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Editorial

Continuing Professional Development : Its Importance and Implement 1
J D Sharma

Original Articles

Hemodynamic Changes following Spinal Anesthesia in Preeclamptic and Normotensive Women Undergone Cesarean Section 2
R Ershad S Yasmin

Attenuation of Haemodynamic Responses to Laryngoscopy and Intubation in Hypertensive Patient : The Influence of Melatonin 6
M M Rubaiat K A Lateef R Ershad

Clinical and Diagnostic Profile of Neonatal Congenital Heart Disease and Immediate Outcome: A Study in a Tertiary Care Hospital 11
N Hamid N N F Begum K Akter J Sultana

Chemotherapy-Induced Cardiotoxicity: A Prospective Study 17
S M Yusuff J F S Safa M R Hasan R S R Biswas F Alam N U Mahmud R A Begum

A Cross Sectional Study on Awareness of Consumers to Adverse Drug Reaction Reporting Related Aspects in a Tertiary Medical College Hospital 21
M Ata R Hoque R S R Biswas A Mostafa S A Shimu S B Mannan R P Chowdhury

Functional Outcome of Epidural Steroid Injection in the Management of PLID with Radiculopathy 25
M Saha M F Karim M Tabassum ABM Z Sadeque T I Khan S A Hasan

Hypertension and its Associated Risk Factors among Military Personnel 31
A S M Z Ali A B M B Hossain

Case Report

A Large Newborn with Hemihypertrophy, Refractory Hypoglycaemia: Backwith Wiedemann Syndrome: A Case Report 36
M M Sarker K Akhter F Jalil

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EDITORIAL

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Continuing Professional Development : Its Importance and Implement

Jhulan Das Sharma[1*]

Continuing Professional Development (CPD) takes a multidimensional approach to long term career development. Any learning activities undertaken by professional for the purpose of developing new skills and enhancing their current capabilities represent elements of CPD.

Patient and the general people expect that doctors remain up-to-date and professionally competent. The formal undergraduate and post-graduate education and training are conducted to bring a behavioral change in a medical practitioner to meet that expectation. The rate and magnitude of change in medical science is such that the contents of text books are not sufficiently up-to-date rather somewhat out of edge and skill of medical practice through which doctors will remain up-to-date. Due to rapid changes in health care delivery system, health professionals needs to transform from a Continuing Medical Education (CME) to a Continuous Professional Development (CPD) model so that they remain "up-to-date" in their knowledge and competency in total care. CPD is broader concept for continuing development of multifaceted competencies inherent in medical practice including medical, managerial, social and personal subjects which are needed for high quality professional performance in modern health care delivery system. Undergraduate and post-graduate medical education is regulated by specific rules and regulation but CPD is the process where the responsibility rests on professionals and individual doctor. People expect what is 'best' rather than what is 'right' for a particular situation and for that level, professionals competence should be combined with improvisation and general oversight. That is why, all over the world the concept of CPD is emerging and developing as a dynamic educational process to improve and upgrade ones professional performance. As a part of the 'global resident' we should be familiar to cope with and should be trying to contribute in these progress and development. This editorial will help us initial understanding and formulating of Continuing Professional Development (CPD).

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ORIGINAL ARTICLE

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Hemodynamic Changes following Spinal Anesthesia in Preeclamptic and Normotensive Women Undergone Cesarean Section

Reza Ershad[1] Shamima Yasmin[2]*

ABSTRACT

Background: Spinal Anesthesia (SA) in c/s is the preferred option when balancing risks and benefits of both mother and fetus. Spinal anesthesia in c/s is thought to be advantageous due to simplicity of techniques, rapid applications and onset of anesthesia reduced risk of systematic toxicity. Spinal anesthesia induced maternal hypotension is the most common complications associated with maternal morbidity and mortality during Cesarean Section (CS). The aim of the study was to compare the incidence and magnitude of Hemodynamic changes after spinal anesthesia in preeclamptic patients and non-preeclamptic patients undergone C/S under SA.

Materials and methods: This study was conducted at Combined Military Medical College and Hospital from March to 1st May 2020. We hypothesized PE parturients are at high risk of S/A induced hypotension's than non PE patients. A total of 90 ASA II and ASA III parturients data were taken consecutively and assigned into two groups where 60 were non-preeclamptics, and 30 preeclamptics. Parturients with cardiac disease, twin pregnancy, chronic hypertension, gestational hypertension, superimposed hypertension, renal disease, diabetes mellitus, coagulopathy (Platelet count < 80 × 109/L) active labor, eclampsia, abruptio placentae, placenta praevia, any adjuvant added with local anesthetics were excluded.

Results: During the study mean age of the Non PE (Non-preeclamptic) and PE (Preeclamptic) group was 26.43 years and 27.55 years. In non PE group all patients got ASA II where as in PE 70% got ASA II group and 30% got ASA III. The incidence of spinal anesthesia-induced hypotension was higher in non-preeclamptic parturients than preeclamptic parturients (75% vs. 46.67%, respectively) and the degree of blood pressure drop was significantly greater in the non-preeclamptic parturients compared to those with preeclampsia; As well intraoperative fluid consumption was significantly greater in the non-preeclamptics parturients compared to those with preeclamptics.

Conclusion : The incidence and magnitude of spinal anesthesia induced hypotension during c/s were less in preeclampsia patients than non-preeclampsia patients. Based on data from this study we can recommend S/A for preeclampsia patients unless otherwise contraindicated.

Key words: Non-preeclampsia patients; Preeclampsia patients; Spinal anesthesia.

Introduction

Only since 1995, when the first randomized research comparing regional vs general anesthesia for cesarean delivery in severe preeclampsia was published, there Spinal Anesthesia (SA) has been regarded as an option in this high-risk group of patients[1]. Even though the patient did not get epidural anesthesia during labor, an editorial published in 1998 suggested that epidural anesthesia be used instead of SA for cesarean delivery, even if the patient had not previously had epidural anesthesia[2]. In the absence of contraindications to regional anesthetic, several recent studies show that SA is safe[3–6]. In healthy parturients, several investigations have indicated that there is less hypotension and a lesser need for vasopressors than during SA.

Fluid loading and vasopressor prophylaxis were found to be beneficial in lowering the incidence of spinal anesthesia-induced hypotension in healthy parturients[7]. However, these precautions may raise the risk of hypertension and pulmonary edema in preeclamptic individuals[8].

Because of varying definitions, the reported prevalence of spinal anesthesia-induced maternal hypotension ranges from 7 to 89.2 percent. As a result, anesthetists have difficulties in managing anesthetics for preeclamptic parturients undergoing Cesarean section[9].

In this study our main goal is to compare the incidence and magnitude of hemodynamic changes in preeclamptic and non-preeclamptic parturients undergone Cesarean section under spinal anesthesia.

To detect the incidence and magnitude of hemodynamic changes in preeclamptic and non-preeclamptic parturients undergoing Cesarean section under spinal anesthesia.

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Journal of Army Medical College Chattogram
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Materials and methods

This cross-sectional study was conducted at Combined Military Medical College and Hospital from March to 1st May 2020. We hypothesized that PE parturients are at high risk of S/A induced hypotension's than non PE. A total of 90 ASA II and ASA III parturients data were taken consecutively and assigned into two groups where 60 non-preeclamptics, and 30 preeclamptics. Parturients with cardiac disease, twin pregnancy, chronic hypertension, gestational hypertension, superimposed hypertension, renal disease, diabetes mellitus, coagulopathy (Platelet count < 80 × 109/L) active labor, eclampsia, abruptio placentae, placenta praevia, any adjuvant added with local anesthetics were excluded.

The data analysis was done using SPSS version 22 statistical software. Student t test, MannWhitney U test and Fisher exact test were used to compare the data. All p values < 0.05 were considered statistically significant.

Results

Table I shows maternal and neonatal factor in the study where mean age of the Non PE and PE group was 26.43 years and 27.55 years. In non PE group all patients got ASA II where as in PE 70% got ASA II group and 30% got ASA III. The following table is given below in detail:

Table I Maternal and neonatal factor in the study

Variable	Non-PE, n=60	PE, n=30
Mean Age (Years)	26.43	27.55
Mean Weight (kg)	63.69	64.95
Anesthesia status: ASA II	60 (100%)	21(70%)
ASA III		9 (30%)
Mean Gestational age (Weeks)	38.86	37.56
Weight of new born	3.03	2.91

Figure 1 illustrates the distribution of the patients according to nulliparas where 46.67% cases were nulliparas in non-PE group where as in PE group it was 50%. The following figure is given below in detail:

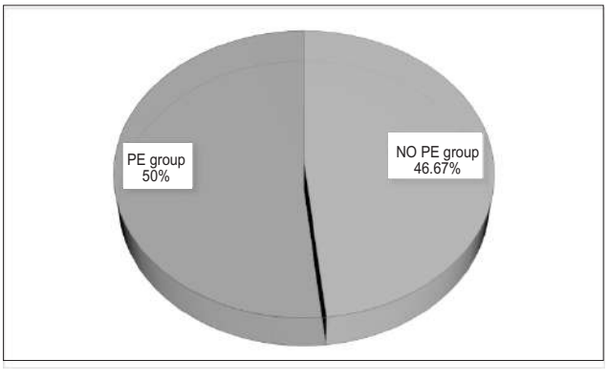

Figure 1 Distribution of the patients according to nulliparas

Figure 2 demonstrates the previous caesarian section of the patients where in non-PE group 31.68% had previous caesarian section where as in PE group it was 20%. The following table is given below in detail:

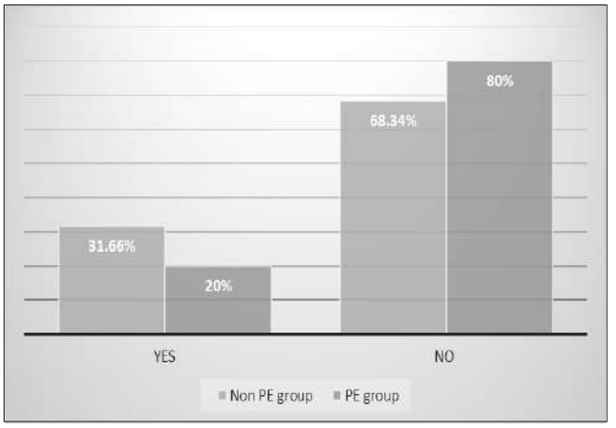

Figure 2 Previous caesarian section of the patients

Table II shows the distribution of the patients according to anesthetic status and procedural position of parturients, where the Speed of spinal administration was higher in the preeclamptic parturients compared to those with non-preeclamptics and though this difference was not statistically significant. The following table is given below in detail:

Table II Distribution of the patients according to anesthetic status and procedural position of parturients

Variable	Non PE, n %	PE n %	p value
Volume of injected bupivacaine (ml)[a]	2.32 ± 0.26	2.25 ± 0.24	0.558
Dose of 0.5% plain bupivacaine (mg)[a]	11.44 ± 1.23	11.37 ± 1.25	0.558
Speed of spinal administration (ml/sec)a	0.17 ± 0.59	0.22 ± 0.09	0.323
Position during spinal procedure n (%):			
Sitting	59(98.8%)	28(95.1%)	
Lateral	1(1.2%)	2(4.9%)	
Position after spinal procedure n (%):			0.479
Supine	58(96.67%)	30(100%)	
Left Lateral Tilt	2(3.33%)		
Parturients treated with adrenaline intraoperatively n (%)			0.550
Yes	3(5%)	30(100%)	
No	57(95%)		

Table III reveals the baseline hemodynamic status of the parturients where the baseline SBP, DBP, MAP, and heart rate were higher in parturients with preeclampsia than the corresponding values among the non-preeclamptic parturients.

Table III Baseline hemodynamic status of the parturients

Variable	Non PE	PE	p value
Baseline SBP (mmHg)	117.81 ± 9.21	133.95 ± 11.70	0.001
Baseline DBP (mmHg)	74.52 ± 8.66	84.80 ± 10.41	0.001
Baseline MAP (mmHg)	82.20 ± 8.44	86.32 ± 10.25	0.219
Baseline heart rate (Beats/minute)	94.90 ± 14.79	98.36± 20.20	0.320

Journal of Army Medical College Chattogram
Volume 4 Issue 1 June 2021; 2-5

Table IV shows fluid consumption, estimated blood loss and surgical conditions where Non-preeclamptic parturients have been taken a higher volume of preload fluid compared with preeclamptics (609.50 ± 279.65 VS 563.44 ± 319.46 ml, p = 0.003) and there was a statistically significant difference in intraoperative intravenous fluid consumption between ml groups, which was higher in non-preeclamptics compared to preeclamptic parturients (1721.46 ± 352.40 vs 1461.40 ± 417.58, p = 0.002).

Table IV Fluid consumption, estimated blood loss and surgical conditions

	Non PE	PE	p value
Crystalloid preload (ml)	609.50 ± 279.65	563.44 ± 319.46	0.003
Intraoperative IV fluid (ml)	1721.46 ± 352.40	1461.40 ± 417.58	0.002
Estimated blood loss (ml)	383.96 ± 134.13	380.02 ± 132.75	0.875
Duration of surgery (minute)	44.90 ± 12.75	41.68 ± 9.15	0.560

Table V demonstrates the distribution of the patients according to incidence and magnitude of hemodynamic changes following spinal anesthesia where the incidence of hypotension in non-preeclamptic parturients (75%) was higher than that of preeclamptic parturients (46.67%).

Table V Distribution of the patients according to incidence and magnitude of hemodynamic changes following spinal anesthesia

Variable	Non-PE	PE	p value
Incidence of hypotension n (%) [b]	45(75%)	14(46.67%)	0.035
Lowest SBP after SA (mmHg)	83.5 ± 2.11	104.30 ± 12.14	-
Decrease from baseline %[a]	25.88± 5.46	22.01 ± 3.05	< 0.001
lowest DBP after SA (mmHg)	54 ± 8.59	66 ± 5.01	-
Decrease from baseline %[a]	26.18 ± 4.07	23.93 ± 4.79	< 0.001
lowest MAP after SA (mmHg)	60.01 ± 7.54	64 ± 0.01	-
A decrease from baseline %[a]	24.64 ± 2.21	20.27 ± 15.13	< 0.001
Mean HR after SA (beats/minute)[a]	91.40 ± 9.94	88.21 ± 12.30	0.567
20% decrease in HR n (%)	58(96.67)	21(70)	0.068
20% increase in HR n (%)	2(3.33)		0.550

Discussion

One study found that SBP, DBP, and MAP measured at the baseline were higher for the patients with preeclampsia, and the lowest mean SBP, DBP, and MAP measured among the preeclamptic patients were higher than the corresponding values among the healthy parturients[10]. This finding was in line with our study result. In this study, the incidence of hypotension after spinal anesthesia in preeclamptic parturients (46.67%) was less than that of non-preeclamptic parturients (75%) (p = 0.035). The discrepancy in the incidence of hypotension is related to preeclampsia related factors. Despite the sympathetic block due to spinal anesthesia, because of exaggerated vasoconstriction, preeclamptic parturients can still maintain their vascular tone that caused only a limited decrease in blood pressure.

Following spinal anesthesia, the mean SBP, DBP, and MAP measured at different time points were higher in preeclamptic parturients than the corresponding values among non-preeclamptic parturients. But this difference was insignificant between groups at 14, 18, 22, 24, 26,35 min in SBP, at 8 and 40 min in DBP, at 10, 14, 24, 35 min in MAP, and thereafter to the end of surgery whereas, the mean pulse rate was comparable between groups at different time points after SA.

Another study found significant differences in SBP, DBP, and MAP at each point of time in both groups[11]. The possible explanation for this discrepancy might be the employment of invasive blood pressure monitoring in their study, in contrast to our study. Similar to our study other report found that severely preeclamptic patients had a less frequent incidence of clinically significant hypotension compared to healthy parturients (16.6% versus 53.3%, p = 0.006)[12].

The incidence of hypotension among preeclamptic parturients in our study was higher than one study result. The likely reason may be the use of different criteria for defining hypotension (20% versus 30% decline to baseline MAP) and the use of the small volume of preload in our study participants compared to other.

In contradiction to our result, another study found that there was no statistically significant difference regarding the occurrence of hypotension after spinal anesthesia between severely preeclamptic and healthy parturients. But the incidence rate of hypotension was high in both groups (84 and 70%, p = 0.45)[13].

This difference may be due to the intraoperative administration of intravenous hydralazine in preeclamptic parturients in their study. In response to that, one study found that the percentage of fall of BP from baseline were significantly greater in the healthy parturients compared to those with preeclampsia (25.8% ± 10.1 vs. 18.8% ± 17.0 for SBP, 28.5% ± 8.8 vs. 22.5% ± 10.4 for DBP, and 31.2% ± 14.2 vs. 18.2% ± 12.6% for MAP, p < 0.05[14]. Likewise, another study conducted by others found that the percentage of fall of DBP and MAP calculated from the baseline was also less in the preeclamptic group (34.5 and 33% in normotensive as opposed to 30.3 and 32.3% in preeclamptics, respectively)[15]. The result of our study was in accordance with the above findings.

