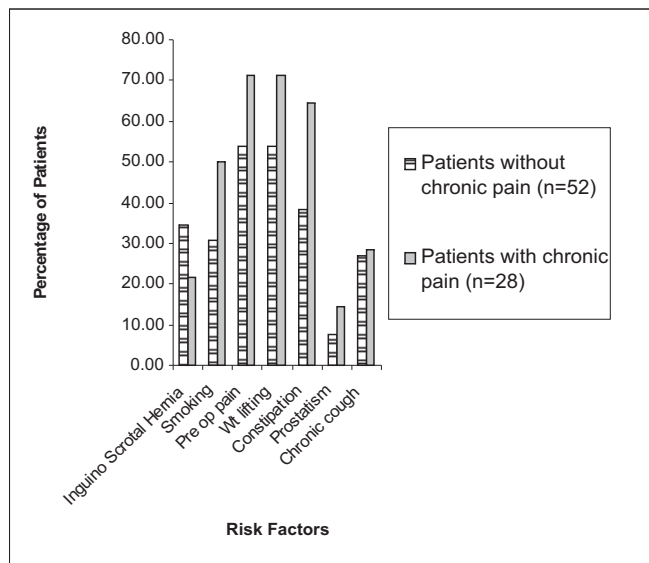


Figure: Preoperative risk factors for chronic pain following Lichtenstein tension free mesh repair

Discussion

The incidence of chronic pain reported in the current literature varies widely. This is probably due to the differences in the technique of surgery, method of assessment of pain, and the duration of follow up. Assessment of pain after three months may indicate a higher prevalence than assessment at six months or one year. In one of the critical reviews on chronic pain following inguinal hernia repair between 1987-2000, Poobalan *et al*, reported a much higher occurrence of pain as of 54% (4), but in 2004, Aasvang and Kehlt, reported a occurrence of 12 % of chronic pain (5) and a similar occurrence was reported by Simon *et al*, in 2007 after a meta-analysis of 29 good quality studies (6).

Definition of chronic pain was another controversial issue in many studies. Some have explained it as pain which persists for more than a year postoperatively (7). Another study has defined it as groin or scrotal pain which lasts for more than a month after surgery (8). According to the IASP (International Association of the Study of Pain) definition any pain which persists beyond a period of 3 months can be labeled as chronic pain (9). We defined chronic pain according to this IASP definition and some other studies have also used the same definition (4).

Quantification of the severity of the pain was the next challenging issue. This probably has led to the wide range of prevalence of chronic pain reported in various studies. In studies where a Visual Analog

Scale (VAS) was used as the tool of pain measurement the incidence of chronic pain was much higher than the studies where simple questions were used as to whether the pain is present or not (6). We used The Wong-Baker FACES (WBF) pain rating scale, to quantify the severity of pain. This scale was originally designed for paediatric patient groups (10), but was later used for adults. We believe that even for adults, it would be much easier to use a pain rating scale with an illustration for a better understanding of the severity of pain than a scale with numbers and/or lines.

The technique of inguinal hernia repair has seen many modifications since the introduction of the modern concept of inguinal hernia repair by Bassini in 1884. It has evolved into the laparoscopic surgery which has indicated a better outcome and less postoperative acute and chronic pain when compared with open-repair of the hernia with or without a mesh (6). But still some authorities recommend the open mesh repair over the laparoscopic repair for inguinal hernia (11).

Preoperative and postoperative factors which may increase the risk of chronic pain following inguinal herniotomy have been assessed in some studies. There is a higher risk with recurrent hernias, patients with previous abdominal surgery, younger patients and patients who had a preoperative groin pain related to the hernia (6,12).

Nociceptive pain due to sutures in the periosteum during Lichtenstein mesh repair is a probable risk factor (13). The risk of damaging the genitofemoral and ilioinguinal nerves during the mesh repair has been considered as a risk factor in some studies (14). Supportive evidence has been provided in another study where the elective ilioinguinal and iliohypogastric nerve resection causing less postoperative persistent pain syndrome (15). Light weight mesh has shown some effect in reducing the incidence of chronic pain (16).

Conclusion

Nearly one third of patients reported pain following Lichtenstein tension free inguinal hernia repair, but mostly it was a mild aching pain which was tolerable and not requiring analgesics. In most instances this pain was related to the mid inguinal point and/or pubic tubercle.

The preoperative duration of hernia, presence of preoperative groin pain, presence of an inguinoscrotal hernia or the type of hernia had no significant association with the occurrence of pain. Except for constipation, rest of the risk factors for inguinal hernia formation, such as smoking, weight lifting, chronic cough, prostatism had no significant association with the incidence of chronic pain following Lichtenstein tension free inguinal hernia repair.

Acknowledgements

The authors would like to thank Mrs. W.W.M. Abeysekera, MSc (Applied Statistics) currently reading for PhD (Theoretical Statistics) Latrobe University, Melbourne, Australia, for the invaluable support in statistical analysis of the study.

To all the patients for their contribution to this study, House Officers, Resident House Officers and the nursing staff of surgical wards 11 and 27 of Colombo South Teaching Hospital.

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Effect of morphological preservation artifacts on the quality of immunohistochemical staining for ER and Her-2

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ABSTRACT

Introduction: The most commonly encountered morphological preservation artifacts in the histological assessment of breast cancer include retraction of tumour cell clusters from the stroma, cytoplasmic retraction and alterations in nuclear morphology. This study intended to assess how these artifacts affect the quality of immunohistochemical (IHC) staining for ER and Her-2.

Methods: For this retrospective study, 120 cases of consecutive breast cancers reported by the 2nd and 3rd authors during 2009 to 2010 were included. Haematoxylin and Eosin stained sections of each breast cancer were assessed to obtain a consensus score for the degree of morphological preservation artifacts present. For each artifact (Retraction of tumour cell clusters, cytoplasmic retraction and alterations in nuclear morphology) a consensus score was given (0, 1, 2, 3) depending on the percentage of cell clusters/cells affected. Each IHC slide was assessed to obtain a consensus score for the quality of IHC staining for ER and Her-2. Parameters measured were uniformity of staining (0, 1), background staining (0, 1, 2), and adequacy of counterstaining (0, 1).