Conclusion

The incidence and magnitude of spinal anesthesia induced hypotension during c/s were less in preeclampsia patients than non-preeclampsia patients. Based on data from this study we recommended S/A for preeclampsia patients unless otherwise contraindicated.

Disclosure

Both the authors declared no competing interest.

Journal of Army Medical College Chattogram
Volume 4 Issue 1 June 2021; 2-5

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ORIGINAL ARTICLE

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Attenuation of Haemodynamic Responses to Laryngoscopy and Intubation in Hypertensive Patient : The Influence of Melatonin

Molla Md Rubaiat[1] Kazi Ashkar Lateef[2] Reza Ershad[3]*

ABSTRACT

Background: Laryngoscopy and endotracheal intubation are known as potent stimuli which lead to increase heart rate and blood pressure. Melatonin (N-acetyl-5-methoxytryptamine) is a pineal gland hormone maintaining normal circadian rhythms. It is normally used for patients with sleep disorders and altered circadian rhythms, such occurs in jet lag, night shift work and various neuropsychiatric disorders. It has been studied mainly for pre-operative anxiolysis and sedation in intensive care unit. A hypothesis is made that melatonin can provide haemodynamic stability during laryngoscopy and intubation in hypertensive patients when given 120 min before the procedure. Assessing the usefulness of oral melatonin in attenuating the pressor response to direct laryngoscopy and tracheal intubation in hypertensive patients.

Materials and methods: Sixty American Society of Anesthesiologists physical status Grade II patients of either gender, 20–50 years old, 50–70 kg body weight, scheduled to underwent elective surgical procedures under general anaesthesia and endotracheal intubation, were assigned into two equal groups–Case Group (Melatonin)) and control group (No medication). Case group received oral melatonin tablets 6 mg 120 min before surgery. The haemodynamic parameters were recorded preoperatively just before taking melatonin and also just before induction of general anaesthesia and thereafterat 1, 3, 5 and 10 min of laryngoscopy and endotracheal intubation. Data were presented as mean ± SD. Unpaired t-test was used for between-group comparison of ratio and interval scale data. Significance was assigned at the level 0.05 or less.

Results: It was observed that in control group, there was a significant increase in blood pressure and heart rate at laryngoscopy and intubation and persisted till 10 min post-intubation. In case (Melatonin) group, there was an insignificant increase heart rate at 1 min after laryngoscopy and intubation which however settled within 3 min post-intubation where blood pressure was very much controlled throughout the mentioned period and was statically significant ($p<0.005$).

Conclusion: Melatonin is an effective drug for attenuation of cardiovascular responses to laryngoscopy and endotracheal intubation in hypertensive patient.

Key words: Haemodynamic response; Laryngoscopy; Melatonin; Pre-operative anxiety.

Introduction

Laryngoscopy and endotracheal intubation are considered potent noxious stimuli which provoke haemodynamic responses leading to a marked increase in heart rate and blood pressure[1]. This is probably of no consequence in healthy individuals. However, these events are especially detrimental in individuals who have limited myocardial reserve due to coronary artery disease, cardiac dysrhythmias, congestive heart failure, hypertension, cardiomyopathy and geriatric age group[2]. Hence, it is mandatory to take measures to attenuate these pressor responses. The mechanisms of these haemodynamic alterations are somatovisceral reflexes due to sympathetic stimulation. During intubation of trachea, the laryngeal and tracheal sensory receptors are stimulated which result in the release of endogenous catecholamines resulting in tachycardia and hypertension[3]. Since the invention of laryngoscopy and endotracheal intubation, various drug regimens and techniques have been used from time to time to attenuate these stress responses. Some of such agents beta receptor blockers (Esmolol, propranolol) calcium channel blockers (Verapamil, diltiazem) sympatholytic (Clonidine, dexmedetomidine and methyldopa) benzodiazepines (Midazolam, alprazolam) barbiturates, propofol, pregabalin and peripheral vasodilators (Sodium nitroprusside, nitroglycerine)[4]. However, each agent has some limitations such as respiratory depression, hypotension, tachycardia, bradycardia, rebound hypertension or allergic reactions. Hence, there has always been a need for a better agent. Melatonin (N-acetyl-5-methoxytryptamine) is an endogenous sleep-regulating hormone secreted by pineal gland. Exogenous administration of melatonin facilitates sleep onset and improves the quality of sleep. It is different from benzodiazepines and their derivatives because it produces natural sleep pattern and does not lead to impairment of cognitive functions[5]. Various researchers have used this drug in different dose patterns as premedication in both adults as well as children. It has been mainly studied in view of pre-operative anxiolysis,

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sedation in intensive care unit, pre-operative cognitive and psychomotor functions[6]. It is assumed that inhibitory actions of melatonin on central nervous system responsible for sedation and anxiolysis may have role in attenuating haemodynamic responses to laryngoscopy and intubation. Based on this, a hypothesis has made that melatonin can provide haemodynamic stability during laryngoscopy and intubation when given 120 min before the procedure. The primary destination was, to study the changes in blood pressure during laryngoscopy and endotracheal intubation during general anaesthesia.

The aim of study was to evaluate the role of melatonin to avoid peri-induction cardiovascular complication in hypertensive patients during general anaesthesia.

Methods and materials

This is a prospective randomized study, was conducted at Department of Anaesthesiology in Combined Military Hospital (CMH) Dhaka from December 2017 to May 2018, with permission from Ethical Committee of Combined Military Hospital, Dhaka.Total 60 patients were selected for the study during pre-anaesthetic checkup strictly following the inclusion and exclusion criteria.The patients were divided into 2 (Two) groups, 30 (Thirty) in each group by lottery.

Inclusion criteria were patients age varied from 20 to 50 years, essential hypertensive patients (Taking single antihypertensive drug) ASA grade-II and mallampatti grade I and II. Exclusion criteria were unwilling patient, emergency surgeries, histories of pregnancy, renal impairment, diabetes mellitus, sleep disorders, obesity, psychiatric and neurological illness, intake of antipsychotics, sedatives, anxiolytics and anti-epileptic drugs, known allergy to the drug and patient taking beta receptor blockers.

After obtaining the informed written consent the patients were explained in detail about the procedure, benefits and complications of the study on the preoperative day. To minimize effect of antihypertensive drug, those patients who were taking single antihypertensive drug were incorporated in the study. Patients taking beta-blocker were omitted from study because of direct negative chronotropic effect on heart.All the patients were advised to take their antihypertensive drug as per schedule. No sedative was advised before night of operation.

One group (Control group) receivedno drug and other group (Case group) received oral melatonin (6 mg) (Two tablets, each tablet contains 3 mg melatonin) was administered 120 min before surgery with sips of water. The study drugs were administered by paramedic in the pre-operative area, and were unaware of the study.

Monitoring of the pulse rate, respiratory rate, blood pressure and arterial oxygen saturation (SpO_2) were done in the pre-operative period before administration of drugs by the paramedics posted in the preoperative room. On receiving the patient in the operation theatre, routine monitoring were commenced which included heart rate, electrocardiogram, arterial SpO_2, $EtCO_2$ and Non-invasive Blood Pressure (NIBP). Inj Fentanyl 1μg/kg body weight was administered intravenously 2 minutes before induction. After 2 minutes, induction was attained with intravenous propofol 2 mg/kg body weight intravenously mixed with 30mg preservative-free 2% lignocaine hydrochloride. Succinylcholine was given intravenously 2 mg/kg body weight. Maintenance of anaesthesia was attained with inhalation of halothane 1 MAC (Minimum alveolar concentration) nitrous oxide: oxygen 60:40 and muscle relaxation with vecuronium bromide administered in the dose of 0.08 mg/kg body weight intravenously as loading dose and one-fourth of the initial dose as maintenance doses. Mechanical ventilation was adjusted to maintain normocapnia ($EtCO_2$ values of 35-40 mmHg). Intravenous injection Tramadol 100 mg administered slowly before completion of surgery for post-operative analgesia. After completion of the surgery, neostigmine 50 μg/kg body weight and injection atropine 25 μg/kg body weight were administered intravenously to reverse the residual neuromuscular blockade.

All parameters such as heart rate, systolic, diastolic and mean blood pressures were measured 120 min after administration of drug just before induction of GA, there after 1, 3, 5 and 10 minutes after induction and intubation.

Just after arrival at the post anaesthesia care unit the patients received the standard post-operative care including oxygen administration via face mask at 5–6 L/min and monitoring of heart rate, NIBP, respiratory rate and SpO_2 at a regular interval throughout postoperative period for 24 hours. We observed for any episodes of nausea, vomiting, dizziness, headache, respiratory depression, arrhythmias, bradycardia, hypotension and restlessness till 24 h postoperatively.

All collected data were checked and rechecked for omissions, inconsistencies and improbabilities. Data analysis were performed by Statistical Package for Social Science (SPSS) version-19. Data were edited, coded and entered into the computer. Statistical analyses were done and level of significance measured by using appropriate procedures like t-test and proportion (d) test and others where applicable. Level of significance (p value) will be set at 0.05 and confidence interval at 95%. Results will be presented as text and tables. Data was presented as mean ± SD. Significance will be assigned at the level 0.05 or less.

Results

To minimize effect of antihypertensive drug on study, those patients who were taking single antihypertensive drug were incorporated.Patients taking beta-blocker were omitted from study because of direct negative chronotropic effect on heart [Table I]. All the patients were advised to take their antihypertensive drug as per schedule. Both the study groups were identical in terms of age, gender distribution, weight, ASA status [Table II]. The patients were informed regarding the study and written consent were taken. After scrutinized according to eligibility criteria 60 patients were finalized thereafter by card sampling, they were divided into 2 groups, named case group and control group patients.

Journal of Army Medical College Chattogram
Volume 4 Issue 1 June 2021; 6-10

The case group was treated with tab Melatonin (3mg) - 2 tabs and the control group without drug. No sedative was advised before night of operation. Each group contained 30 Patients. Data regarding demographic profile, vital signs were recorded, compiled, edited and results were plotted into tabular and figure form.

Systolic blood pressure was higher from baseline values in placebo group during laryngoscopy and intubation. Thereafter, this increase persisted at all points of time until 10 min ($p < 0.001$). In case group, there was no rise of systolic blood pressure and the patients were stable at all points of time after the administration of the study drug ($p < 0.001$) [Table III]. Similar trends were observed for diastolic and mean blood pressure ($p < 0.001$) [Tables IV and V].

In control group, there was a rise in heart rate from baseline values at laryngoscopy which attained statistical significance at 1 min and persisted thereafter till 10 min. In case group, there was a rise in heart rate from baseline values at the time of laryngoscopy, but it was not statistically significant and returned to previous values within 1 min. Thereafter, it was maintained at lower values at all points of time till 10 min after laryngoscopy and intubation ($p < 0.001$) [Table VI].

In the control group, one patient had nausea and vomiting, two patients were agitated and restless in the immediate post-operative period. In the case group, one patient had nausea and vomiting in the post-operative period. None of the patients had respiratory depression or hypotension.

Table I Patients who were taking antihypertensive drugs in this study (n=60, 30 in each group)

Drugs	Case (n=30)	Control (n=30)	Total (n=60)
Angiotensin receptor blocker	21(70%)	23(76.67%)	44(73.33%)
Calcium channel blocker	9(30%)	7(23.33%)	16(26.67%)

It is mentioned that patients who were taking single antihypertensive drug, included in this study and patients taking beta-blocker were omitted from this study.

Table II Anthropometric profile (n= 60, 30 in each group)

Anthropometric variables	Case (n=30)	Control (n=30)
Mean weight (Kg)	67.96±6.73	63.19±7.55
Mean height (in cm)	163.17±5.92	164.32±6.74
Mean BMI (kg/m^2)	23.16±1.67	24.09±0.98

Table III Systolic blood pressure (mm of Hg) in both groups at various points of time (n=60, 30 in each group)

Blood pressure	Case (n=30)	Control (n=30)	p-value
Baseline (Mean±SD)	124.43±6.65	123.63±5.79	0.618^{NS}
120 minutes after administration of drug just before induction (Mean±SD)	119.10±8.36	124.80±6.30	0.004^{S}
1 minute after Induction and intubation (Mean±SD)	121.60±9.69	140.50±9.80	0.001^{S}
3 min after GA (Mean±SD)	115.83±7.52	137.57±9.73	0.001^{S}
5 min after GA (Mean±SD)	107.30±9.57	129.70±6.86	0.001^{S}
10 min after GA (Mean±SD)	105.47±8.39	127.07±5.79	0.001^{S}

S: Significant, NS: Not significant, p-value was calculated by student's t test.
p-value was significant at <0.05.

Table IV Diastolic blood pressure (mm of Hg) in both groups at various points of time (n=60, 30 in each group)

Diastolic Blood Pressure	Case (n=30)	Control (n=30)	p-value
Baseline (Mean±SD)	79.17±6.34	80.87±4.52	0.621^{NS}
120 minutes after administration of drug just before induction (Mean±SD)	75.50±5.73	85.20±5.740	0.001^{S}
1 minute after Induction and intubation (Mean±SD)	79.43±6.75	95.53±6.00	0.001^{S}
3 min after GA (Mean±SD)	78.80±7.12	92.00±3.40	0.001^{S}
5 min after GA (Mean±SD)	76.30±6.14	88.70±3.78	0.001^{S}
10 min after GA (Mean±SD)	75.67±5.72	85.87±3.41	0.001^{S}

S: Significant, NS: Not Significant, p-value was calculated by student's t test.
p-value was significant at <0.05.

Table V Mean blood pressure (mm of Hg) in both groups at various points of time (n=60, 30 in each group)

Blood pressure	Case (n=30)	Control (n=30)	p-value
Baseline (Mean±SD)	94.27±6.44	95.12±4.94	0.55^{NS}
120 minutes after administration of drug just before induction (Mean±SD)	90.03±6.60	98.40±5.92	0.001^{S}
1 minute after Induction and intubation (Mean±SD)	93.49±7.73	110.52±7.26	0.001^{S}
3 min after GA (Mean±SD)	91.14±7.25	107.20±5.51	0.001^{S}
5 min after GA (Mean±SD)	86.63±7.28	102.37±4.81	0.001^{S}
10 min after GA (Mean±SD)	85.60±6.61	99.60±4.20	0.001^{S}

S: Significant, NS: Not Significant, p-value was calculated by student's t test.
p-value was significant at <0.05.

Journal of Army Medical College Chattogram
Volume 4 Issue 1 June 2021; 6-10

Table VI Heart rate at various points of time (n=60, 30 in each group)

Blood pressure	Case (n=30)	Control (n=30)	p-value
Baseline (Mean±SD)	80.43±9.25	81.10±4.76	0.727^{NS}
120 minutes after administration of drug just before induction (Mean±SD)	88.97±6.45	98.43±5.54	0.001 ^{S}
1 minute after Induction and intubation (Mean±SD)	90.27±5.97	110.33±6.99	0.001^{S}
3 min after GA (Mean±SD)	81.57±6.78	107.13±4.83	0.001^{S}
5 min after GA (Mean±SD)	79.79±6.35	102.87±4.25	0.001^{S}
10 min after GA (Mean±SD)	78.47±5.72	100.17±4.19	0.001^{S}

S: Significant, NS: Not Significant, p-value was calculated by student's t test.
p-value was significant at <0.05.

Discussion

The present study is aimed at assessing the role of melatonin (Available at local market, brand name "Tab. Filfresh-3mg") in attenuating haemodynamic responses to laryngoscopy and intubation in case of hypertensive patients who are taking only single antihypertensive drug. Melatonin (N-acetyl-5-methoxytryptamine) is a pineal gland hormone which controls the circadian rhythm. It is used for sleep disorders, jet lag, perioperative anxiolysis, sedation, cognitive and psychomotor functions[7,8]. It is assumed that inhibitory actions on central nervous system responsible for sedation and anxiolysis may have a role in attenuating haemodynamic responses to laryngoscopy and intubation. Rosenberg et al studied the role of perioperative melatonin in the modification of surgical stress response indicating that melatonin has sympatholytic activity[9]. This is in support of our assumption. The peak effect of exogenous melatonin ranges from 60 to 150 min[10]. Based on this, a hypothesis had been made that melatonin can provide haemodynamic stability during laryngoscopy and intubation when given 120 min before the procedure.In a study, it was shown that effective dose of melatonin for antihypertensive with minimal side effect was 5 to 10 mg. Hence, 6 mg melatonin has been administered 120 min before induction of anaesthesia.

It is observed that in melatonin group, systolic blood pressure was lower than baseline values at all points of time till 10 min after intubation as compared to the placebo group in which there was a significant rise. Similar trends were observed for diastolic and mean blood pressure. It has been studied that melatonin reduces mean blood pressure in healthy volunteers[11]. A study on rats revealed that pinealectomy resulted in hypertension[12]. Mohammed et al compared the role of oral melatonin 6 mg and 9 mg with placebo administered 1 h before surgery in attenuating pressor response to laryngoscopy and intubation. They observed that there was a reduction of blood pressure with regard to systolic, diastolic and mean blood pressure and perfusion index in both melatonin groups as compared to the placebo group[13].

The mechanism of effect of melatonin on circulation is complex. The blood pressure lowering effect may be attributed to the specific binding of melatonin to melatonin receptors in the blood vessels, interfering with the vascular response to catecholamines. It may interfere with the peripheral as well as central autonomic system, causing a reduction in adrenergic outflow and resulting catecholamine levels. Furthermore, it may induce relaxation of arterial wall smooth muscle by enhancing the availability of nitric oxide[12]. In addition, it may also act via specific receptors melatonin type 1 or melatonin type 2 located peripherally in the blood vessels and centrally in blood pressure regulating area of the brain[14]. It also has free radical scavenging effect leading to dilatation of blood vessels, and it may work via epigenetic mechanism at area postrema in the brain. The blood pressure lowering effect could also be due to the sedative action of orally administered melatonin. The sedative effect is mainly due to binding at GABA-A receptor and exerting its anaesthetic effect[15,10].

It is observed that heart rate was also lower than baseline values at all points of time in melatonin group as compared to the placebo group. However, in a similar study, no difference was observed in the changes of heart rate in the melatonin groups as compared to the placebo group[13]. The heart rate lowering effect of melatonin may be attributed to its anxiolytic actions. The underlying mechanism is probably the synergy between melatonergic and GABA-ergic systems. It also has analgesic effects as observed by various investigators and this may also contribute to the haemodynamic stability[16,17].

Moreover, the magnitude of the haemodynamic responses is directly proportional to the duration of laryngoscopy and to the force applied during laryngoscopy. Hence, those patients requiring more than one attempt for intubation were not included in the study. Since this study is regarding haemodynamic responses to hypertensive patients,agents that maydesensitize the autonomic receptors such as sedative drug night before operation is not advised. Diabetic patients usually have some degree of autonomic neuropathy, age progresses blood vessel wall gets atherosclerosis may interfere with the results; hence, these patients were excluded from the study.

In the study, there were no significant side effects such as bradycardia, arrhythmias, respiratory depression, restlessness, nausea and drug interactions. Various studies indicate that melatonin has an excellent safety profile. Very high doses up to 300 mg/day orally for 2 years have been administered safely. Even in children doses up to 20 mg have been used without any significant side effects apart from sedation[15]. There is no liability to cause dependence and addiction. It may cause fatigue (4%) or nausea (3%). Diziness, headache and irritability may be seen in some

Journal of Army Medical College Chattogram
Volume 4 Issue 1 June 2021; 6-10

patients with use of very high doses in some previous studies of melatonin done for its anxiolytic action. Thus, proving that melatonin is a useful drug for use as an adjunct in anaesthesia. The correct dosage in humans seems largely unknown and requires further studies.

The role of melatonin in anaesthesia and critical care has been elaborately discussed in the literature; it has been mentioned as a wonder drug with a wide spectrum of beneficial uses in anaesthesia, postoperative care and critical care including antioxidant and neuroprotective properties besides hypnosis, anxiolysis, analgesia and others[15]. The use of melatonin for attenuation of haemodynamic responses before laryngoscopy and intubation is superior to few other drugs studied for the same purpose like esmolol, dexmedetomidineetc[18, 19].

Conclusion

Melatonin by virtue of its multiple functions has the potential to take a place in the anaesthetic drug armamentarium, because it can be an attractive option for pre-medication as an antihypertensive as well as anxiolytic (Decrease heart rate) for the induction of general anaesthesia as an adjuvant which can provide favourable operative conditions. It may be concluded here thatpre-treatment with 6 mg melatonin administered orally 120 min before induction of general anaesthesia is effective for attenuating haemodynamic responses to laryngoscopy and intubation.

Disclosure

All the authors declared no competing interest.

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ORIGINAL ARTICLE

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Clinical and Diagnostic Profile of Neonatal Congenital Heart Disease and Immediate Outcome: A Study in a Tertiary Care Hospital

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ABSTRACT

Background: Congenital Heart Disease (CHD) contributes a lot in neonatal mortality rate in our country. The purpose of the study to identify, classify neonatal CHD and to see their immediate outcome. Early detection of neonatal CHD will help to reduce neonatal mortality rate as well as the smooth growth and development of an infant.

Materials and methods: This was an observational study, carried out in the Department of Pediatrics & Pediatric Cardiology of a tertiary care Military Hospital, Dhaka from 15 May 2018 to 14 October, 2018. Among 523 neonate, 52 cases were confirmed by history, physical examination & echocardiography and recorded in pre formed data sheet and statistical analysis was done.

Results: 73.07% cases were acyanotic and cyanotic patients were (26.92%). Majority of cases (48.07%) presented with symptoms before they completed 1 wk of age. Most common presentations was rapid respiration (80.7%). Others were feeding difficulties (67.3%), Poor weight gain (53.84%), cyanosis (38.46%), forehead sweating (48.7%). Among Cardiac findings murmur (38.46%) and cardiomegaly (26.92%) were the most frequently observed features. Echo Findings revealed majority (19.23%) had Atrial Septal Defect. VSD and PDA were found in same no of patients (15.38%). Among cyanotic patients (26.92%) most common two CHD were TGA (7.62%) and TOF (5.76%). Immediate outcome with the symptomatic treatment showed 38.46% patient was improved, 16.66% patients shunt closed spontaneously and 11.53% patient was expired because of severe type congenital heart disease.

Conclusion: The clinical presentation of congenital heart disease varies according to the type and severity of the defect. Nearly one third to half of all the congenital heart diseases is critical, requiring intervention in the first year of life. With the advances in Pediatric cardiac care in the last few decades many condition are now correctable.

Key words: Acyanotic congenital heart disease; Atrial Septal defect (ASD); Congenital Heart Disease (CHD); Cyanotic congenital heart disease; Patent Ductus Arteriosus (PDA); Transposition of Great arteries (TGA); Tetralogy of Fallot (TOF); Ventricular Septal Defect (VSD).

Introduction

Congenital heart disease is a general term used to describe abnormalities of the heart or great vessels that are present from birth. Most such disorders arise from faulty embryogenesis during gestational weeks 3 through 8, when major cardiovascular structure develop[1]. Congenital heart disease is defined as "an abnormality in cardiocirculatory structure or function at birth even it is discovered much later"[2].

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The incidence of congenital heart disease varies in different studies but is commonly noted to be 5 to 8 per thousand live birth[1,3]. The incidence has been relatively constant over the years and in different parts of the world[4]. More recent higher incidence figure appear to be due to the inclusion of more trivial form of congenital heart disease. Such as tiny ventricular septal defect that redetected more frequently by higher sensitive echocardiography[5]. The relative frequency of the most common lesions are Ventricular Septal Defect (36%), Atrial Septal defect (5%), Patent Arterial Duct (9%), Atrioventricular Septal Defect (4%), Pulmonary Stenosis (9%), Aortic stenosis (5%), Coarctation of Aorta (5%), Transposition of great Arteries (4%), Tetralogy of Fallot (4%). The other 20% of congenital heart disease consists of many rare or complex lesions[6].

The cause of most Congenital heart defects is unknown. Most cases are thought to be multifactorial and result from a combination of genetic predisposition and environmental stimulus[3].

The timing of presentation and accompanying symptomatology depends on i) The nature and severity of the anatomic defect ii) The in utero effects of the structural lesions iii) The alterations in cardiovascular physiology secondary to the effects of the transitional circulation: closure of the ductusarteriosus and the fall in the pulmonary vascular resistance[5].

Journal of Army Medical College Chattogram
Volume 4 Issue 1 June 2021; 11-16

Most congenital defects are well tolerated in the fetus because of the parallel nature of the fetal circulation. Even the severe cardiac defects (Hypoplastic left heart syndrome) can usually, be well compensated by the fetal circulation. It is only after the birth when the fetal pathways are closed that the full hemodynamic impact of an anatomic abnormality becomes apparent[3].

Although the most significant transitions in circulation occur in the immediate perinatal period, the circulation continues to undergo changes after birth, and these later changes may also have a hemodynamic impact on cardiac lesions and their apparent incidence. As pulmonary vascular resistance falls over the first several weeks of life, left to right shunting through intra cardiac defects increases and symptoms become more apparent. Thus, in patients with a ventricular septal defect, heart failure is often manifested between 1 and 3 months of age. The severity of various defects can also change dramatically with growth, some VSDs may become smaller and even close as the child ages. Alternatively, stenosis of the aortic or pulmonary valve, which may be mild in the newborn period, may become worse if valve orifice growth does not keep pace with patient's growth[3].

The clinical presentation of congenital heart disease varies according to the type and severity of the defect[7]. The clinical manifestations reported in different studies include asymptomatic, breathlessness, cough, fatigue, recurrent respiratory tract infection, feeding difficulty, growth failure,cyanosis, clubbing, polycythemia, oedema, tachycardia, cardiomegaly, murmur etc[8-11].

Complications of different congenital heart disease are growth retardation, failure to thrive (FTT), recurrent respiratory tract infection, heart failure, infective endocardities, paradoxical embolism, cerebrovascular accidents and abscess, pulmonary hypertension, shunt reversal etc[3].

As Combined Military Hospital, Dhaka is a tertiary level hospital, a significant number of neonate suffering from congenital heart disease are admitted in PCICU (Paediatric Cardiac Intensive Care Unit) and NICU (Neonatal Intensive Care Unit). To diagnose congenital heart disease properly, their clinical features should be recognized first. Routine neonatal examination fails to detect more than half of the babies with heart disease; examination at six weeks misses one third. A normal examination does not exclude heart disease[11].

Objectives of the study was to detect neonatal CHD, classification of the cases, their clinical presentation, echo findings and to see immediate outcome. In our country very few studies available on neonatal CHD. Therefore this study was undertaken in this hospital to highlight these basic epidemiological issues. This might help the health care planner and providers to formulate programs that will contribute to earlier case detection, urgent referral to appropriate center and effective management as well as prevention of CHD.

Materials and methods

This is an observational study was carried out in the Department of Pediatrics & Pediatric Cardiology of Combined Military Hospital Dhaka from 15 May 2018 to 14 October 2018. The study population was the entire neonate admitted in NICU and PCICU of this hospital during the study period. Total 513 neonates got admitted in that period. In all cases detail history was obtained from the parents. History included the presenting complaints of the patients, e.g breathlessness, cough, feeding difficulty, fatigue ability, bluish coloration of lips, tongue and extremities, history suggestive of cyanotic spell, fast breathing, poor weight gain, recurrent chest infection etc. Onset of symptoms and duration were noted. Baby's detail of birth history including ante-natal history was taken. Next a thorough general physical examination was performed in all cases. All the routine anthropometric measurements (Length, weight, and occipitofrontal circumference) and vital signs (Pulse, respiratory rate, BP-all four limbsand temperature) were noted in all cases. Patients were carefully examined for any dysmorphic faces (e.g Down syndrome, Turner Syndrome, Edward syndrome, Patau Syndrome, Marfan syndrome etc) shortness of breath, labored breathing, cyanosis, radio-femoral delay, polycythaemia, edema, enlarged liver and basal crepitation. Hyperoxia test was done all neonate. Detail cardiovascular examination was done in all cases and careful attention was given to note the position and character of apical impulse, presence of thrill, parasternal heave, palpable P2, character of apical impulseetc. If murmur was found, its location, character and radiation was noted. If the history and physical examination findings were suggestive of congenital heart disease then the patient was suspected as a case of congenital heart disease.

Then for diagnostic purpose chest X-ray, ECG and echocardiography were done in those 68 clinically suspected cases. Routine Blood examination (e.g total and differential count of WBC, Hb%, ESR) and other relevant investigations were also done. Among 68 clinically suspected cases, congenital heart disease was confirmed in 52 cases by echocardiography. After confirming diagnosis data was noted in a preformed data sheet. To see the immediate outcome, patients were closely monitored during their hospital staying period. Verbal and written consent was taken from the parents. Ethical clearance was taken from hospital ethical clearance committee.

Inclusion criteria

Neonate delivered in term and post term irerespective of birth weight with any type of CHD where diagnosis was confirmed by Hyperoxiatest, chest-Xray, ECG and Echocardiography.

Exclusion criteria

Neonate age > 28 days and baby born before 37 completed weeks.

Journal of Army Medical College Chattogram
Volume 4 Issue 1 June 2021; 11-16

Data was analyzed by SPSS V-21. Some common abbreviations used in this study-VSD (Ventricular Septal Defect), PDA (Patent Ductus Arteriosus), DORV (Double Outlet Right Ventricle), TA (Tricuspid Atresia), PS (Pulmonary Stenosis), TOF (Tetralogy of Fallot) ESM (Ejection Systolic Murmer), PSM (Pan Systolic Murmur).

Results

Table I Baseline demographic features: Age, Sex, birthwt, Gestationalage, Consanguinity
(n-52)

Age Range	No of Pt.	Percentage
>2 wks	17	32.69%
1-2wks	15	28.84%
<1wks	25	48.07%
Sex: Male	28	53.84%
Female	24	46.15%
Birth wt:1.5-2.4 kg	13	25.00%
2.5-2.9 kg	25	48.07%
3.0-4.0 kg	10	19.23%
>4.0kg	04	07.69%
GA:37-38 wks	32	61.53%
39 wks-40 wks	11	21.15%
>40 wks	09	17.30%
Appropriate for GA	38	73.07%
Small for GA	10	19.23%
Large for GA	04	07.69%
Consanguineous	05	09.61%
Non consanguineous	47	90.38%

This table revealed most of the patients presented within one wk of age- 48.07%, then >2 wks-32.69%, rest of the pt presented within 1-2 wks of age-28.84%, male: female ratio

1: 0.85,48.07% of patient having birth wt 2.5-2.9 Kg. Low birth wt was noted only 25%, more no of patient having CHD delivered in 37-38 wks of gestation that is 61.53%, most of the neonates were AGA that is 73.07%. SGA was observed 19.23% of cases, only 5 cases was borne to consanguineous married couple that is only 9.61%.

This study revealed more common basic type of CHD in neonate was Acyanotic heart disease, that is 73.07% and less common type was detected in Cyanotic heart disease that is 26.92% (Table I).

Table II Incidence of various types of CHD in neonate (n=52)

Name of the lesion	no of pt.	Percentage
Acyanotic (n-38): Atrial Septal Defect (ASD)	10	19.23%
Ventricular Septal Defect (VSD)	08	15.38%
ASD+PDA (Patent Ductus Arteriosus)	03	5.76%
ASD+VSD	04	7.69%
CoA (Coarctation of Aorta)+ASD	02	3.84%
ASD+PS (Pulmonary Stenosis)	02	3.84%
PDA	05	9.61%
ASD+VSD+A-V Canal defect	03	5.76%
AS (Aortic Stenosis)	01	1.92%
Cyanotic (n-14): Single Ventricle+TA	01	1.92%
DORV+VSD+PS	02	3.84%
TAPVR	01	1.92%
TGA+ASD	03	5.76%
TGA+VSD	01	1.92%
TOF	03	5.76%
Trancus Arterisious +VSD	02	3.84%
Ebstein Anomaly+PDA	01	1.92%

Table showing most common shunt anomaly in is ASD (19.23%), then VSD (15.38%) among acyanotic CHD & TOF and TGA is common type of cyanotic congenital heart disease among the cases that is 5.76% (Table II).

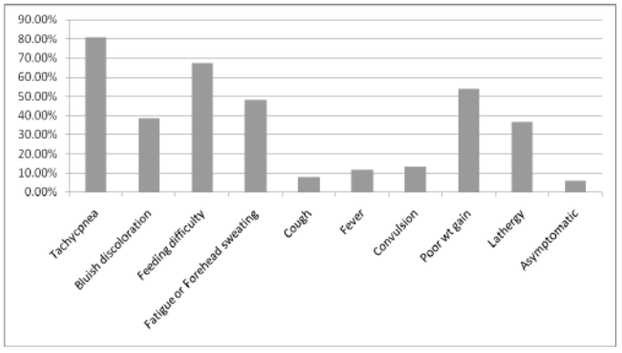

Figure 1 This graph shows more common symptoms is tachypnea (80.76%), then feeding difficulty (67.30%) and poor wt gain (53.84%)

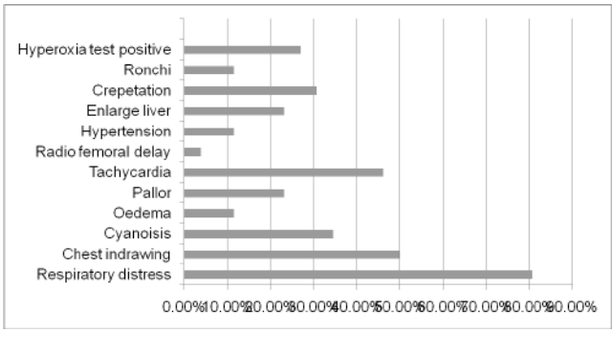

Figure 2 This graph showing most common physical findings are respiratory distress 80.76%, chest indrawing 50% and tachycardia 46.15%

Most common cardiac finding revealed cardiomegaly (26.92%), then murmur that is only 38.46%. Most prominent is Pan systolic murmur (45%), then Ejection systolic murmur that is 40% and Continues murmur 15%. Palpable P2 detected in 19.23%, Fixed splitting of S2 was found in 23.07%, Single S2 elicitted 9.69%.11.53% neonate presented with persistence fetal circulation following birth, Heart failure 23.07% and Pulmonary hypertension 19.23%.