Results: The study included a total of 120 consecutive breast cancer cases. There was no statistically significant relationship between the consensus score for the commonly encountered morphological preservation artifacts and the quality of IHC staining of ER ($p=0.44$) and Her-2 ($p=0.51$).

Conclusions: Commonly encountered morphological preservation artifacts have no significant effect on the quality of IHC staining for ER and Her-2 measured in terms of uniformity of staining, background staining and adequacy of counterstaining.

Keywords: Morphological preservation artifacts, Immunohistochemistry

Introduction

Immunohistochemistry (IHC) is a widely used ancillary test in the histopathological diagnosis and prognostication of tumours (1). The primary advantage of IHC is that antigen can be detected in the context of architectural and cellular morphology of the tissue in contrast to biochemical assay (2). Therefore morphological preservation of tissue at microscopic level is important in the assessment.

Of the most commonly used predictive and prognostic factors of breast cancer, expression of

oestrogen receptors (ER), progesterone receptors (PR) and amplification of human epidermal growth factor receptor 2 (Her-2) are assessed by IHC. Adjuvant treatment for breast cancer is based on these predictive and prognostic factors. Hence accurate IHC assessment of ER, PR and Her-2 are extremely important in making the most appropriate therapeutic decision for breast cancer patients. Patients with ER and PR positive tumours are treated with adjuvant hormone therapy while metastatic breast carcinomas expressing strong positivity for

Her-2 are given trastuzumab as targeted therapy. Hormone receptors are expressed in the nucleus while Her-2 antigen is found in the cell membrane. Hence the morphological preservation of these sites of antigen expression is important for IHC assessment of breast cancers.

Formalin is the most commonly used fixative in IHC (3). The speed of penetration of tissues by 10% buffered formalin is about 1mm/hour (4). Due to the slow penetration of formalin, breast cancer situated deep in a mastectomy specimen does not get fixed adequately, unless it is sliced soon after the surgery, facilitating early contact with the fixative. Poor fixation is the most common cause of morphological preservation artifacts which are detected in H&E stained slides. This study intended to assess how the commonly encountered morphological preservation artifacts affect the quality of IHC staining for ER and Her-2 as markers which are localized in different parts of breast cancer cells.

Methods

This was a retrospective study. All breast cancers reported by the 2nd and 3rd authors during 2009 to 2010 were retrieved from the files of the Diagnostic Immunohistochemistry Laboratory of our institution.

Manual IHC staining had been performed on the histological sections prepared from 10% formalin fixed breast cancer tissue embedded in paraffin wax. Streptavidin Biotin method had been used. Dako (Glostrup, Denmark) monoclonal mouse antihuman ER α , clone 1D5 (M7047), polyclonal rabbit antihuman c-erbB-2 oncoprotein (A0485) and Universal LSAB2 kit/HRP Rabbit/mouse with Streptavidin/HRP (K0675, K0673) were used for the IHC staining. For each IHC staining a positive control had been used.

Based on the observations made in day to day breast cancer reporting three commonly encountered morphological preservation artifacts were selected for the assessment (Figure 1).

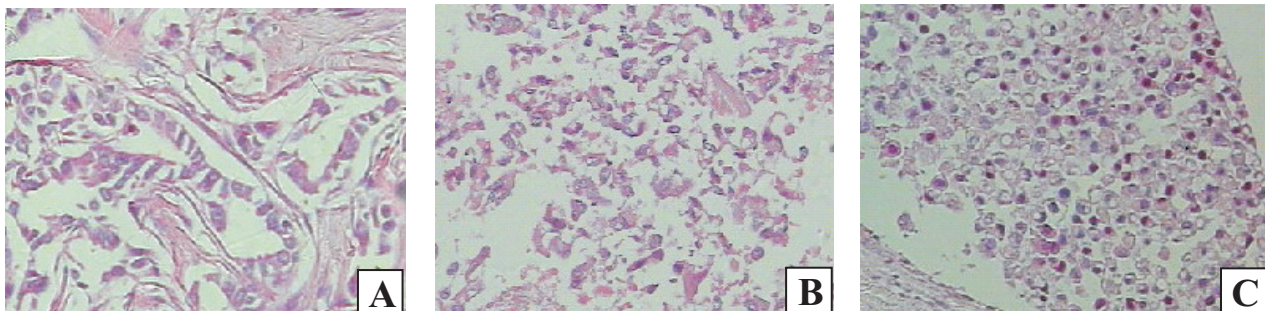


Figure 1: Commonly encountered morphological preservation artifacts in the IHC stained breast cancer tissues. A) retraction of tumour cell clusters from the stroma; B) cytoplasmic retraction; C) alterations in nuclear morphology - shrunken and condensed nuclei. (400x)

These included retraction of tumour cell clusters from the stroma, cytoplasmic retraction and alterations in nuclear morphology. To objectively quantify the artifacts in breast cancer tissue, the investigators devised a scoring system based on the percentage of cells/cluster of cells affected. These three artifacts were assessed separately. When there was no artifact score = 0, <10% of cells with artifact score = 1, 10-75% cells with artifact score = 2 and >75% of cells with artifact score = 3.

A Haematoxylin and Eosin stained (H & E) section of each breast cancer was assessed over a binocular multi-head microscope to obtain a consensus score for the preservation artifacts. Shrunken and condensed nuclei in breast cancer cells were considered the features of alteration in nuclear morphology. In assessing altered nuclear morphology, apoptotic nuclei among preserved breast cancer cells were excluded.

Each IHC slide was assessed for the quality of IHC staining out of a possible score of 4 (Table 1).