Journal of Army Medical College Chattogram
Volume 4 Issue 1 June 2021; 11-16

Most common radiological abnormality was detected Plethoric lung field 28.84% then Cardiomegaly 26.92%, Pulmonary Opacity 19.23%, Olegaemic Lung field 11.53%, Dextro Cardia 3.84% and Boot Shape heart 1.92%.
Most common ECG feature identified as RVH 40.07% then RAD 38.46%, Biventricular hypertrophy 28.84%, P-Pulmonale 15.38%, rSr' QRS in V1 13.46%, LAD & LVH 9.61%. Extreme RAD was found 7.69% and Prolong P-R 3.84%.

Table III Echocardiography findings different types of lesion in neonate (n-52)

Type	Frequency	Percentage
ASD (n-25): Premium	04	16.0%
Secundum	21	84.0%
Small	13	52.0%
Medium	07	28.0%
Large	05	20.0%
VSD (n-20): Small	05	20.0%
Medium	09	45.0%
Large	06	24.0%
Malaligned	04	20.0%
Membranous	13	65.0%
Muscular	03	15.0%
PDA (n-8): Small	02	25.0%
Midium	03	37.5%
Large	03	37.5%
PS (n-7): Moderate	04	57.14%
Severe	03	43.0%
TOF (n-3): Severe	01	33.3%
Moderate	02	66.6%
A-V canal defect (n-03):		
Ostium Premium defect	02	66.6%
Endocardial Cushion def	01	33.3%
Shunt direction (n-52):		
Lt to Rt	30	57.69%
Rt to Lt	06	11.53%
Bidirectional	16	30.76%

This table shows 84% secundum ASD, 24% large VSD, 37.5% large & medium PDA and 57.69%Lt to Rt shunt (Table III).

Table IV Management given to patient under study (n-52)

Modalities of treatment	No. of pt.	Percentage
Medical		
• Ibuprofen to PDA	02	3.84%
• Frusemide	02	3.84%
• Frusemide + Spironolactone		
• Digoxin + Frusemide	08	15.38%
• After load reducing drug (Captopril/Analpril)+Digoxin+Sildenafil	05	9.61%
• High flow oxygen+Captopril+Sildenafil	10	
• β Blocker (Propranolol)		
• Prostaglandin-E +Frusemide	06	11.53%%
• Lonotrope+other drugs	05	9.61%
	02	3.84%
	12	23.07%
Catheter Intervention		
Balloon Atrial Septostomy	02	3.84%
PDA Stenting	01	3.84%
Ballon Angioplasty	01	1.92%
Surgery (Plan)	12	23.07%

Table V Immediate outcome of cases under study (n-52)

Outcome	No of pt	%
Improved	20	38.46%
Closed Spontaneously (ASD, VSD, PDA)	09	16.66%
Advised for routine follow up	09	17.30%
Expired	06	11.53%
Referred to specialized Cardiac Surgery Centre	08	15.38%

Discussion

Congenital heart decease occur in 0.5-0.8% of life birth[3]. However many studies have reported the incidence as 8 / thousand live births[12,13,2]. In a previous study conducted in CMH Dhaka 1st September 1999 to 31st August 2000 by NN Fatema et all found incidence of CHD among neonate 25/1000 live birth. But in this study revealed incidence of CHD among neonate is 10.13/100 admitted case in NICU and PCICU as all the live birth (Study period was not included).

In this study commonest type of congenital heart disease was Atrial Septal Defect (19.23%). This correlates with many studies like Fatema et al, Rahman et al, Siddique et al but differ from other study like Mitchell et al, Fyler DC et al, Hussan M et al, Mollah MAH et al [14,15,10,16,12,8,11]. They found VSD is the commonest lesion. This difference in observation might be due to they took sample form neonate to all age group children. A significant proportion of ASD closed spontaneously before end of infant period or most of them remain asymptomatic in neonate or childhood period and are diagnosed for the first time when they are adult. On the other hand a significant number 30-50% of small VSD close spontaneously most frequently during first 2 years of life[17].

In the study of Nahar et al found acyanotic heart disease was 85.4% & cyanotic heart disease 10.9% but we found acynotic 73.07% & cyanotic 26.92% possible due to small sample size[14]. They found male female ratio 1:1 but this study revealed male female ratio 1:0.85.

Journal of Army Medical College Chattogram
Volume 4 Issue 1 June 2021; 11-16

In this study we found 48.07% of cases presented with symptoms before they complete 1 wk of age. It is similar to Ravilala VK et al[18]. Most of the severe forms of congenital heart disease, like TGA, TOF, HLHS, HRHS, single ventricle, large VSD manifest in first week of life[19]. Similarly in a study conducted in Pakisthan on 44 neonates, the mean age of presentation was 5 days, with majority admitted on 1st day of life[20]. Present study correlates above study.

In the present study most common presentation was rapid respiration, feeding difficulty, Poor weight gain, convulsion, cyanosis, forehead sweating and heart failure. In a study conducted by Joshi et al in Mumbai, the commonest symptoms was hurried respiration, failure to thrive and refusal to feed[21]. It is also similar to Ravilala VK et al[18]. The observations were correlated with other studies in Bangladesh and western countries[14,22,4,23].

Cardiac findings revealed murmur (38.46%) and cardiomegaly (26.92%) were the most frequently observed features. Cardiomegaly was found mostly in VSD (80% cases). This observation is similar to that of keith[24]. In a study conducted in India, 2603 newborns were screened for the presence of a murmur and murmur was detected in 62 babies (2.3%) of whom 8 (45%) had a cardiac malformation[25]. This difference might be due to all neonate were not screened for murmur and also small sample size.

Most of ASD was secundum defect (84% of ASD) and VSD was membranous type 65% all VSD cases. Small, large and moderate PDA was found 15.38%. Left to right shunt was prominent which very close to other study[8]. Pulmonary hypertension was found 19.23% of all patient which is also close to other study[26].

In a study N N Fatema et al found 93 cases of persistent pulmonary hypertension of newborn or persistent fetal circulation among 6200 newborn over one year, but we found 6 cases out of 52 that is 11.53% as all the newborn was not included in this study[14].

In a study conducted in Pakistan, 36.4% of the newborn with congenital heart disease expired and all of them had severe type of congenital heart disease[20]. All the neonates were given symptomatic treatment and some cases immediate intervention was done. Immediate outcome with the treatment showed 38.46% patient was improved, 16.66% patients hunt closed spontaneously, 11.53% patient expired because of sever type congenital heart disease and delay in surgery. 17.30% patient was advised for routine follow up, 15.38% patient was sent for surgical management. In this study less percentage patient expired because of prompt management and available of all facilities in this center.

Conclusion

Congenital heart disease contributes a lot in neonatal mortality rate in our country. But mostly remain undiagnosed due to shortage of skill manpower, equipment in peripheral hospitals. High risk newborn screening program may be introduced to reduce the mortality rate. Early detection of neonatal CHD will help to reduce neonatal mortality rate as well as the smooth growth and development of infant.

Recommendation

Though the sample is small but the findings of this study will create a necessity for further study in a larger scale and scope for health planner and care provider to formulate a better planning to reduce neonatal mortality rate in our country and ultimately achieve Sustainable Development Goal-3.

Disclosure

All the authors declared no competing interests.

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Volume 4 Issue 1 June 2021; 11-16

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ORIGINAL ARTICLE

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Chemotherapy-Induced Cardiotoxicity: A Prospective Study

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ABSTRACT

Background: Cancer has become a major public health issue in Bangladesh over the last few years. For 20 most common malignancies, the overall ten year survival rate is 50%. For breast, melanoma, lymphoma and uterine cancers this number is even more high i.e. approximately 80%. Contrary to the improved long-term cancer survival rates there has been an increase in adverse cardiac effects of cancer treatment. The purpose of the study conduct the review ongoing chemotherapy regimens.

Materials and methods: This prospective analytical study was conducted at Chittagong Medical College Hospital and Center for Specialized Care and Research (CSCR) from January to December 2017. Total 610 participants were enrolled who received chemotherapy contains Doxorubicin, Trastuzumab, Gemcitabine, Palbociclib, Abiraterone Acetate for variouis malignancies. Patients were observed for cardiac events during and after the treatment for three years.

Results: Anthracyline chemotherapy has remained a mainstay treatment approach for cancer patients. Cardiotoxic side-effects of anthracyline chemotherapy regimens often limits their dosing. Although anthracylines and other drugs have been associated with improved cancer outcomes, there remains an increased risk of cardiovascular morbidity and mortality. Doxorubicin-induced cardio toxicity was 3%, Trastuzumab cardio toxicity was 6.67%, Gemcitabine induced cardiotoxicity was 6%, Palbociclib induced cardiotoxicity was 20% while Abiraterone Acetate cardio toxicity was 25%. The estimated cardio toxicity rate for our two-year follow-up was 6.39% for all specified chemotherapy regimens.

Conclusion : To conclude with perspective on model development needed to facilitate further progress and understanding on chemotherapy induced cardiotoxicity.

Key words: Anthracyclines; Cancer; Cardio toxicity; Gemcitabine; LVEF; Trastuzumab.

Introduction

Cancer has become a major public health issue in Bangladesh over the last few years.The number of prevalent cases (5-years) of cancer in Bangladesh was 270866 in 2020[1]. New cancer cases in 2020 were156775 and number of death due to cancer in 2020 were 108990 in Bangladesh[1]. In a lifetime, cancer affects more than one in three people. Cancer along with cardiovascular disease are the two leading causes of death in developed countries[2]. As per literature, the overall ten-year survival rate for cancer is at 50% across the 20 most common malignancies. However, the ten-year survival rate is even more high, i.e. approximately 80% or higher for breast, melanoma, lymphoma, and uterine cancers[2]. These mortality trends reflect a significant improvement in overall cancer survival rates. Contrary to the improved long-term cancer survival rates there has been an increase in adverse cardiac effects of cancer treatment. There has been a shift in cancer treatment from cancer survival to cancer survivorship[2]. Anthracyclines have remained the primary treatment for majority of solid tumours and hematological malignancies. Anthracyclines have remained an important treatment component for adult malignancies such as lymphoma, breast cancer, and sarcoma since their introduction in the 1960's[3]. Advancement in cancer treatment has led to increased long-term cancer survivors. However, the clinical use of anthracyclines have been associated with cardiac toxic effects which is based on the cumulative dose. Anthracycline-induced cardiac toxicity may ultimately lead to irreversible or severe forms of cardiomyopathy[4]. Even though recent advances in oncologic - therapy allow patients to live a prolonged life, severe complications such as the different types of therapy-induced toxicity, are still the main cause of death. Cardiac toxicity is the second cause of morbidity and mortality in breast cancer survivors[5]. Given the prolonged life expectancy due to new therapies, it is crucial to diagnose and prevent further cardiac dysfunction (Such as left ventricle dysfunction and cardiomyopathy) since early detection can

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Volume 4 Issue 1 June 2021; 17-20

mprove the outcome due to existent therapeutic measures[6,7]. Magnetic Resonance Imaging (MRI) and nuclear angiography can be used for the detection of cardiac toxicity[8]. However, echocardiography can be used as a cheaper and non-radioactive technique. It is easily available and presently considered as the best choice for continued cardiac toxicity evaluation. Continuous monitoring of patients using echocardiography should remain the mainstay for evaluating cancer treatment related cardiac toxicity. Although chemotherapy agents improve survival rate, assessing and monitoring cardiac toxic effects should be an integral part of patient management.

Chemotherapy is essential for most of the cancer treatment. But some chemotherapy causes cardio toxicity. The early detection of cardio toxicity by appropriate follow-up and monitoring is essential. Evaluation of patients using LVEF as a key parameter would help prevent irreversible cardio toxic events. Our purpose of the study this preliminary report may act as a base for researchers and academicians to conduct and review ongoing chemotherapy regimens.

Materials and methods

The prospective analytical study was carried out at Chittagong Medical College Hospital and Centre for Specialized Care and Research (CSCR). Patients diagnosed with different malignancies who were planned for chemotherapy regimen containing Doxorubicin, Trastuzumab, Gemcitabine, Palbociclib, Abiraterone Acetate were enrolled in this study from January 01, 2017 to December 2017. Total 610 patients were enrolled. All patients were observed for three years. A detailed examination of cardiovascular system was done at baseline and at each follow up. Participants were screened for hypertension, chest pain, breathlessness andoedema over feet during follow up. Renal function tests, liver function tests, ECG, chest X-ray and echocardiography was done at baseline and after every three cycles of chemotherapy and wherever indicated. Decrease in LVEF by 10% or symptoms related to decrease in cardiac activity (Dyspnoea, lower imboedema, pulmonary oedema) were taken in to consideration to determine cardio toxicity. A clinically significant decline in LVEF was defined as per standard criteria, i.e. a final LVEF of less than 50% or a 10% change from baseline. Anon-clinically significant decline in LVEF was defined as a drop of 10% but a final LVEF of more than 50%.

Chemotherapy Regimen

Doxorubicin

- For Breast patients : 50-60 mg per meter square body surface area per dose. Repeat cycle every three weeks.
- For Non-Hodgkin's Lymphoma : 50 mg per meter square body surface area per dose. Repeat cycle after three weeks.
- Hodgkin's lymphoma : 25 mg per meter square area per dose, repeat cycle after two weeks.

Gemcitabine

- 850 mg to 1000 mg per meter square body surface area per dose (Day 1 and day 8). Repeat dose after 3 weeks.

Trastuzumab

- Loading dose 8mg/kg and maintenance dose 6mg/kg

Palbociclib

- 125 mg orally per day for 21 days. Repeat cycle after 4weeks.

Abiraterone Acetate

- 1000 mg orally per day.Up to resistance.

Results

The study included a total of 610 patients of which 383 were females and 227 were males. A total of 250 (40.98%) of patients had breast cancer, 230 (37.7%) had Lung cancer and 40 (6.55%) had lymphoma, 70 (11.47%) had pancreatic cancer, 20(3.27%) had prostate cancer (Table I). The mean age and dose of each chemotherapy drug has been stated in Table II. All patients had their 2D-echo performed. Doxorubicin-induced cardio toxicity was 3%, Gemcitabine-induced cardio toxicity was 6%, Trastuzumab-induced cardio toxicity was 6.67% while Palbociclib cardio toxicity was 20% and Abiraterone Acetate cardio toxicity was 25% (Table III). The estimated cardio toxicity rate for our two-year follow-up was 6.39% for all aforementioned chemotherapy regimens.