Table 1: Scoring system for quality of IHC staining

Criteria for scoring	0	1	2
Uniformity of IHC staining	Not uniform throughout	Uniform throughout	NA
Background staining	Excessive background staining interfering with the interpretation	Background staining with no interference to the interpretation	No background staining
Adequacy of counter staining	Inadequate	Adequate	NA

NA - not applicable. [A modified version of the scoring system developed by Maxwell and McCluggage, 2000]

This is a modified version of the scoring system developed by Maxwell and McCluggage in 2000 (5). The intensity of staining and the specificity of staining which were considered in original scoring system were omitted as those two parameters have no value in the assessment of ER negative and Her-2 negative tumours.

Data analysis was done using SPSS Version 11 package. Cases were categorized into three groups (Grade 1, 2 and 3) depending on the total score for commonly encountered preservation artifacts. Analysis of variance was used to compare the mean values of the quality of IHC staining (for ER and Her-2 separately) for the above groups. Both scoring systems were pre-tested before using on the study sample.

Ethical approval was obtained from the Ethical Review Committee of our institution, before commencing the study.

Results

This study included a total of 125 consecutive breast cancer cases. H&E slides and IHC slides for ER were available for all 125 cases. However, only 123 cases had the corresponding Her-2 stained slides.

There were 103 (82.4%) mastectomies, 7 (5.6%) lumpectomies, 1 (0.8%) wide local excision, 9 (7.2%) axillary lymph nodes with metastasis and 5 (4%) Tru-cut biopsies. Since Tru-cut biopsies are immediately immersed in formalin and do not show preservation artifacts they were excluded from the sample. Therefore a total of 120 breast cancer cases were included in the study.

Commonly encountered morphological preservation artifacts

The expected total score for the morphological preservation artifacts ranged from 0 to 9 where 0 signified the absence of the assessed artifacts. There were eight cases which had the maximum total score of 9 for the preservation artifacts but none had score 0 (Table 2).

Table 2: Frequency distribution of commonly encountered morphological preservation artifacts total score

Score	1	2	3	4	5	6	7	8	9	Total
Frequency (%)	12 (10.0)	18 (15.0)	13 (10.8)	14 (11.7)	11 (9.2)	15 (12.5)	18 (15.0)	11 (9.2)	8 (6.7)	120 (100)

Depending on the total score for the artifacts, cases were categorized into three groups. A score ranging from 0 - 3 (Grade 1) = minor degree of artifacts, 4 - 6 (Grade 2) = moderate degree of artifacts and 7 - 9 (Grade 3) = high degree of artifacts (Table 3).

Quality of IHC staining ER

IHC stained slides for ER was available for all 120 cases. The best staining quality was indicated by a score of 4. The majority (63.3%) of the IHC stained slides scored 3 or 4 and thus indicating good quality of IHC staining (Table 4).

The majority of the cases had uniform staining throughout the section and background staining did not interfere with the interpretation. Most of the cases had adequate counter staining (Table 5).

Table 3: Mean values of the quality of IHC staining for the degree of preservation artifacts

	Degree of preservation artifacts (grade)	Mean (SD)
Total Score for ER	1 (n=43)	2.6 (0.8)
	2 (n=40)	2.3 (1.1)
	3 (n=37)	2.5(0.8)
Total Score for Her-2	1 (n=41)	2.7 (0.8)
	2 (n=40)	2.5 (0.9)
	3 (n=37)	2.6 (0.7)

Table 4: Score for the quality of IHC staining for ER and Her-2

Total Score	ER Frequency (%)	Her-2 Frequency (%)
0 (Poor quality)	3 (2.4)	2 (1.6)
1	20 (16.0)	13 (10.6)
2	24 (19.2)	26 (21.1)
3	72 (57.6)	75 (61.0)
4 (Best quality)	6 (4.8)	7 (5.7)
Total	125	123

Table 5: Quality of IHC staining for ER and Her2; according to the features assessed for the quality

	Uniformity of IHC staining		Background staining			Adequacy of counter staining	
	0	1	0	1	2	0	1
ER	42 30.8%	83 69.2%	24 20.0%	89 74.2%	7 5.8%	14 7.5%	111 92.5%
Her2	36 26.3%	87 73.7%	17 14.4%	93 78.8%	8 6.8%	13 6.8%	110 93.2%

Quality of IHC staining Her-2

IHC stained slides for Her-2 was available for only 118 cases. The best staining quality was indicated by a score of 4 as for ER. The majority, 79 (66.9%) cases scored 3 or 4 indicating good quality of IHC staining (Table 4).

As for ER, the majority of the cases had uniform staining throughout the section and background

staining did not interfere with the interpretation. Most of the cases had adequate counter staining (Table 5).

The average scores of the quality of IHC staining for ER and Her-2 were calculated separately for the 3 grades (Table 5). ANOVA was used as the statistical method to find out whether the preservation artifacts have a significant effect on the quality of IHC

staining. Preservation artifacts did not have a statistically significant effect on the quality of IHC staining for ER ($p = 0.44$) and the quality of IHC staining for Her-2 ($p = 0.50$).

Multiple comparisons were done using Post Hoc test which did not reveal a statistically significant effect.

Discussion

Immunohistochemistry has become an integral part of histopathological diagnosis and it provides essential data predictive of clinical evolution and of therapeutic responsiveness (6). Therefore it is essential to identify factors which affect the quality of IHC staining in order to maintain the reliability of the test. There are many publications in the literature on the effects of fixation and other pre-analytical factors on the quality of staining (7). However publications on relationship between commonly encountered morphological preservation artifacts and quality of IHC staining are sparse.

For the present study we assessed the effect of commonly encountered morphological preservation artifacts (Table 1). The quality of IHC staining was assessed in terms of uniformity of staining, background staining and adequacy of counter-staining. Intensity of staining was not considered as done by Maxwell and McCluggage because the intensity of ER depends on how much oestrogen receptors are expressed in the nucleus (5). Specificity of staining was also not considered as the study sample included both negative and positive breast cancers.

None of the breast cancers included in the study had score 0 for preservation artifacts. This indicates that all the specimens had at least a minor degree of morphological preservation artifacts. There was nearly one third of the total amount of cases in each Grade of preservation artifacts (Table 3). Minimum degree of preservation artifacts was present in Grade 1 and maximum degree of preservation artifacts was present in Grade 3 cases. This is inversely related to the percentage of cells that are preserved in the breast cancer sections.