Table I Types of malignancies reported in study population

Malignancy	Breast Cancer	Lung Cancer	Lymphoma	Pancreatic	Prostate
Males	0	139	26	42	20
Females	250	91	14	28	0
Total	250	230	40	70	20

Table II Chemotherapy drugs, mean age and average dose in study population

	Doxorubicin	Gemcitabine	Trastuzumab	Palbociclib	Abiraterone Acetate
No. of Patients	200 (M=32, F=168)	300 (M=165;F=135)	60 (M=0, F=60)	30 (M=0, F=30)	20 (M=20, F=0)
Mean Age	47.25	49.7	47.6	48.34	53.35
Dose	25-60 mg per meter square body surface area per dose	850 mg to 1000 mg per meter square body surface area per dose	Loading dose 8mg/kg and maintenance dose 6mg/kg	125 mg orally per day for 21 days. Repeat cycle after 4weeks	1000 mg orally per day. Up to resistance

Table III Cardiac toxicity status in study population

Name of Medication	No. of patients with cardiac toxicity	Percentage
Doxorubicin	6 out of 200	3%
Gemcitabine	18 out of 300	6%
Trastuzumab	4 out of 60	6.67%
Palbociclib	6 out of 30	20%
Abiraterone Acetate	5 out of 20	25%
Total	39 out of 610	6.39%

Journal of Army Medical College Chattogram
Volume 4 Issue 1 June 2021; 17-20

Discussion

Anthracyline chemotherapy has remained a mainstay treatment approach for cancer patients. Cardiotoxic side-effects of anthracyline chemotherapy regimens often limits their dosing. Although anthracylines have been associated with improved cancer outcomes, there remains an increased risk of cardiovascular morbidity and mortality[9]. Trastuzumab and anthracylines are well-known cardio-toxins. The rates of asymptomatic and symptomatic changes in LVEF differ among different patient populations[10]. This current retrospective study aimed at assessing the real-world implications and outcomes of trastuzumab and anthracyline use. This is one of the few studies that examines the different risk factors, specifically decline in LVEF in a general cancer cohort. Cardio toxicity increases with an increase in total cumulative dose of trastuzumab or anthracyclines[11]. We report a cardio toxicity rate of 3% due to doxorubicin. Trastuzumab-induced cardio toxicity was 6.67%. Shrum et al published a retrospective analysis of the case notes of 156 patients to further investigate and assess clinical features which may predispose patients to developing new-onset gemcitabine-induced cardiomyopathy[12]. All of the patients had received gemcitabine for various cancers in 1st or subsequent lines of treatment, 51 patients in ovarian cancer and 105 patients with breast, lung, pancreas and bladder cancer. Patients with new-onset congestive heart failure were compared with patients without new-onset congestive heart failure. 4.5% of patients developed new-onset congestive cardiac failure[13]. We report a cardio toxicity rate of 6% due to Gemcitabine. Limited data are available on the cardiac safety of CDK4/6 inhibitors. In the phase II PALOMA-1 trial, one patient in the palbociclib arm and one patient in the placebo were diagnosed with coronary artery disease and cardiac failure respectively[14]. In MONALEESA-2 and PALOMA-1, pulmonary embolism was found in two and four patients (0.6% and 5%) in the ribociclib and palbociclib arm, respectively, and in no patient in the placebo arm[14,15]. Here we found cardio toxicity in 6 out 20 patients who received Palbociclib, where cardio toxicity rate was 20%. Raphael et al shows that an increased risk of all-grade and grade ≥3 cardiovascular events for abiraterone[16]. Chopra et al reported a significant increase of cardiac toxicity and hypertension in patients receiving abiraterone[17]. Here we report a cardio toxicity rate of 25% due to Abiraterone.Patients who had symptoms of heart failure were treated with beta blockers, Angiotensin-Converting Enzyme (ACE) inhibitors and diuretics. Dexrazoxane is a derivative of Ethylene-Diamine Tetracyclic Acid (EDTA) that readily penetrates cell membranes and act as an intracellular iron, which may decrease anthracycline-induced free radial generation. Follow-up of patients with reported heart failure symptoms was conducted. All patients with a decline in LVEF and symptoms of heart failure were discontinued from ongoing chemotherapy.

Limitation

The study did not include biomarkers essential for assessment of cardio toxicity in cancer patients receiving cardio toxicity.

Conclusion

This is one of the very few prospective studies conducted in Bangladesh to highlight chemotherapy induced cardio toxicity. The early detection of cardio toxicity by appropriate follow-up and monitoring is essential. Disseminating knowledge on cardio toxic events in cancer patients is highly recommended to ensure higher standards of treatment and quality of care.Identifying drug-induced cardiac adverse effect as early as possible will help to prevent irreversible cardiac damage and to ameliorate the long-term morbidity and mortality rates as well as to improve the patients quality of life. This study may act as a base for researchers and academicians to conduct and review ongoing chemotherapy regimens.

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Disclosure

All the authors declared no competing interest.

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Journal of Army Medical College Chattogram
Volume 4 Issue 1 June 2021; 17-20

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ORIGINAL ARTICLE

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A Cross Sectional Study on Awareness of Consumers to Adverse Drug Reaction Reporting Related Aspects in a Tertiary Medical College Hospital

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ABSTRACT

Background: *Adverse Drug Reaction (ADR) monitoring and reporting is a multidisciplinary approach. Not only for health care Professionals (HCPs) but also for consumer. The present study was conducted to assess the awareness of consumers on ADR reporting in a tertiary medical college hospital.*

Materials and methods: *This was a descriptive cross sectional study in tertiary medical college hospital. Study period was March 2020 to July 2020 which was conducted on 300 patients as consumer of drug. Self administered questionnaires were distributed to a convenient sample of consumer.*

Results: *A total of 300 consumers from indoor department were included. It was found that 23% consumers were not aware of term ADR. 45% consumers or his/her family members experienced ADR of which 51.11% did not report it to anyone. Others (48.88%) reported it to doctors, nurses, drug sellers but no one reported to National pharmacovigilance centre i.e Directorate General of drug Administration (DGDA). Consumers who did not report to anyone mentioned that they (87%) did not know to whom and where to report. Most of the consumers (97%) were not aware that ADR should be reported to the DGDA. Majority (32%) of the consumers preferred telephonic method for reporting followed by online reporting system (24%).*

Conclusion: *Even though the acceptable attitude, consumers have poor knowledge and lack of awareness on ADR reporting and it could be improved by introducing educational interventional programs.*

Key words: Adverse drug reaction reporting; Pharmacovigilance; Consumers.

Introduction

No doubt that medicine is blessings for humanity and it fight against disease & sufferings but has also inherent risks along with their use, called Adverse Drug Reaction (ADR). ADR defines as 'any response to a drug that is noxious and unintended, and that occurs at doses used in humans for prophylaxis, diagnosis, or therapy, excluding failure to accomplish the intended purpose'[1]. Though most of the cases these reactions are mild but have possibility to cause disability even death. 4.2-6.0% of all hospital admission is due to ADR & ADR occur in about 10-20% of all hospitalized patient[2-3]. Identification, assessment & prevention of ADR i.e Pharmacovigilance (PV) is globally is one of the main tools used to patient safety and care. The importance of pharmacovigilance is increasing day by day because the frequency of ADR and percentage of hospital admission due to ADR is increasing day by day[4]. Among the various method of PV, spontaneous reporting being the most widely used successful method which has traditionally been solitary responsibility of Health Care Professionals (HCPs). In addition to HCPs, drug consumers also play a vital role to strengthen the pharmacovigilance programme[5]. If spontaneous report coming from consumers as well as patients, it promotes better understanding, more detailed and direct and explicit than indirect reports from HCPs[6]. Early detection of ADRs, ADRs reporting of Over the Counter Drug (OTC) alternative medicine and promotion of consumer's right are the advantage of consumer's reporting. Considering importance of consumers reporting, direct consumer's reporting system subsists in many countries[7]. Direct ADR reporting system by the consumers exist in 44 countries which represent 9% of the total ADR reports, the rest coming from HCPs[8]. Consumer's reporting is a new concept. It will add the additional layer for good pharmacovigilance as they have the first hand knowledge of experience with ADR[9-11]. In 1960, The United States commenced

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Journal of Army Medical College Chattogram
Volume 4 Issue 1 June 2021; 21-24

first program where the consumers had opportunity to report directly to the Food and Drug Administration (FDA). In 2006, Belgium received ADR reports from a consumer and transfers them to Federal Agency of Medicine & Health Products (FAMHP). The United Kingdom also made robust efforts to promote consumer reporting. Since 2010, Norwegian Medicine Agency started to accept electronic reports from consumers[12]. In 2007, Malaysia initiated patient reporting[13].

In Bangladesh, Pharmacovigilance was introduced and practiced under supervision of WHO-UMC (WHO- Uppsala Monitoring Committee). Adverse Drug Reaction Monitoring (ADRM) cell was established under Directorate General of Drug Administration (DGDA) in 1996[14]. Spontaneous ADR report submission is encouraged by all private and government institutional health care professionals (Doctors, nurse and pharmacist). Not only HCPs but also patient or consumers can also report of ADR if they suspect. Questions can be arises on the consumer reporting of ADRs regarding the quality of reports. Study showed that no countries had reported poor quality of consumer's report[6]. Major drawback of spontaneous reporting system is underreporting. Unfortunately it was seen that Directorate General of Drug Administration (DGDA) authority received only 50 ADR reports in the last 20 years period (1994-2013). Only 10 reports of which were properly completed[15]. More than half of the study population experienced ADRs but they were unfamiliar with the existence of ADR reporting body of Bangladesh. Many of the study population were unknown about the reporting process, while some had fear of legal liabilities associated with ADRs reporting[14]. Simple awareness regarding drug safety which may be taken in the form of pharmacovigilance is needed by the HCPs (Doctors, nurses) drug seller and even patients as consumers. Many people in our country are unaware about the existence function and purpose of national ADR reporting procedure. Due to lack of this awareness people are staying behind the pioneer role in saving lives. Moreover in Bangladesh where the scenario of ADR reporting practice by the physician is not satisfactory currently and hence to start the culture of ADR reporting by the consumer is highly challenging[16]. Mass media involvement in creating the awareness among general people should be raised more. Emphasis should be placed to create awareness on ADR reporting practice among HCPs as well as Consumers. Consumers should know that they have also right to report ADR. In our neighbor country India Consumer's ADR reporting rate was very low but in Bangladesh no such data was found[17]. The most important determinants of consumer's ADR reporting are their awareness about ADR reporting. Hence the present study was planned to determine awareness regarding ADR reporting among consumer.

Materials and methods

This was a descriptive cross sectional questionnaire based study in a tertiary medical college hospital during the period of March 2020 to July 2020. A total of 300 questionnaires were used as samples by convenient sampling technique. 300 questionnaires were distributed to indoor patients as consumers. Before filling up the questionnaire, the objectives of the study and the contents of the questionnaire were personally briefed to each participant. The respondents were asked to answer and return the questionnaire. The study was conducted by using self designed pre tested questionnaire to obtain information on awareness of consumers towards adverse drug reaction reporting along with their experience on adverse drug reactions and reporting, preferred method of reporting. Data was analyzed using SPSS software (version 18).

Inclusion criteria:

- All the patients admitted to the inpatient departments.
- Patients agreed to participate and willing to co-operate during the study.
- Patient with at least primary school pass, so that she/he can read and understand the questionnaire.

Exclusion criteria:

- Patients visiting out-patient departments were excluded.
- Patient who are not primary school pass were excluded.

Ethical permission was taken from IRB of CMOSHMC.

Results

The analysis in the study is based on the 300 respondents who participated in the study. The age range of the 300 patients was 18-70 years (Mean age was 31.92 years, SD ± 11.59). 59% of respondents were found to me female and 41% were males. Most of the respondents (27%) were SSC pass, 23 % were graduates, 18% were HSC pass, 8% primary school pass and 8 % were post graduates. Demographic details of the respondents are shown in Table I.

Table I Demographic characteristics of respondents (n=300)

Characteristics	Respondents
Age group	
18-25	47%
26-50	47%
>50	6%
Gender	
Male	41%
Female	59%
Education Level	
Primary school	8%
High school	16%
SSC	27%
HSC	18%
Graduate	23%
Post graduate	8%

Journal of Army Medical College Chattogram
Volume 4 Issue 1 June 2021; 21-24

The analysis of the questionnaire showed that 77% respondents were aware of term ADR. 45% consumer's or his/her family member experienced ADR. Among the respondents who experienced ADR, 48.88% respondents reported it and 51.11% did not report to anyone. Among the respondents who reported ADR, 68.18% reported to doctor, 9.09% reported to nurse and 22.72% reported to drug seller but no one reported directly to the DGDA. The findings from our study indicate that many consumers (51.11%) did not report to anyone even though they experienced ADR. The Reasons for not reporting to anyone was mainly due to most of the consumers (87%) did not know to whom and where to report and 78.3% were fully unaware that it has to be reported. Other reasons for not reporting to anyone are shown in Table II.

Table II Reasons given by the consumers for not reporting of ADR

Reasons	Respondents
The side effect was not serious enough	17.4%
As soon as I stopped the drug the reaction was healed by itself	17.4%
I was not sure that the reaction was due to drug	30.4%
I felt it would resolve itself	21.7%
I was fully unaware that it has to be reported	78.3%
I did not know to whom and where to report	87%
Reporting process is complicated for me	0

*Multiple answers allowed. *n= number of consumers who experienced ADR but did not report it to anyone.

97% consumers did not know that any ADR should be reported to DGDA and 98 % consumers did know that the DGDA office is situated in the Mohakhali, Dhaka. However, 92% consumers did not know that he or she has right to report directly to the DGDA. Moreover, 96% consumers were willing to report themselves directly to the DGDA. The respondent's preferred method for ADR reporting in future was telephonic method (32%) followed by online reporting (24%) and mobile app (24%). Other consumers preferred e mail and hospital drop box (Figure1).

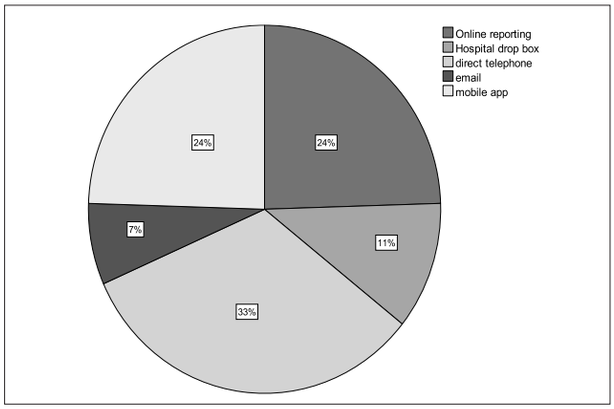

Figure 1 Preferred method for ADR reporting

Discussion

The most important determinants of consumer's ADR reporting is awareness of the ADR and it's reporting. 23% respondents did not know term ADR. Many consumers (45%) experienced ADR but among them 51.1% did not report it to anyone and those who reported ADR they reported it to the Health Care Professionals (HCPs) or drug seller but no one reported it to our National reporting system (DGDA). This indicates lack of awareness of ADR reporting process of our country. Similar study was found in India where only 8.9% consumers thought of reporting it and also in developed country consumers reporting rate of ADR was only 23.4%[18,19]. In this study, 68.8% reported ADR to doctors whereas in a study in India consumers considered that for reporting of ADR, only doctors are to be the right person[18]. The reasons behind not reporting of ADR to any one was mainly many of the consumers (78.3%) were fully unaware that it has to be reported which possibly indicate ignorance about their health issue. The another important reasons were found that many of them (87%) did not know to whom and where to report. This reason reflects their unawareness about the reporting system. 97% consumers were unaware that ADR should be reported to DGDA. This similar findings were also observed in India where most of the respondents were unaware about their National ADR reporting programme[18,19]. 96% consumers intended to report ADR directly to DGDA if there is a convenient way to report which indicate positive attitude towards ADR reporting. So it is essential to provide them the knowledge about how to report to our National reporting system so that they can contribute to generate more report and take part to enrich and strengthen our reporting system. Consumers were asked to choose one preferred method for their reporting. Most of the consumers (33%) preferred telephonic method to report ADR which is in line with the Indian Study[20]. Many consumers (24%) also preferred online reporting process and mobile app. This study revealed that in maximum cases, consumers do not report drug reaction to anybody but in some cases they report to HCPs and drug seller. Most of them are not aware of our National ADR reporting system. Steps should be taken to make the consumer aware of reporting adverse effect of drug as there is a Government body for receiving report of adverse effect of drug i.e DGDA.

Limitations

This study was done in one hospital setting and sampe size was not large enough due to pandemic situation of COVID 19.

Conclusion

The present study reveals a basic idea about the awareness of consumers for ADR reporting. This result reflects poor awareness of the consumers towards ADR reporting system. This situation could be improved a lot by introducing educational intervention program in hospitals and clinics. Mass media may develop awareness and motivate consumers to report ADR. HCPs may also encourage the consumers to report ADR and this will bring out a basic and fruitful improvement in ADR reporting.

Journal of Army Medical College Chattogram
Volume 4 Issue 1 June 2021; 21-24

Recommendation

The consumers should be informed of the procedure for reporting. In that case, mass media, social media may play a very important role. HCPs those who are aware of it, they should transmit the knowledge to their colleagues and also to their patient. Government may also arrange publicity in this respect.

Acknowledgement

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Disclosure

All the authors declared no competing interest.

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ORIGINAL ARTICLE

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Functional Outcome of Epidural Steroid Injection in the Management of PLID with Radiculopathy

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ABSTRACT

Background: A Prolapsed Lumbar Intervertebral Disc (PLID) causes Low Back Pain (LBP) incapacitating musculoskeletal disorder with considerable social and economic burden. It is common in people with age range from 20 to 45 having clinically significant sciatica in 4-6% of the population. Different conservative, nonsurgical varieties for treating PLID or radicular pain exist, including medications, physical therapy, manipulation and alternative therapy. Surgery is associated with a failure rate of 25%, henceforth Epidural Steroid Injection (ESI) is highlighted amongst the most widely recognized nonsurgical treatments for PLID. The aim of this study was to evaluate functional outcome of ESI in the management of PLID with radiculopathy in Rajshahi Medical College Hospital, Rajshahi that may contribute to more appropriate management of patients with LBP due to PLID with radiculopathy.

Materials and methods: A prospective comparative study was carried out in the Department of Physical Medicine & Rehabilitation at Rajshahi Medical College Hospital, Rajshahi for a period of one year from July 2015 to June 2016. A total number of 130 patients with PLID of both sexes who fulfilled the selection criteria were included in the study. Patients were randomly divided into two groups, as study group 'A' and control group 'B'. Each group was containing 65 patients. Group 'A' patient were treated with Epidural Steroid Injection (ESI) plus other conservative treatment and group 'B' patients were treated with conservative measures only. The follow up of the all patients of both groups were done at 3, 6 and 12 weeks of first visit. The outcome of patient assessed by Straight Leg Raising (SLR) test Visual Analogue Scale (VAS) for pain, Finger To Floor Distance (FTFD) and Ronald Morris Disability Questionnaire (RMDQ) score.

Results : In the distribution of 130 PLID patients male was predominant than female with mean age 36.64±9.6 in group A and 37.62±8.0 in group B. Comparison of VAS pain score between two groups is statistically significant in first follow up but not significant in 2nd and 3rd follow up. Mean consumption of diclofenac sodium 50 mg in group A was 17.5±3.5 tab/week in week 0, 13.5±2.11 tab/week in week 3, 11.7±2.9 tab/week in week 6 and 7.6±5.25 tab/week in week 12 . In group B it was 16±3 tab/week in week 0, 13.6±1.4 tab/week in week 3, 12±2.96 tab/week in week 6 and 8.85±3.25 tab/week in week 12. SLR score between two groups is statistically significant in first follow up but not significant in successive follow up. Comparison of FTFD score between two groups is statistically significant in first follow up but not significant in 2nd and 3rd follow up.

Comparison of RMDQ score between baselines to each follow up in group A is statistically significant. In case of group B the score between baselines to 1st follow up is not significant but baseline to week 6 and week 12 follow up is significant.

Conclusion: The study revealed that ESI group has statistically significant improvement of all parameters in week 3 follow up. Comparison between two groups in every parameter (VAS, FTFD, RMDQ and SLR) of outcome revealed that study group had statistically significant improvement in week 3 follow up but in successive follow ups improvement is insignificant, therefore epidural steroid injection has better outcome only for a short term period.

Key words: Disc herniation; Epidural steroid; LBP; Radiculopathy; Ultrasound.

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Introduction

A Prolapsed Lumbar Intervertebral Disc (PLID) is a spinal condition that can cause Low Back Pain (LBP) as well as numbness, tingling, a "pins and needles" feeling and muscle weakness in the lower body[1]. It is a widespread and incapacitating musculoskeletal disorder with considerable social and economic importance[2].

It can happen to people of all ages, but is most common in people 20 to 45[1]. Most lumbar disc prolapses are located laterally and give symptoms from one or at most two spinal roots of the sciatic nerve[3]. The life time incidence LBP is 50-70% and the incidence of sciatica may be as high as 40%[4]. However, clinically significant sciatica due to disc prolapse occurs in 4-6% of the population[5].

Journal of Army Medical College Chattogram
Volume 4 Issue 1 June 2021; 25-30

The degeneration of intervertebral disc from a combination of factors can result in herniation, particularly at the L_4-L_5 and L_5-S_1 levels in more than 90% of the cases[4]. The presence of pain radiculopathy and other symptoms depend on the site and degree of herniation. Magnetic Resonance Imaging (MRI) may help to confirm the diagnosis. Different conservative, nonsurgical varieties for treating PLID or radicular pain exist, including medications, physical therapy, manipulation and alternative therapy[6]. If conservative treatment fails, then surgery, the most invasive treatment modality is commonly carried out for chronic persistent pain of disc herniation with or without radiculopathy[7]. Unfortunately, surgery is associated with a failure rate of 25% in well-reviewed patients[8]. On the other hand Epidural Steroid Injection (ESI) is highlighted amongst the most widely recognized nonsurgical treatments for PLID[9]. Suppression of the biochemical factors of inflammation is the rationale behind the use of corticosteroids in LBP leading to reduction in soft-tissue swelling, oedema, pressure, soft adhesions and slow regression of disc herniation[10]. Epidural Steroid Injections (ESIs) localize the drug around the area of affected nerve roots, thereby decreasing systemic effects and side-effects. There is a chance of exposure of radiation in case of fluoroscopy guided ESI in comparison to Ultrasound (US) where there is no chance to exposure of radiation[11]. A curved-array, low-frequency (2–5 MHz) probe is recommended because the wide field of view and deeper penetration improve recognition of anatomy and image quality respectively There are three approach of ESI: Interlaminar, trans foraminal and caudal approach. Among these, interlaminar approach with or without fluoroscopy or ultrasono guide is a popular approach for the lumbar region[12,13,14,15]. Agents commonly used are methylprednisolone acetate, triamcinolone acetonide and dexamethasone. Among these triamcinolone is more safe and inexpensive but similar in efficacy[16,17,18]. ESIs are administered with dilution using local anesthetics. Bupivacaine is a potent local anesthetic agent with a long duration of action. 0.125% Bupivacaine acts as adequate analgesic agent. Interlaminar approach with or without fluoroscopy or ultrasono guide is a popular approach for the lumbar region. Considering more availability and user friendly in outdoor setting, Ultrasound (US) guide support is taken in this study with the aim to study the functional outcome of epidural steroid injection in the management of PLID with radiculopathy.

Materials and methods

A prospective comparative study was carried out in the Department of Physical Medicine & Rehabilitation at Rajshahi Medical College Hospital, Rajshahi for a period of one year from July 2015 to June 2016. A total number of 130 patients with PLID of both sexes who fulfilled the selection criteria were included in the study.

Inclusion criteria

- Age 20-50 years
- Body Mass Index (BMI) between 15-30 kg/m^2
- LBP with radiculopathy on either left or right lower limb up to six months
- MRI evidence of lumbar intervertebral disc prolapse.

Exclusion criteria

- Symptoms requiring early surgical intervention
- Structural spinal deformities (Scoliosis >40°, Spondylolisthesis)
- Received any spinal injection, low back surgery, chemonucleolysis, or nucleotomy
- Associated with Inflammatory LBP.

Patients were randomly divided into two groups, as study group 'A' and control group 'B'. Each group was containing 65 patients. Group 'A' patients were treated with Epidural Steroid Injection (ESI) plus other conservative treatment and group 'B' patients were treated with conservative measures only.

Intervention: US Guided Epidural Steroid Injection

During performing the procedure patient was in prone position placing a pillow under the abdomen to help open up the lumbar interlaminar space by reversing lumbar lordosis. With all aseptic precautions epidural steroid in the form of triamcinolone acetonide 80 mg along with local anesthetic agent in the form of 0.125% Bupivacaine injection had been given. The procedure was performed under the guidance of ultrasound which helped to locate the epidural space as well as maintain the accuracy. Patients were kept under observation for 1 hour after the procedure. If patient is still symptomatic, ESI should be repeated till a maximum of 210 mg/year of triamcinolone injections.

Conservative Therapy

Conservative therapy in both the groups included drugs as: NSAIDs-diclofenac sodium 50mg three times daily or as required, muscle relaxant-baclofen 10 mg twice daily, neuropathic pain reliever-pregabalin 75 mg two to three times daily and tricyclic antidepressant-amitriptyline 10 mg once daily. Activities Daily Livings (ADLs) instructions and individualized therapeutic exercise according to the phase of PLID were prescribed to both groups for pain management and restoration of functional deficit associated with disc injury.

Follow Up and Outcome Measures

The follow up of the all patients of both groups were done at 3, 6 and 12 weeks of first visit. The following examinations are performed to assess the outcome of the study:

i) Straight Leg Raising (SLR)[1] test: Restriction of angles to 60^0-<90^0, 30^0-<60^0, <30^0 was considered as mild (Grade 1) moderate (Grade 2) and severe (Grade 3) respectively.

ii) Finger To Floor Distance (FTFD) [1]: The degree of flexion was recorded by measuring the distance between the finger tip and the floor.

iii) Visual Analogue Scale (VAS): The patients were asked to mark on 100 mm horizontal line, the point that they feel to represent their perception of current state[19].

Journal of Army Medical College Chattogram
Volume 4 Issue 1 June 2021; 25-30

iv) Roland-Morris low back pain Disability Questionnaire (RMDQ)[20, 21].

The research protocol was approved by the ethical committee of Rajshahi Medical College. Informed consent was taken from each patient. The procedure, risks and benefits of this study were explained to the respondent. Data was collected using a preformed data collection sheet and presented on a categorical scale compared between the groups using Chi-square and Fisher's Exact Probability test, while the data presented on a quantitative scale was compared between the groups using student's 't' test. Statistical analysis was performed by using SPSS-17.

Results

A total number of 130 PLID patients completed follow up for this study. Among these 65 patients were in study group (Group A) and 65 patients were in the control group (Group B). Baseline characteristics of patients mentioned in the following tables are gender, age, NSAID score and pain score.

Table I Distribution of the study population according to gender

Gender	Group A(n=65)	Group B(n=65)	p value
Male	55 (84.6%)	53 (81.5%)	0.645
Female	10 (15.4%)	12(18.5%)	
Total	65 (100.0%)	65 (100.0%)	

Table I shows the distribution of patients according to gender. In group A male was predominant than female which were 55(84.6%) cases and 10(15.4%) cases respectively. In group B male was also predominant than female which was 53(81.5%) cases and 12 (18.5%) cases respectively. The difference between these two groups was not statistically significant.

Table II Distribution of the study population according to age

Age (years)	Group A(n=65)	Group B(n=65)	p value
20-30	12 (19.2%)	13 (19.7%)	0.400
31-40	30 (45.2%)	22 (34.4%)	
41-50	23 (35.6%)	30 (45.9%)	
Total	65 (100%)	65 (100.0%)	
Mean age	36.64±9.6	37.62±8.0	

Table II shows distribution of patients according to age. In group A, majority of the patients was in the age group of 31- 40 years which was 30 (45.2%) cases followed by 41-50 years 23 (35.6%), then 20-30 years group 12 (19.2%). In group B, majority of the patients were in the age group of 41 - 50 years which was 30 (45.9%) cases followed by 31 - 40 years group and 20-30 years age group which were 22 (34.4%) cases and 13(19.7%) cases respectively. The mean age of the patients was 36.64±9.6 in group A and 37.62±8.0 in group B. The difference of age between these two groups was not statistically significant.

Table III Distribution of patients according to VAS pain score at week 0 : Group A (n=65) vs. Group B (n=65)

VAS score	Group A Mean±SD	Group B Mean±SD	p value
Week 0	9.5±.809	8.9±1.009	0.023

Table III shows that distribution of VAS pain score between two groups (Group A and Group B) on baseline (Week 0) was not statistically significant.

Table IV Distribution of the patients according NSAID intake

	Group	Mean± SD	p value
Week 0	Group A	17.5±3.5	0.055
	Group B	16±3	
Week 3	Group A	13.5±2.11	0.772
	Group B	13.6±1.4	
Week 6	Group A	11.7±2.9	0.675
	Group B	12±2.96	
Week 12	Group A	7.6±5.25	0.176
	Group B	8.85±3.25	

From Table IV it was seen that in case of group A, mean consumption of diclofenac sodium 50 mg was 17.5±3.5 tab/week in week 0, 13.5±2.11 tab/week in week 3, 11.7±2.9 tab/week in week 6 and 7.6±5.25 tab/week in week 12. And in case of group B, the mean consumption of diclofenac sodium 50 mg was 16±3 tab/week in week 0, 13.6±1.4 tab/week in week 3, 12±2.96 tab/week in week 6 and 8.85±3.25 tab/week in week 12. The P value between the two groups were 0.055, 0.772, 0.675 and 0.176 in week 0, week 3, week 6 and week 12 respectively which were not statistically significant.

The outcome of patient assessed by Straight Leg Raising test (SLR), Visual Analogue Scale (VAS) for pain, Finger To Floor Distance (FTFD) and Ronald Morris Disability Questionnaire (RMDQ) score (Table V – Table VIII).

Table V Comparison of patients according to VAS pain score Group A (n=65) vs. Group B (n=65)

VAS score	Group A Mean±SD	Group B Mean±SD	p value
Week 0	9.5±.809	8.9±1.009	0.023
Week 3	5.69±1.9	6.02±1.6	0.041
Week 6	4.4±2.04	4.2±1.66	0.392
Week 12	2.34±1.26	3.06±1.8	0.228

Table V shows that :-

- In case of group A, comparison of VAS pain score between baseline (Week 0) and each follow up (Week 3, week 6 and week12) was statistically significant.
- In case of group B comparison of VAS pain score between baseline (Week 0) and 1st follow up (Week 3) was not

Journal of Army Medical College Chattogram
Volume 4 Issue 1 June 2021; 25-30

significant (p value =0.06). But between baseline and week 6 and week 12 follow up was significant· Comparison of VAS pain score between two groups (Group A and group B) was statistically significant in first (Week 3) follow up (p value=0.041) but was not significant in 2nd (Week 6) and 3rd (Week12) follow up.

Table VI Comparison of the patients according to SLR

	Group A Mean±SD	Group B Mean±SD	p value
Week 0	43.04±16.48	53.15±17.68	0.056
Week 3	63.69±14.84	64.24±14.72	0.031
Week 6	69.67±14.6	72.93±10.25	0 .940
Week 12	81.4±10.5	78.26±11.7	0.557

Group A (n=65) vs. Group B (n=65).

Table VI shows that comparison of SLR score between two groups (Group A and Group B) was statistically significant in first (Week 3) follow up (p value=0.031) but was not significant in 2nd (Week6) and 3rd (Week12) follow up.

Table VII Comparison distribution of the patients according to FTFD

	Group A Mean±SD	Group B Mean±SD	p value
Week 0	42±15.05	32.96±15.3	0.056
Week 3	23.28±13	27.20±12.9	0.047
Week 6	17.9±9.76	16.35±10.8	0.104
Week 12	11.83±10.95	11.54±11.4	0.809

Table VII shows that :-

- In case of group A comparison of FTFD score between baseline (week 0) and each follow up (Week 3, week 6 and week12) was statistically significant.
- In case of group B comparison of FTFD score between baseline (Week 0) to 1st follow up (week3) was not significant (p value =0.064). But baseline to week 6 and week 12 follow up was significant.
- Comparison of FTFD score between two groups (Group A and Group B) was statistically significant in first (week 3) follow up (p value=0.047) but was not significant in 2nd (Week 6) and 3rd (Week 12) follow up.

Table VIII Comparison of the patients according to RMDQ Score
Group A (n=65) vs. Group B (n=65)

	Group A Mean±SD	Group B Mean±SD	p value
Week 0	17.30±3.67	16.20±2.9	0.056
Week 3	11.33±4.26	12.22±3.6	0.045
Week 6	8.93±4.43	8.54±4.08	0.468
Week 12	4.89±3.28	5.46±4.16	0.536

Table VIII shows that :-

- In case of group A comparison of RMDQ score between baseline (Week 0) and each follow up (Week 3, week 6 and week 12) was statistically significant.
- In case of group B comparison of FTFD score between baseline (Week 0) and 1st follow up (week 3) was not significant (p value =0.059). But baseline to week 6 and week 12 follow up was significant.

Discussion

The distribution of 130 PLID patients according to gender revealed male was predominant than female which were 55(84.6%) in group A and 53(81.5%) in group B. The difference between these two group was not statistically significant (p=0.645).

In group A, majority of the patients were in the age group of 31 to 40 years (45.2%) followed by 41 to 50 years group (35.6%) and 20 to 30 years age group (19.2%). In group B, majority of the patients were in the age group of 41 to 50 years (45.9%) followed by 31 to 40 years group (34.4%) and 20 to 30 years age group (19.7%). The mean±SD age of the patients was 36.64±9.6 and 37.62±8.0 in group A and group B respectively. The difference of age between these two groups was not statistically significant (p=0.400). Borman et al (2003) have reported that most of the cases PLID occur after the age of 35 years which is very similar to the present study[22].

The outcome of patient was assessed by visual analogue scale, Straight Leg Raising (SLR) test, Finger To Floor Distance (FTFD) and Ronald Morris Disability Questionnaire (RMDQ) score. For the assessment of pain a visual analog scale was used. In group A, at the beginning of treatment, the mean VAS score of the respondents was 9.5±0.809 cm. The VAS score gradually decreased in week 3, week 6 and week 12. And the comparison of VAS pain score between week 0 and each follow up of group A was statistically significant, p value of which were 0.01, 0.009, 0.003 for 1st, 2nd and 3rd follow up respectively. In group B, at the beginning of treatment, the mean VAS score of the respondents was 8.9±1.009 cm. Here also the VAS score gradually decreased in week 3, week 6 and week 12. The comparison of VAS pain score between week 0 and 1st follow up was not significant but the 2nd and 3rd follow up was significant, p value of which were is 0.06, .02, .005 in 1st, 2nd and 3rd follow up respectively. But between two groups in 1st follow up p value is 0.041, in 2nd follow up p value=0.392 and 3rd follow up p value=0.228 i.e. the difference was significant in 1st follow up but not significant in 2nd and 3rd follow up. The similar result was found in the study done by Col Rashmi Datta et al 2011 where it was seen that steroid group and placebo group result was not significant[18].