Morphological preservation artifacts can be seen in the IHC stained slides because of the delay in exposure of the center of a surgical specimen to formalin (8). Most often our laboratories receive specimens, not soon after the surgery but a few hours

to several days later. To avoid autolysis the whole mastectomy specimen is sent in 10% formalin. However they are unsliced and by the time they reach the pathologist the central part of the tumour may have already undergone autolysis although the gross specimen is in 10% buffered formalin due to the slow penetration of formalin. Therefore we do encounter the morphological preservation artifacts very often in the mastectomy and lumpectomy specimens although they are hard to find in Tru-cut biopsies.

Another reason for morphological preservation artifacts is dehydration which occurs in tissue processing. This is believed to be due to the difference in the consistency of tumour and stroma (9). Therefore the presence of retraction of tumour cell clusters from the stroma may have occurred, at least in some cases, during processing and not related to fixation. Cellular discohesion is a feature of poorly differentiated tumours (10). Distinction between cellular discohesion and artifactual cytoplasmic retraction can be made on the arrangement of the cell membranes of the adjacent cells. The cell membranes of the neighboring discohesive cells are randomly arranged and show cytoplasmic processes (10). We did not include the tumors with cellular separation due to discohesion into the tumors with artifacts in order to separately identify the true artifactual retraction of tumour cells.

Ibarra *et al* (11) have stated that delayed fixation of the center of the surgical specimen may be responsible for false-negative results because of the inadequate necessary cross-links between protein and nucleic acids required for proper IHC analysis (11). We did not assess the false negative rate in the present study.

In routine laboratory practice, pathologists examine the specimens macroscopically and microscopically and select the well preserved areas for the preparation of slides. This may be the reason why preservation artifacts were seen only in a proportion of cells in the section. Therefore the effect of preservation artifacts can be eliminated by choosing preserved areas when assessing the ER and Her-2 status.

Apart from many analytical factors antigen diffusion prior to fixation is a pre-analytical cause of background staining outside the expected antigen site (12). Most of the breast cancer cases of our study had background staining probably due to the poor

preservation, but it did not interfere with the interpretation in the majority.

In conclusion, the commonly encountered morphological preservation artifacts; retraction of tumour cell clusters, cytoplasmic retraction and alterations in nuclear morphology do not affect the quality of IHC staining for ER and Her-2, measured in terms of uniformity of staining, background staining and adequacy of counter staining. We believe that our pilot study encourages further studies to find out the causes of morphological preservation artifacts and their effect to the quality of IHC staining.

Acknowledgements

The authors would like to thank Dr. B. Perera, Senior Lecturer, Department of Community Medicine, Faculty of Medicine, University of Ruhuna, Sri Lanka for his guidance in the statistical analysis and Mrs. G.G.D.D. Gunawardhana, Senior Staff Technical Officer, Department of Pathology, Faculty of Medicine, University of Ruhuna for the preparation of H&E and IHC slides.

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Adherence to the current guidelines in the management of paraquat poisoning; an audit

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ABSTRACT

Background: Self-poisoning with paraquat (PQ) is a major health problem with 60 -70% fatality. Fuller's earth is the mainstay of therapy as other treatment modalities are controversial. Current management guidelines of paraquat poisoning recommend the administration of Fuller's earth / activated charcoal until they are detected in stools and also immunosuppression therapy. The aim of the study was to look at the adherence to the existing guidelines in the management of PQ poisoning by the ward staff.

Methods: In this cross-sectional study consecutive patients admitted to two selected hospitals due to PQ poisoning were recruited. Current practice in management of PQ poisoning in these hospitals was compared with the National guidelines.

Results: There were 145 patients (111 males) admitted with paraquat poisoning during the study period. Fuller's earth was given to 130 (89.6%) patients. One patient refused and one died before the treatment. Twelve (8.3%) patients did not receive Fuller's earth. Among them five died with the median of 3 (range 1-13) days after the hospital admission. Nineteen (14.6%) patients out of 130 who received PQ did not notice Fuller's earth in their stool. Forty patients either did not observe Fuller's earth in their stools or the data was not available. Eighty four (58%), 14 (10%) and 57 (39%) patients received cyclophosphamide, dexamethasone and methylprednisolone, respectively.

Conclusion: Among the patients who received Fuller's earth at least 14% did not fulfill the criteria of proper administration. Education of health care people on administration of Fuller's earth may be required. Even though immunosuppression therapy is controversial, more than 50% of patients received it.

Keywords: Herbicide, Immunosuppression, Paraquat, Therapeutics

Introduction

Paraquat (PQ) (1,1' - dimethyl-4,4' - dipyridyl) is a bipyridyl compound. It was first marketed in 1962 as a broad-spectrum, non selective and contact herbicide after having been first described by Weidel and Rosso in 1882 (1,2). Self-poisoning with PQ is a major health problem as it has the highest individual case fatality rate of around 65% for any given poison in Sri Lanka (3). PQ is highly corrosive. It is

absorbed poorly after inhalation but is extremely toxic if ingested. After PQ ingestion, mucosal oedema, burns or ulceration may be seen in the mouth, oesophagus, stomach and intestines. Death usually occurs within 48 hours of ingestion of 50 mg/kg or more than 20 ml of 20% preparation of PQ (4). At lower doses death may be delayed for several weeks (1). Toxicity of paraquat is due to the pulmonary accumulation of the bipyridyl compound. PQ is transported actively into

pulmonary cells resulting in pulmonary oedema or fibrosis. The major cause of death in PQ poisoning is respiratory failure due to an oxidative insult to the alveolar epithelium with subsequent obliterating fibrosis (4).

The principles of pharmacological management of PQ poisoning include Fuller’s earth or activated charcoal, immunosuppressants (cyclophosphamide, dexamethasone and methyl prednisolone) and fluids. The role of immunosuppressants is not completely clear. Therefore administration of Fuller’s earth is the mainstay of therapy. Fuller’s earth is an adsorbent and PQ gets inactivated as soon as it comes in contact with Fuller’s earth. If Fuller’s earth is not available activated charcoal can be used (5).

We aimed to look at the adherence to the existing guidelines in the management of PQ poisoning by the ward staff.

Materials and Methods

A cross-sectional study was conducted at Teaching Hospital, Galle and General Hospital, Matara from June 2008 to June 2010. Consecutive patients admitted to the hospitals due to PQ poisoning confirmed by positive urine sodium dithionite test, were recruited to the study. This study was approved by the Ethical Review Committee, Faculty of Medicine, University of Ruhuna, Sri Lanka.

Informed consent was obtained from the patient or a close relative present at the time of admission if the patient was unable to give the consent.

Current practice of management of PQ poisoning in the two hospitals was compared with the guidelines published by the National Poisons Information Center, National Hospital of Sri Lanka, Colombo.

Results

There were 145 patients (111 males) admitted with paraquat poisoning to the collaborating hospitals during the study period. The median age of the patient was 29 years (Inter quartile range, 21 - 47).

One hundred and thirty (89.6%) patients received Fuller’s earth. One patient refused the treatment, one patient died before administration of Fuller’s earth, the data of administration of Fuller’s earth was not available in one patient and 12 patients did not receive Fuller’s earth. Among the 12 patients who did not receive Fuller’s earth, two patients received activated charcoal. The details of patients who did not receive Fuller’s earth are shown in Table 1. Twenty-five patients received both Fuller’s earth and activated charcoal.

Table 1: Characteristics of patients who did not receive Fuller’s earth

Patient	Amount Ingested (ml)	Duration of Hospital Stay (days)	Outcome
1	10	3	Died
2	Unknown	6	Left against medical advice
3	No evidence of ingestion	3	Discharged
4	Unknown	13	Died
5	5	4	Left against medical advice
6	5	12	Left against medical advice
7	15	4	Discharged
8	3	7	Died
9	10	11	Discharged
10	15 - 30	11	Discharged
11	Unknown	1	Died
12	750	1	Died

Eighty-five out of 130 (65.4%) patients who received Fuller's earth observed Fuller's earth in their stools. One patient died a few hours after the commencement of Fuller's earth. Nineteen (14.6%) patients did not notice Fuller's earth in their stools. Forty patients either did not observe Fuller's earth passed with their stools or the data was not available.

None of the patient received humidified oxygen except one patient, who was given oxygen at his terminal stage.

The immunosuppression therapy practiced in the collaborating hospitals and the number (%) of patients who received them are given in Table 2.

Table 2: Regimens of immunosuppression therapy practiced in the collaborating hospitals

Immunosuppression therapy	General Hospital, Matara (n=61)		Teaching Hospital, Galle (n=84)	
	Regimen	Number (%) of patients who received the treatment	Regimen	Number (%) of patients who received the treatment
Cyclophosphamide	1g stat (IV) 250mg twice daily for three days (oral)	53 (87%)	15mg/kg/daily for two days (IV)	31 (37%)
Dexamethasone	8mg thrice daily (oral)	3 (5%)	8mg thrice daily for 14 days (oral)	11 (13%)
Methylprednisolone	1g twice daily for three days (IV)	53 (87%)	1g/daily for three days (IV)	4 (5%)

IV - intravenous

Discussion

Ninety percent of patients admitted following PQ poisoning received Fuller's earth but at least 15% of patients did not receive an adequate dose to be detected in the stools. Majority of patients received immunosuppression therapy.

Fuller's earth is the only specific management currently available for paraquat poisoning. Proper administration of Fuller's earth may minimize the mortality and morbidity of patients with paraquat poisoning. The reason for 8% of patients not receiving Fuller's earth was not clear in the current study. According to the current guidelines, except the patients who did not have evidence of ingestion all others should receive Fuller's earth. According to the expert committee on essential medicines, both Fuller's earth and activated charcoal are included in the National list of Essential Medicines in Sri Lanka. Therefore Fuller's earth and activated charcoal should be available all the time in the hospitals.

Hence all patients with paraquat poisoning should receive Fuller's earth. Activated charcoal can be given if Fuller's earth is not available. Fuller's earth is available as powder for oral suspension. Once it is prepared the supernatant does not contain particles of Fuller's earth. Therefore the suspension has to be well mixed while it is administered. People who give Fuller's earth to patients may not be aware of this fact, so patient may be given the supernatant to take while Fuller's earth may remain at the bottom of the container. This may be a reason why some patients did not observe Fuller's earth in the stools after administration. Proper administration of Fuller's earth has to be emphasized to the patients and care givers.

Chen et al (2002), Lin J L et al (1999 and 2006) showed promising effects on PQ poisoning with a combination of cyclophosphamide, methylprednisolone and dexamethasone. They used 1g of methylprednisolone (IV) daily for three days,

15mg/kg of cyclophosphamide (IV) daily for two days and preceding 5 mg dexamethasone (IV) three / four times per day or 10mg dexamethasone (IV) thrice daily for 14 days. The dose of methylprednisolone given at the General Hospital, Matara was higher than that in the previous studies. The dose of cyclophosphamide regimen practiced at the two collaborating hospitals were more or less equal to the studies done previously, except the administration of cyclophosphamide via the oral route from the second dose onward at the General Hospital, Matara. The collaborating hospitals in the current study practiced slightly higher doses of oral dexamethasone compared to the previous studies, but the previous studies administered dexamethasone intravenously.

The reason why a smaller percentage of patients received cyclophosphamide & methylprednisolone at the Teaching Hospital, Galle is that they had been recruited for the double blind placebo controlled immunosuppression trial (Gawarammana I, et al. unpublished data).

Conclusion

Although 90% of paraquat poisoned patients received Fuller's earth, either the amount administered or the way of administering was not satisfactory. Proper education of health care personal on administration of Fuller's earth may be required.