In case of Straight Leg Raising (SLR) test it was revealed that in group A, at the beginning of treatment the mean SLR score of the respondents was 43.04±16.48. The SLR score gradually increased in week 3, week 6 and week 12.

Journal of Army Medical College Chattogram
Volume 4 Issue 1 June 2021; 25-30

The comparison of SLR score between week 0 and each follow up in group A was statistically significant, p value of which were 0.041, 0.017, 0.008 in 1st, 2nd and 3rd follow up respectively. In group B, at the beginning of treatment, the mean SLR score of the respondents was 53.15±17.68. Here also the score gradually increased in week 3, week 6 and week 12. The comparison of SLR score between week 0 and 1st follow up was not significant but in the 2nd and 3rd follow up comparison was significant, p value of which were 0.053, 0.025, 0.016 in 1st, 2nd and 3rd follow up respectively. But comparison of SLR score between two groups, in 1st follow up p value is 0.031, in 2nd follow up p value is 0.94 and in 3rd follow up p value was 0.557 i.e the difference was significant in 1st follow up but was not significant in 2nd and 3rd follow up. The similar result was found in the study done by Col Rashmi Datta et al where it was seen that comparison between steroid group and placebo group result was not significant[18].

In case of Finger To Floor Distance (FTFD) was seen that in group A, at the beginning of treatment, the mean FTFD score of the respondents was 42±15.05cm. The FTFD score gradually decreased in week 3, week 6 and week 12. The comparison of FTFD score between week 0 to each follow up of group A is statistically significant, p value of which were 0.009, 0.004, 0.0012 in 1st, 2nd and 3rd follow up respectively. In group B, at the beginning of treatment, the mean FTFD score of the respondents was 32.96±15.33cm. Here also the score gradually decreased in week 3, 6 and week 12. The comparison of FTFD score between week 0 and 1st follow up is not significant but in the 2nd and 3rd follow up p value was significant which were 0.064, 0.003 and 0.0016 in 1st, 2nd and 3rd follow up respectively. But in comparison between the two groups in 1st follow up p value was 0.047, in 2nd follow up p value was 0.104 and in 3rd follow up p value was 0.809 i.e the difference was significant in 1st follow up but not significant in 2nd and 3rd follow up. The similar result was found in the study done by Col Rashmi Datta et al where it was seen that comparison between steroid group and placebo group result was not significant[18].

In case of Ronald Morris Disability Questionnaire (RMDQ) score, it was revealed that in group A, at the beginning of treatment the mean RMDQ score of the respondents was 17.3±3.67. The RMDQ score gradually decreased in week 3, week 6 and week 12. And the comparison of RMDQ score between week 0 to each follow up of group A was statistically significant, p value of which were 0.04, 0.017, 0.002 in 1st, 2nd and 3rd follow up respectively. In group B, at the beginning of treatment, the mean RMDQ score of the respondents was 16.2±2.9. Here also the score gradually decreased in week 3, week 6 and week 12. The comparison of RMDQ score between week 0 to 1st follow up was not significant but the 2nd and 3rd follow up was significant, p value of which were 0.059, 0.023, 0.01 in 1st, 2nd and 3rd follow up respectively. But comparison RMDQ score between the two groups, in 1st follow up p value was 0.045, in 2nd follow up p value=0.468 and 3rd follow up P value=0.536 i.e the difference is significant in 1st follow up but not significant in 2nd and 3rd follow up. The similar result was found in the study done by Col Rashmi Datta et al where it was seen that comparison between steroid group and placebo group result was not significant[18].

Conclusion

From this study it is seen that comparison between baseline and follow ups ESI group has statistically significant improvement in week 3 follow up according to Visual Analogue Scale (VAS), Finger To Floor Distance (FTFD), Ronald Morris Disability Questionnaire (RMDQ) score and Straight Leg Raising test (SLR). But in next follow ups both the groups show statistically significant improvement.

Comparison between the two groups (Study group and control group) in every parameter (VAS, FTFD, RMDQ and SLR) of outcome revealed that study group had statistically significant improvement in week 3 follow up but in successive follow ups improvement is insignificant. So it can be said that epidural steroid injection has better outcome only for a short term period.

Recommendations

Further studies with larger sample size are needed in our country for better understanding to evaluate the efficacy of epidural steroid injection in the management of PLID patients.

Disclosure

All the authors declared no competing interest.

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Journal of Army Medical College Chattogram
Volume 4 Issue 1 June 2021; 25-30

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ORIGINAL ARTICLE

Journal of Army Medical College Chattogram
Volume 4 Issue 1 June 2021; 31-35

Hypertension and its Associated Risk Factors among Military Personnel

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ABSTRACT

Background: Hypertension is a major public health problem all over the world because of its high prevalence and its association with increased risk of cardiovascular disease and other complications. It is a silent killer and most patients are detected to have it incidentally when they are admitted to hospital for unrelated disease or subjected to pre-employment or pre-operative medical checkups. The aim of the study was to find out the prevalence of hypertension and status of its risk factors among the soldiers of Rangpur Cantonment.

Materials and methods: This descriptive cross-sectional study was conducted at Medical Inspection (MI) room, Combined Military Hospital (CMC) Rangpur from July 2018 to December 2018. A total of 151 cases were selected through purposive sampling technique. Data collection was carried out by the researcher through face to face interview.

Results: Out of 151 respondents 15.9% were hypertensive. Most of the respondents (55.0%) were NCO (Non-Commissioned Officer). Among the participants 90.1% were married. Majority of the respondents (38.8%) were in the age group of 31-40 years. There is a strong association between hypertension and smoking ($p<0.05$) and also between hypertension and weekly consumption of beef or mutton ($p<0.05$).

Conclusion: Among all 151 respondent 84.1% were normotensive and 15.9% were hypertensive. The Prevalence of hypertension was more common among those habituated with smoking, taking extra salt with meal, fast food intake and increased consumption of beef. Regular screening program can detect the undiagnosed or asymptomatic cases so that timely intervention and follow up treatment can be given.

Key words : Hypertension; Military personnel; Risk factor.

Introduction

Hypertension is a major health problem throughout the world due to its high prevalence and its association with increased risk of cardiovascular disease[1-4]. Hypertension causes around 7.5 million deaths or 12.8% of all annual deaths worldwide[5]. This disease is predicted to be increased to 1.56 billion by the year 2025[6]. High blood pressure is a major risk factor for chronic heart disease, stroke and coronary heart disease.

Blood pressure is the force of blood against the arteries. Blood pressure has two components-the systolic pressure and the diastolic pressure. It varies from person to person and by ages.

Hypertension or high blood pressure is defined as abnormally high arterial blood pressure. According to the Joint National Committee 7 (JNC7) Normal blood pressure is a systolic BP<120 mm Hg and diastolic BP<80 mm Hg. Hypertension is defined as systolic BP level of ≥140 mm Hg and or diastolic BP level ≥90 mm Hg. The grey area falling between 120-139 mmHg systolic BP and 80-90 mm diastolic BP is defined as "prehypertension"[7, 8]. Although prehypertension is not a medical condition in itself, pre-hypertensive individuals are at more risk of developing Hypertension[1].

Hypertension is a silent killer as very rarely any symptom can appear in its early stages until a severe medical crisis takes place like heart attack, stroke or chronic kidney disease[8-10]. As people are unaware of excessive blood pressure, it is only through measurement that detection can be done. Majority of the patients with hypertension remain asymptomatic, but some people with hypertension report headaches, light headedness, vertigo, altered vision or fainting episode[11]. There are several factors predisposing to hypertension. These factors vary from country to country and even there is difference between urban and rural regions of the same place[12].

Globally, cardiovascular disease accounts for nearly one third of the total global death[13]. High blood pressure is the leading cause of CVD. Hypertension is responsible for at least 45% of death due to heart disease and 51% deaths due to stroke[14]. Currently, 80% of deaths due to cardiovascular disease occur in low and middle income countries, where the burden of hypertension has increased over the past decade due to population growth, ageing and increase in behavioral risk factors.

Hypertension is an increasingly important medical and public health issue because it is common and increases the risk of cardiovascular and kidney disease. High incidence

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Journal of Army Medical College Chattogram
Volume 4 Issue 1 June 2021; 31-35

of metabolic syndrome, and lifestyle related factors like obesity, high salt intake and less physical activity may play important role in the pathophysiology of HTN.

Physical fitness is the prime requirement for military service to perform complex and difficult task effectively. Hypertensive individual is not allowed to join in military service though it is observed that hypertension is found in early age among military persons. It is presumptive that most of the soldiers might have suffered from mental stress due to service conditions though they do physical exercise regularly and take normal diet, they have tendency to hide symptoms to avoid the effect of medical category which affect their career.

Hypertension or raised blood pressure is now a days becoming an alarming threat to the life of modern society. It cuts life short. If the associated risk factors of hypertension are known earlier then reduction of complications of the disease is possible. The aim of this study is to find out the asymptomatic patients of hypertension through screening and evaluate their relevance in making early diagnosis, proper treatment and standardized follow-up care to minimize the mortality and morbidity from complication of hypertension. The present study is designed to determine the blood pressure status of soldiers in Rangpur Cantonment.

Materials and methods

This descriptive cross-sectional study was conducted at Medical Inspection (MI) room of Combined Military Hospital (CMH) Rangpur from July to December 2018. A total of 151 cases were selected through purposive sampling technique. Data were collected by face to face interview with structured questionnaire. A standard questionnaire was developed in accordance with the study objectives to obtain relevant information. An interview schedule with questionnaire was prepared. This interview schedule was worked out first and pre-tested in another population outside the study population for clarity. After necessary correction, addition, exclusion and modification, final questionnaire was prepared. Research tools and equipment were: Stethoscope, Sphygmomanometer, Weighing scale and measuring tape. After explaining the purpose of the study to the respondents, data were collected through face to face interview. Blood pressure was measured with an aneroid sphygmomanometer with the subjects in sitting position, relaxed for 5 minutes and at least 30 minutes after last smoked, ingested caffeine or exercised. The mean of the two measurements of blood pressure were taken for consideration.

Results

This descriptive type of cross-sectional study was carried out among 151 purposively selected study population at MI room of CMH Rangpur, with an aim to find out the prevalence of hypertension and its associated risk factors among the soldiers. The results of the study are presented as follows:

Table I Distribution of respondents by socio-demographic and characteristics of hypertension

Characteristics		Frequency	Percentage
Age group (In years)	<30	50	33.1
	31-40	58	38.4
	41-50	32	21.2
	>50	11	7.3
	Total	151	100.0
Mean age=36.88, SD= ±1.91			
Educational status	SSC Passed	80	53.0
	HSC Passed	61	40.4
	Graduation or above	10	6.6
	Total	151	100.0
Marital status	Married	136	90.1
	Unmarried	15	9.9
	Total	151	100.0
Living condition	Barrack house	90	59.6
	Govt house	38	25.2
	Hired house	23	15.2
Rank of respondents	Sainik	41	27.1
	NCO	83	55.0
	JCO	27	17.9
	Total	151	100.0
Systolic BP mmHg	100	31	20.5
	110	38	25.2
	120	44	29.1
	130	24	15.9
	140	14	9.3
	Total	151	100.0
Diastolic BP mmHg	70	77	51.0
	80	43	28.5
	90	23	15.2
	100	8	5.3
	Total	151	100.0
Status of hypertension	Normotensive	127	84.1
	Hypertension	24	15.9
	Total	151	100.0
Family history of hypertension	Yes	77	51.0
	No	74	49.0
	Total	151	100.0

Journal of Army Medical College Chattogram
Volume 4 Issue 1 June 2021; 31-35

Table II Distribution of respondents by associated risk factors

Characteristics		Frequency	Percentage
Smoking habit	Yes	20	13.2
	No	131	86.8
	Total	151	100.0
Habit of extra salt intake	Yes	100	66.2
	No	51	33.8
	Total	151	100.0
Habit of exercise in leisure	Yes	115	76.2
	No	36	23.8
	Total	151	100.0
Weekly consumption of eggs	3 eggs	45	29.8
	4 eggs	95	62.9
	6 eggs	11	7.3
	Total	151	100.0
Weekly consumption of Beef/Mutton	1 meal	51	33.8
	2 meal	77	51.0
	≥3 meal	23	15.2
Weekly intake of fast food	Total	151	100.0
	1 time	67	44.4
	≥2 time	29	19.2
	No intake	55	36.4
Status of BMI	Total	151	100.0
	Normal weight	139	92.1
	Overweight	12	7.9
Co-morbid condition	Total	151	100.0
	No	141	93.4
	DM	4	2.6
	Renal disease	2	1.3
	COPD	2	1.3
	Gout	2	1.3
	Total	151	100.0

Table III Association between blood pressure and related risk factors

Age Group	Blood pressure status		Total
	Normotensive	Hypertensive	
<30	44 (88.0%)	6 (12.0%)	50 (33.1%)
31-40	48 (82.8%)	10 (17.2%)	58 (38.4%)
41-50	28 (87.5%)	4 (12.5%)	32 (21.2%)
>50	7 (63.6%)	4 (36.4%)	11 (7.3%)
Total	127 (84.1%)	24 (15.9%)	151 (100.0%)
Rank status			
Sainik	35 (85.4%)	4 (9.8%)	41 (27.1%)
NCO	69 (83.1%)	14 (16.9%)	83 (55.0%)
JCO	23 (85.2%)	6 (22.2%)	27 (17.9%)
Total	127 (84.1%)	24 (15.9%)	151 (100.0%)
Family history of HTN			
Yes	63 (81.8%)	17 (22.1%)	77 (51.0%)
No	64 (86.5%)	7 (9.5%)	74 (49.0%)
Total	127 (84.1%)	24 (15.9%)	151 (100.0%)
χ^2=3.63 df= 1 p>0.05			
Smoking			
Yes	7 (35.0%)	13 (65.0%)	20 (13.2%)
No	120 (91.6%)	11 (8.4%)	131 (86.8%)
Total	127 (84.1%)	24 (15.9%)	151 (100.0%)
χ^2=41.56 df=1 p=0.000			
Extra salt in diet			
Yes	81 (81.0%)	19 (19.0%)	100 (66.2%)
No	46 (90.2%)	5 (9.8%)	51 (33.8%)
Total	127 (84.1%)	24 (15.9%)	151 (100.0%)
χ^2=2.13 df=1 p>0.05			
Weekly intake Beef or Mutton			
1 meal	47 (92.2%)	4 (7.8%)	51 (33.8%)
2 meal	71 (92.2%)	6 (7.8%)	77 (51%)
≥3 meal	9 (39.1%)	14 (60.9%)	23 (15.2%)
Total	127 (84.1%)	24 (15.9%)	151 (100.0%)
χ^2=40.99 df=2 p=.000			
Body Mass Index			
Normal	120(86.3%)	19 (13.7%)	139 (92.1%)
Overweight	7 (58.3%)	5 (41.7%)	12 (7.9%)
Total	127 (84.1%)	24 (15.9%)	151 (100.0%)

Mean age of the respondent was 36.88 ± 1.91 years. Out of 151 respondents majority (38.4%) respondents were in the age group 31-40 years, SSC passed 53.0%, Married 90.1%, living in the barrack 59.6%, NCO 55.0%. 29.1% respondents had systolic BP 120 mmHg, 51% respondents had diastolic BP 70 mmHg, among all respondents 84.1% were normotensive, 15.9% were hypertensive and 51.0% respondents had positive family history (Table I).

It was revealed that among the respondents 13.2% had smoking habit. Habit of consumption of extra salt with meal was 66.2%, Habit of exercise during leisure 76.2%, Weekly consumption of 4 eggs 62.9%, weekly consumption of beef or mutton 2 meals 51.0%, Habit of weekly intake of fast food 44.4%. Out of all 151 respondents 92.1% had normal body weight and 6.5% had co-morbid conditions (Table II).

Proportion of hypertension are more in the age group >50 years, which is 36.4% and in rank status of JCO, which is 22.2%. Among 24 hypertensive cases 17 had family history of hypertension, history of smoking in 13 cases and habituated with taking extra salt with meal in 19 cases. Total 23 cases had the habit of taking beef or mutton three times weekly, among them, 14(60.9%) had hypertension. Out of 24 hypertensive cases, 12 were overweight and 41.7% overweight population were hypertensive (Table III).