Acknowledgements

We would like to thank the participants, the Consultants who gave their patients for the study, administrative staff and health care professionals at the Teaching Hospital, Galle and the General Hospital, Matara, Heads and the staff members of the Department of Pharmacology and the Department of Medicine, Faculty of Medicine, University of Ruhuna, Sri Lanka, and the members and the Clinical Research Assistance of the South Asian Clinical Toxicology Research Collaboration. A special word of thanks is extended to Professor N.A. Buckley, Professor A.H. Dawson, Professor K.D. Pathirana, Professor P.L. Ariyananda and Dr. Bilesha Perera.

Source of funding

This study was supported by a Welcome Trust and NHMRC International Collaborative Research Grant (GR071669MA).

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Have thirteen beggars been killed by a serial killer?

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ABSTRACT

Introduction: From 2010-2011, several murders of beggars were reported from Colombo and suburb. The motive of such killings was not obvious and some parties suspected an attack targeting beggars by an organized group.

Objective: To analyse the medico-legal aspects of the series of killing.

Methods: Data of beggars who had been killed, serially, under similar circumstances in Colombo and suburbs were collected from January 2010 to December 2011.

Results: There were 14 murders (12 males) in 9 towns. The bodies were left on the location of killing without being moved. The causes of death had been blunt force trauma to head. No suspects were arrested. Sole eye witness confirmed the presence of 'rituals' and 'cooling-off period' in suspect. In November 2011, a beggar was arrested while attempting to kill another beggar when the latter was a sleep. The suspect was produced for medico-legal examination and later referred to a Psychiatrist. He was diagnosed to have anti-social traits. On a subsequent day, he admitted that he had murdered altogether 14 beggars. He had shown all the crime scenes to the investigators. He was sent for inward psychiatric treatment and is awaiting trial.

Conclusions: Usually serial killers are males with past criminal records who kill strangers, perform 'rituals', leave 'signature', display the dead bodies and remove souvenirs. All above characteristics except the last two were evident in this case. Fourteen independent, planned murders with potential "cooling-off periods" indicate that the suspect could be the highest 'potential serial killer' in Sri Lanka. The importance of the establishment of a National Criminal Investigating Centre is suggested to investigate such unsolved crimes.

Keywords: Serial killer, Cooling off period, Rituals, Signature, Displaying, Souvenirs

Introduction

The most practical definition of a serial murder is three or more independent, planned murders committed by the same individual or individuals, and separated by a "cooling-off" period (1). According to this definition, it is the "cooling-off" period that separates serial killers from other types of multiple murderers (1).

From 2010 - 2011, a series of beggars were found to have been killed with head injuries, on the pavements of Colombo city and suburbs.

General public were thoroughly disturbed by the reports in the media. Some believed that this was an attempt to eliminate beggars from the Colombo city. In one occasion, even a complaint was made to an international human rights organisation alleging lackadaisical attitude of police on such murders.

This study analysed the medico-legal aspects of this series of killings to determine the nature and characteristics of the killer.

Methodology

Data of beggars who were killed with head injuries in the pavements of Colombo and suburbs were collected from 2010 January to 2011 December. The data were collected from media reports, crime scene data of Scene of Crime Officers (SOCO), police records, court records and from clinical examination and investigation of the alleged perpetrator.

Secondary data were collected from journals, text books, internet etc. Analysis of the features of the murders and the suspect was done and compared with the reported incidents of serial killings in medical literature.

Results

There were 14 murders in 9 towns. They were as follows;

1st murder - At Wellawatta, a male beggar was alleged to have been killed with head injuries from a granite stone while sleeping. Autopsy was done on 10th April 2010 and the cause of death (COD) was blunt force trauma to head.

2nd murder - A female beggar was found dead at Kotahena with head injuries. Autopsy was done on 13th of April 2010 and the COD was blunt force trauma to the head.

3rd male beggar was found murdered at Kotahena on the 1st of May 2010 and the 4th male beggar was found murdered at Slave Island on the 13th of May 2010. Large blood stained granite stone was found near the 3rd body (Picture). The autopsy reports revealed the same cause of death for both cases.



Picture: The blood stained granite stone

5th murder - Another female beggar was found murdered at Colpetty with head injuries. The autopsy was done on 14th May 2010 and the COD was blunt force trauma to head.

Four more (6th - 9th) male beggars were murdered at Slave Island on 15th of June 2010, at Mount Lavinia on 28th of June 2010, at Kotahena on 7th of September 2010 and at Paliyagoda on 16th of July 2011 respectively in a similar manner. The autopsy reports revealed the CODs as blunt force trauma to head.

10th murder - A drunken male was found killed with head injuries at Paliyagoda. The relatives of the deceased complained to an international human rights organization of alleged lackadaisical attitude of the authorities regarding these killings. The autopsy done on 21st July 2011 revealed the COD as blunt force trauma to head.

11th murder - Body of a male beggar was found at Moratuwa on the 16th of August 2011, about 4.00am. An eye witness stated that he had seen a man, who had his hands raised towards the sky for a while and then assaulted another beggar who was sleeping alone, robbed him and then walked away. This was the only instance where an eye witness was available. He had followed the murderer about 1km until he was threatened. The autopsy was done on 16th August 2011 and the COD again was blunt force trauma to head.

Three more (12th - 14th) male beggars were found murdered at Paliyagoda on the 19th of September 2011, at Kiribathgoda on 22nd of September 2011 and at Kelaniya on the 2nd of October 2011, respectively. The autopsy reports revealed the CODs as blunt force trauma to head.

Out of 14 deaths, 13 were beggars (11 men) and one was a drunken man sleeping on the pavement. All had been killed probably while sleeping on the pavements. The alleged mechanism of death was an assault with heavy stones on head. In all cases, the COD had been blunt force trauma to head. Only one case had an eye witness. No suspect was arrested in these homicides.

According to the description of the eye witness, there was definite “cooling-off” period in the homicide No. 11. In other cases, the potential shortest cooling-off period is one day and the longest could be as long as 10 months. All 14 dead bodies were not moved away from the site of killing.

On 30th of November 2011, at 2.30am a beggar was arrested while standing near a concrete block on the pavement at Mount Lavinia. He was produced before the author and was referred for Psychiatrist assessment. Psychiatric assessment was incomplete as he pretended to be dumb. He appeared calm and innocent.

He was reproduced from the remand prison and was reviewed on 24th of February 2012 by the author. He claimed that the scar of a cut injury found on the postero-lateral aspect of the upper part of the neck was caused by an assault with a knife by another beggar in 2001.

He disclosed that on the day of the arrest, he was about to kill a beggar who was sleeping alone on the pavement. Further, he said that he killed all above 14 victims by dropping heavy stones on their head. He said that he tried to sexually abuse one of the female victims.

Psychiatrist assessment revealed “anti-social personality traits” in the suspect and he was sent to the National Institute of Mental Health, Angoda, Sri Lanka for inward observations.

Finally, the suspect had shown the crime scenes accurately to the investigators.

Discussion

These murders were ‘independent’, because there was no relationship among the victims and the victims to the suspect except for the fact that the victims were beggars. According to the definition of ‘serial murder’ the ‘planning’ is defined as any action committed by an offender in preparation of a murder and involves the accumulation of items for use in the abduction, murder, disposal and selection of a victim (1). In this series, all the cases were well ‘planned’, such as killing in the mid night while sleeping alone on the pavement in order to avoid eye witness.

According to the description of the eye witness, there was definite ‘cooling off period’ in the 11th homicide. In all the other cases too, a potential ‘cooling off’ periods were present.

Fourteen ‘independent’, ‘planned’ murders with ‘cooling-off periods’ indicate that this suspect could be a serial killer in Sri Lanka who killed the highest number of victims.

This is not the first time that serial killers are reported in Sri Lanka. In 2003 a mobile vendor, from Madugoda, Kandy, killed several women. He could be the first serial murderer in the recent criminal history of Sri Lanka (2). The said person had visited houses to sell domestic items between 10.00 am - 12.00 noon and when he found a suitable opportunity he used to kill women mostly by strangulation. He had derived sadistic satisfaction by killing these women (2).

In 2004, an army officer, who was suffering from post-traumatic stress and personality disorder following frontal lobe injury caused by a fragment of a grenade, killed five people.

In 2011-2012, Kahawatta in Ratnapura District became under mass fear following mysterious murders. At least seven elderly women were killed and some of the victims had been raped by an unknown killer. Later, the Police arrested several suspects alleged to be connected with these murders. But the Police Department had not sought assistance from Psychologists / Psychiatrists to determine whether these suspects were serial murderers (2).

For comprehensive understanding of serial murder, investigators must review crime-scene photographs, police reports, laboratory reports, media accounts of cases, behavioral characteristics of murderers and victimology information, interact with other parties and interview the offenders as well (3). That was the methodology applied in the investigation of this case series.

The perpetrator of serial murder may not appear like a conventional criminal. Instead, can appear calm and well-mannered (3). The perpetrator in this series too presented calm, quiet and innocent.

All researches are in agreement that the majority of serial murderers are male and have a criminal history (4), exactly as seen in this case.

After committing a murder, the serial killer is not emotionally shocked by the feelings of guilt instead, the perpetrator is emotionally numbed (4). According to the description of the eye witness as well as clinical examination findings, this suspect too displayed similar features.

Most studies have found that the majority of the victims of serial murder were strangers to the offenders. There is no prior relationship between the

victim and the attacker (4). In this series, though the victims were fellow beggars, there had been no prior relationship with them and the victims were strangers to the killer.

Studies of serial murderers have reported several methods of killing used by offenders, including strangulation (both manual and ligature), stabbing, cutting, blunt-force trauma and firearms. Majority use strangulation or stabbing (5). But in this series, a single method had been used. That is blunt force trauma to head by a stone.

There are two basic body disposal scenarios; either leave at the site of killing or move away from the site of killing. If the offender leaves the victim at the scene, the victim's body can be left as it is or the offender may position the body in a bizarre or suggestive manner or the offender may attempt to conceal the victim at the scene (5). If the offender moves the body away from the murder site, one of the three scenarios can occur: the victim can be dumped, concealed, or displayed. Many serial murder crimes involve more than one crime scene or event site (5). But in this case series, the suspect left the body at the site of killing.

Many serial offenders reflect unusual behaviour that can be attributed to their fantasies such as displaying the victim's body and/ or removal of souvenirs from the scene (6). In this case series no special displaying or removal of souvenirs occurred.

Other features generally found with serial murder are method of operation (*modus operandi*), ritual and signature (7).

"Rituals" are the symbolic acts reflective of behavior committed by the offender during the course of the crime that are not necessary for the successful completion of the crime (7). In this case, the eye witness had seen the suspect raising his hands to the sky for some time before committing the crime. This could be considered a 'ritual'.

'Signature' is defined as the unique combination of method of operation and ritual that allows one serial case to be linked to others (7). All the cases in this series possessed a signature. All victims were killed probably while sleeping on the pavement by assaulting with heavy stones on head.

Most of the serial killers suffer from Anti-Social Personality Disorders. There are many reasons why

serial killers commit murders. Eg: profit, passion, hatred, power or domination, revenge, opportunism, fear, contract killing, desperation, compassion, ritual etc (5). In this case series, he accepted that he did these murders with anger to take the revenge of the cut injury to his neck caused by a fellow beggar in 2001. Anger motivated serial killings are often directed toward a targeted segment of the community (5). In this series, the target group was beggars.

Majority of serial killers kill the victim for sexual motivations (5). In this study, such motivation was noted only in the homicide number 5.

According to the Anomie Theory, serial killers lack any bonds tying them to the society. They feel isolated, alienated and rejected by the society (8) as seen in this case.

It creates immense difficulties for the medico-legal community to investigate, identify and prosecute a serial murderer. The medico-legal community should seek the assistance and expertise of professionals including Forensic Psychiatrists.

Awareness among the community plays a key role in prevention of crimes committed especially by the deviant killers. It is each and everyone's duty to be cautious and vigilant and in the same time to maintain the optimal social equilibrium to prevent such crimes.

Similar to the National Child Protection Authority (NCPA), a National Criminal Investigation Centre with a database on crime records is an essential institute for the country. This is with a view to collect reports, maintain records, analyse all unsolved crimes, provide information for investigators and law makers.

Conclusions

Features such as male gender, murdering strangers, past criminal history, 'rituals' and 'signature' favour the suspect to be a serial killer. Displaying of dead bodies and removal of souvenirs were not evident in this case. Fourteen independent, planned murders were executed with cooling-off periods indicate that the suspect could be the highest potential serial killer in Sri Lanka.

The importance of establishment of a National Criminal Investigation Centre to investigate in to such unsolved crimes is reiterated.

Acknowledgment

T. Sugathapala, Chief Inspector and Officer In charge of Crimes, Police Station, Mount Lavinia, Sri Lanka, for collecting samples.

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IMAGE

Vitamin D: Can we use higher doses for wider indications?

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Vitamin D is a unique substance with properties of both a vitamin and a hormone. Over many decades it has been considered an essential vitamin for bone mineral homeostasis. In the recent past there has been growing appreciation for its role in many other areas of human health including immune regulation, metabolic and cell proliferation and differentiation (1). These pleiotropic effects of vitamin D are called non-classic actions of vitamin D.

In response to the awareness of these recently recognised health benefits there has been a continuous debate about vitamin D's safety and efficacy. Most of these benefits related to the classic actions of vitamin D occur with much higher doses than what is considered safe and nutritionally sufficient dose, a long ago.

Before 1997, adequate daily intake of vitamin D as advocated by the Food and Nutrition Board (FNB) was 200 IU, which is similar to half the amount found in a teaspoon of cod liver oil. According to Vieth, however, there is no adequate evidence to prove that this dose of vitamin D has any effect on the serum 25(OH) D concentrations which is the correct and objective way of determining vitamin D status in the body (2).

Although most people believe that the daily intake of vitamin D is 200 IU, in 1997 the tolerable upper limit of (UL) vitamin D was increased up to 2000 IU / day by the FNB (3). Subsequently, there have been many well designed human clinical trials where the safety and tolerability of higher vitamin D doses were established.

The method of calculating the safe tolerable UL of vitamin D by the FNB consists of three steps; identification of hazards, dose response evaluation and derivation of UL.

Identification of hazards includes evaluation of data regarding the substance in relation to its adverse effects towards human. Type and severity of adverse effects are identified in this step. In dose response evaluation, oral intake and adverse effects that result from the substance are evaluated quantitatively. This step identifies the No Observed Adverse Effect Level (NOAEL), Lowest Observed Adverse Effects Level (LOAEL) and degree of uncertainty assigned by a numerical value. If someone is selecting vitamin D dose as the NOAEL, which has been tested in one or more adequately designed randomised control trial/s that is free of adverse effects we can use 1 as the uncertain factor (UF).

FNB used the following equation to calculate the UL.

$$UL = NOAEL / UF$$

FNB selected 60 microgram as the NOAEL from the clinical trial by Narang et al (4). They considered 1.2 as the UF which gave the UL as 50 micrograms.

$$\text{Vit D UL} = 60 \mu\text{g} / 1.2 = 50 \mu\text{g} = 2000 \text{ IU}$$

Using the same method European Commission Scientific Committee on Food (SCF) considered NOAEL 100 micrograms from the study by Vieth et al and considered 2 as the UF (5). So the UL declared by SCF was 50 micrograms (6).

$$\text{Vit D UL} = 60 \mu\text{g} / 1.2 = 50 \mu\text{g} = 2000 \text{ IU}$$

After formulating these levels many clinical trials have shown that vitamin D oral intake can be increased to a higher level without causing harm to human. Current recommendations have obtained UL of vitamin D using a higher uncertainty factor because of unwarranted fear towards vitamin D. It has, restricted its health benefits. If NOAEL and UF are taken from the recently published literature the UL will invariably be higher than 2000 IU / day.

Trivedi et al (2003) in a randomised control trial on elderly adults reported no acute toxicity or adverse outcomes after giving 100,000IU bolus dose once every four months. Duration of this trial was 5 years (7).

Barber Lux et al (1998) administered vitamin D₃ of 25, 250, 1250 micrograms (50,000 IU) per day to healthy men for eight weeks and reported no adverse effects (8). In this clinical trial mean (SD) baseline serum calcium was 9.58 (0.29) mg/dL. After receiving 1250 micrograms of vitamin D₃ per day for eight weeks serum calcium level increased up to 9.7 (0.19) mg/dL. This increase was not statistically significant.

Stern et al, (1981) used vitamin D₃ 100,000 IU as a single morning dose for four days in 24 adults and no adverse effects were observed (9). These are only few to illustrate the point that the much higher doses of vitamin D can be safely used without any evidence of toxicity.

The fact that toxic signs of vitamin D are primarily mediated through elevation of serum calcium was known for a long time. These include fever, chills, vomiting, anorexia, conjunctivitis, thirst and polyuria. There is, however, no consensus on the dose of vitamin D which causes these symptoms. Considering the reports on the adverse effects of vitamin D, many of them were due to accidental consumptions in which the exposures were far above those given in human clinical trials. These are good examples to support that acute toxic potential of increased serum calcium concentrations could occur only with very large doses of vitamin D.

Mixing of vitamin D₃ in its crystalline form into the table sugar resulted in an intake of 42,000 micrograms per day and continuing this dose for several months produced symptoms of hypercalcaemia in two people (10). Administering 2.4 million IU of vitamin D over days to a two year old boy produced toxic symptoms due to hypercalcaemia (11).

Therefore scientists are continuously challenging the current UL of vitamin D of 2000 IU, as weight of evidence support for a much higher dose (10,000 IU / day) as the UL of vitamin D.

Recognition of the traditional therapeutic dose as the safe UL of vitamin D can potentially restrict research efforts and prevent obtaining additional health benefits of vitamin D.

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