Journal of Army Medical College Chattogram
Volume 4 Issue 1 June 2021; 31-35

Discussion

In this study mean age of the respondent was 36.88 ± 1.91 years, where majority 38.0% respondents were in the age group 31-40 years. Among the respondents 55.0% were NCO, Married were 90.1%, living in the barrack house 59.6%, normotensive 4.1% and respondents with family history of hypertension 51.0% (Table-I).

The frequency of hypertension among the soldiers was 15.9% (Table-I). According to WHO[15]. Study on non-communicable disease risk factor survey Bangladesh 2010, the prevalence of self reported (Documented) hypertension was 12.5% (Men 10.9% and women13.9%). The prevalence of hypertension was more in urban area (19.9%) than rural area (15.9%). The later finding is quite closer to this study result. Another study conducted by Islam SMS et al found prevalence of high blood pressure in an urban community (Dhaka) to be 25.6% in male and 24.7% in female[16]. The dissimilarity may be due to differences in population and sample size.

The present study revealed that the proportion of hypertension is more common in the age group above 50 years which is 36.4% (Table-III), which is consistent with the study conducted by Vokonus PS et al in USA where it is evident that risk in the elderly of both sexes was approximately twice as great as that observed for younger persons at the same levels of systolic blood pressure[17]. The risk of cardiovascular disease increases proportionally with increasing diastolic blood pressure in older men.

It has been observed that in this study the occurrence of hypertension was more among person with positive family history of hypertension. Out of 24 hypertensive cases 22.1% had family history of hypertension. Genetic influence or familial trends have been observed in this study, which is consistent with the study conducted by Paul GK et al where he found among hypertensive cases 86.6% had a positive family history of hypertension[18].

In this study, it was evident that 65.0% hypertensive cases belonged to the smoker group and 8.4% hypertensive cases were non-smoker group. The association between high blood pressure and habit of smoking are statistically significant, which is consistent with the study conducted by Mahesar H et al in Hyderabad, where it was found that prevalence of hypertension was higher (23.5%) in smokers against non-smokers (16.4%)[19].

The present study revealed that out 24 hypertensive cases 19.0% were habituated with taking extra salt with meal and 9.8% hypertensive did not take extra salt (Table-III). So, the proportion of hypertension was found to be more common among extra salt takers, which is consistent with the finding of study conducted by G Radhika et al where they found subjects in the highest quintile of salt intake had significantly higher prevalence of hypertension than those in the lowest quintile[20].

In the present study it was depicted that the occurrence of hypertension among overweight persons was more than normal weight person. Out of 12 overweight cases 41.7% had hypertension compared to 13.7% in normal weight persons (Table-III), which is similar with the finding of the study conducted by AKM Alamgir et al where it was revealed that the positive significant relation of both systolic and diastolic blood pressure increment with increment of body weight[21].

In the present study it was shown that all cases had the habit of taking beef or mutton, at least one meal per week. Those who had the habit of three or more meal, two meal, one meal per week developed hypertension (60.9%), (7.8%), (7.8%) respectively which is statistically significant ($p<0.05$) and almost similar to the finding of the study conducted by Lea Borgi, MDa, et al[22]. Singapore, where in all three cohorts, participants consuming ≥ 1 serving per day of any type of animal flesh had a higher BMI. Higher consumption of any individual type of animal flesh was significantly and independently associated with an increased risk of incident hypertension ($p<0.001$).

Conclusion

The study revealed that the prevalence of hypertension among military personnel of Rangpur Cantonment was 15.9%. Majority (38.4%)of the respondents were in the age group 31-40 years.The Prevalence of hypertension was more common those were habituated with smoking, taking extra salt with meal, habit of fast food intake and increased consumption of beef. Hypertension is one of the leading cause of death in the world. It considered one of the major cardiovascular problem and public health importance. Majority of our population with hypertension remains undetected and therefore untreated.

Recommendations

The useful findings may help to implement control measures against serious complications of hypertension like stroke, coronary heart disease, renal failure.Attention must also be given for achieving the primary prevention of hypertension by safe exercise, diet control and by good behavioral means to curve down the disease burden.

Disclosure

Both the authors declared no competing interests.

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Journal of Army Medical College Chattogram
Volume 4 Issue 1 June 2021; 31-35

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CASE REPORT

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Volume 4 Issue 1 June 2021; 36-38

A Large Newborn with Hemihypertrophy, Refractory Hypoglycaemia: Backwith Wiedemann Syndrome: A Case Report

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ABSTRACT

Background : *Beckwith–Wiedemann Syndrome (BWS) is a human genomic imprinting disorder presented with a wide spectrum of clinical features including overgrowth, abdominal wall defects, macroglossia, neonatal hypoglycaemia and predisposition to embryonal tumors. Estimated incidence is one in 13700. This genetic syndrome has its apparent origin in an alteration of the expression of genes from chromosome 11, which can be sporadic (85%) and inherited (15%). Clinically, it presents in diverse forms, it is most common features being macroglossia (97-100%) defects of the abdominal wall (77-80%), hypoglycemia (63%) and macrosomy (68%). There are other minor clinical expressions. Prognosis for normal intellectual development appears to be good in patients without hypoglycaemia. The objective of the study is to keep in mind of BWS which is rarely seen in new born presented with respiratory distress, hypoglycaemia and hemihypertrophy.*

Case Report : *A 30 min old male newborn admitted in the NICU of CMH Chattogram with a history of respiratory distress after birth and delivery of large baby at 38 weeks of gestation. Baby delivered by emergency LSCS due to fetal distress. Examination on admission: Baby was dyspneic, cyanosed, macrosomic, birth weight was- 5.25 kg. He had macroglossia, right sided hemihypertrophy, hepatomegaly, nevus flemus at anterior abdominal wall and neck and left sided complete inguinal hernia. During NICU admission the patient developed Persistent Pulmonary Hypertension (PPHN), refractory hypoglycaemia and neonatal jaundice which were treated accordingly. Patient is now on outdoor follow up after being discharged from NICU. During this period from19 April 2020 to 01 April 2021, he was stable and doing well. His clinical features were suggestive of BWS, as it is a genetic disorder that needs molecular DNA analysis to confirm the diagnosis.*

Conclusion: *In general, the prognosis of BWS is very good, but needs follow up for tumor (Wilms tumor) risk and hypoglycaemia.*

Key words: Beckwith-Wiedemann syndrome; Macroglossia; Wilms tumor.

Introduction

Beckwith–Wiedemann Syndrome (BWS) is a pediatric overgrowth disorder involving an increase chance of tumor development[1,2]. Beckwith-Wiedemann Syndrome (BWS) was described independently by two investigators. In 1963 Beckwith presented 3 postmortem cases with macroglossia, omphalocele, cytomegaly of the fetal adrenal cortex, renal medullar dysplasia and visceromegaly. On the other hand, Wiedemann in 1964 reported 3 cases of siblings with similar clinical characteristics, adding diaphragm defects and hypoglycemia[3,4]. Beckwith-widemann syndrome has estimated incidence of one in 13700. The exact incidence of BWS is unknown because of marked variability in the syndromes presentation. This genetic syndrome has its apparent origin in an alteration of the expression of genes from chromosome 11 region p15.5, which can be sporadic (85%), inherited (15%) or because of chromosomic abnormalities (1%)[2]. This alteration has been found primarily on the IGF2 genes, which is a fetal growth factor, and in the H19 gene, which is thought to be a tumor suppressor gene[5]. Clinically, it presents in diverse forms, its most common features being macroglossia (97-100%) which can be asymmetric, defects of the abdominal wall (77-80%), hypoglycemia (63%) and macrosomy (68%)[6-8]. There are other minor clinical expressions that sometimes are unnoticed such as the predisposition to neoplasms or embrionary tumors likes wilms tumor, hepatoblastoma, rhabdomyosarcoma, placentomegaly, grooves in the earlobe, cleft palate, renal alterations, visceromegaly, refractory hyperinsulinemia, polydactyly, mental retardation[9,10,8]. However, the neurologic engagement is rare[5]. It is a disease of low prevalence, however, it represents one of the most common overgrowth syndromes[2,6]. The number of reported infants born with BWS is most likely low because many are born with BWS, but have clinical features that are less prominent and therefore missed. BWS has been documented in a variety of ethnic groups and occurs equally in males and females. Children conceived through In vitro fertilization

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Journal of Army Medical College Chattogram
Volume 4 Issue 1 June 2021; 36-38

have a three to four fold increased chance of developing BWS. It is thought that this is due to genes being turned on or off by the IVF procedures[11,12]. There is very few reported case of BWS in Bangladesh so we like to present this rare case, BWS admitted to our NICU.

The objective of the study is to keep in mind BWS which is rarely seen in new born presented with respiratory distress, hypoglycaemia & hemihypertrophy.

Case Report

30 min old male newborn admitted in NICU of Combined Military Hospital Chattogram on 1.04.2020 at 0730 hours with the history of delivery of large baby at 38 weeks of gestation, cyanosis and respiratory distress after birth.

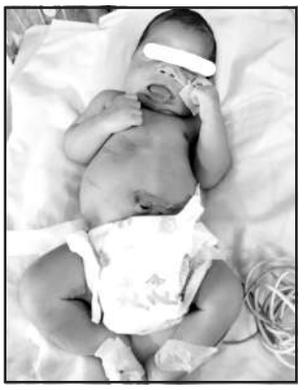
Baby was delivered by emergency LSCS due to fetal distress. He was 4th issue of nonconsanguenous parents. There was no history of delayed cry after birth, maternal diabetes and Beckwith-Widemann syndrome in family.

Mother was on regular antenatal checkup and antenataly diagnosed of large fetus.

Examination on admission, the baby was macrosomic : birth weight was 5.25 kg which was above 97% of growth chart, had macroglossia, right sided hemihypertrophy, baby was dyspneic , respiratory rate was 88-90/min, SPO_2 in room air 88%, heart rate -140 to 150/min,hepatomegaly, left sided complete inguinal hernia, nevus flammeus at trunk and neck.

During the NICU admission period baby developed refractory hypoglycaemia, Persistent Pulmonary Hypertension (PPHN), neonatal jaundice. For PPHN The baby was treated with high flow oxygen with Continuous Positive Airway Pressure (CPAP) ventilatory support for 4 days, for persistent hypoglycaemia I/V infusion of 10% dextrose which was gradually increased up to 12.5 %. Inspite of high dextrose infusion the baby had refractory hypoglycaemia so was treated with I/V inj Hydrocortisone for 5 days, hypocalcaemia was treated with intravenous inj. 10% Ca^{++} gluconate followed by oral Tab. Calcium carbonate supplementation. Neonatal jaundice was treated with continuous phototherapy and with other routine and supportive care. Patient was discharged on 19.04.21 on his 19 day of his age after being completely stable.His investigations findings were, Hb:18.4 gm/dl, TWC: 7x10^9/L, N: 30%, L: 60%, TPC: 200x10^9/L, CRP: Negative, Blood C/S: no growth, RBS: 0.3mmol/L on admission, RBS after treatment: 4.6 mmol/L, RBS on discharge: 4.6 mmol/L, S.Ca^{++}: 6.4 mg/dl on admission, S.Ca^{++}- 8.6 mg/dl after treatment, S. Bilirubin (On 40 hours of age) : total 19.4 mg/dl, direct- 0.5 mgm/dl, indirect: 18.1mg/dl, S.Bilirubin after phototherapy: total 06 mg/dl, direct: 0.5 mgm/dl, indirect: 05.5 mg/dl, Blood urea: 18 mg/dl, S. creatinine: 0.5 mg/dl, Serum Na^+: 139 mmol/l, Serum K^+: 4.5mmol/l, S.TSH-5.6µmol/ml, S.FT4- 14.8 pmol/L, X-ray chest A/P view: normal, USG whole abdomen- Hepatomegaly, nephomegaly with left sided hydronephrosis, S. α-fetoprotein- 13 ng/ml , S.ALT- 42U/L, Echocardiogram reveals normal findings.In case of our patient all the clinical feature are suggestive of BWS. As it is a genetic disorder, needs it molecular DNA analysis to confirm the diagnosis. Due to lack of facility we don't do the molecular DNA study yet.

Our patient of Beckweith-Wiedemann syndrome:



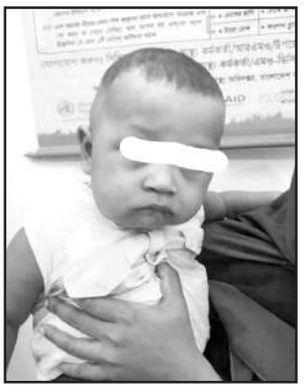


Figure 1 At the age of 4 day **Figure 2** At the age of 9 mont

Figure 3 At the age of 13 month

The baby is on routine out-door follow-up and he is now 13 month old. During the follow-up from 19.04.20 to 1.04.2021 for neurodevelopmental assessment, Hypoglycaemia, tumor risk and renal function assessment, his blood sugar, α-fetoprotein, renal functions all were normal, USG- revels left sided hydonephosis grade- III, his intelligence and motor skills are normal according to his age so far.

Discussion

The BWS appears either sporadically or as familial cases. The clinical manifestations however do not allow for a differentiation between familial and sporadic cases[6]. In familial cases it is now clear that the mutant gene is located in the short arm of chromosome 11 and the lesion appears to be dominant only when inherited through the female line[6]. However, the majority of cases are sporadic as in our patient. Our patients had symptomatic refractory hypoglycaemia for 8 days which was treated according to standard protocol. A similar observation was made by Thorburn in Jamaica' and Verma in India". Hamel in Tanzania' and AdeyokulUlu in Nigeria' reported neonatal hypoglycaemia in a number of their patients[3]. Our patient doesnot have exomphalos. Although the syndrome has many features, the presence of macroglossia or exomphalos or both should alert the clinician to the dual threat of possible early

Journal of Army Medical College Chattogram
Volume 4 Issue 1 June 2021; 36-38

neonatal hypoglycaemia and various intra-abdominal malignancies later in life for which long term follow up by a pediatrician is warranted. The prognosis for normal intellectual development appears to be good in patients without hypoglycaemia[3]. Our patient has left sided hydronephrosis; in BWS nonmalignant renal abnormalities occur with an incidence of up to 59%[2,6]. Macroglossia, a large tongue, is a very common (>90%) and prominent feature of BWS. Infants with BWS and macroglossia typically cannot fully close their mouth in front of their large tongue, causing it to protrude out. Macroglossia in BWS becomes less noticeable with age and often requires no treatment, but it does cause problems for some children with BWS. In severe cases, macroglossia can cause respiratory, feeding and speech difficulties. In our patient its does not cause breathing and feeding difficulty. Hemihypertrophy (Hemihyperplasia) is an abnormal asymmetry between the left and right sides of the body occurring when one part of the body grows faster than normal. Isolated hemihypertrophy is associated with a higher risk for cancer[10,13]. As a result, children with hemihypertrophy should be followed up with the general cancer screening protocol for BWS. Hemihypertrophy can also cause various orthopedic problems, so children with significant limb hemihyperplasia should be evaluated and followed by an orthopedic surgeon. Most children (>80%) with BWS do not develop cancer; however, children with BWS are much more likely (600 times more) than other children to develop certain childhood cancers, particularly Wilms tumor, pancreatoblastoma and hepatoblastoma, neuroblastoma and rhabdomyosarcoma[6,10]. Our patient is on regular follow up schedule for neurodeplopmental assessment and malignancy screening and renal function assessment. Now he is 11 months old and his intelligence and motor skills are normal according to his age so far; and no malignancy detected yet and his renal function is normal.

Limitation

Due to lack of facilities we are unable to perform the molecular DNA study.

Conclusion

In general, the prognosis of BWS is very good. Children with BWS usually do very well and grow up to become the heights expected based on their parents height. As the patient with BWS has chance of hypoglyceamia and chance of childhood cancer is high so they need follow up for good prognosis.

Recommendation

Creating further awareness and provididing advanced management screening procedure of DNA analysis may be followed.

Disclosure

All the authors declared no competing interest.

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Introduction should not exceed more than 500 words. Methods should be including type of study, time and place of the study, population, procedure and statistical procedure for data analysis and approval of the study by the Ethical Review Committee. Results should be presented in logical sequence in the text, tables and illustrations. The whole body of the text should not exceed 6000 words (Excluding abstract, table, figure, reference). The total number of references will not be more than 25 and less than 15 for the original article.

Tables

All tables should be in result section. It should be simple and self explanatory. It also should be using roman numerical which numbered consecutively using roman numerical (eg. Table I, II). A short descriptive title should appear above each table with a clear legend and any footnotes suitably identified below. Captions should be typed, double-spaced, on a separate sheet.

Figures/Graphs

Should be submitted in original as brief as possible. Figure should be numbered in Arabic numerical (eg. Fig 1, 2) followed by the legend on the bottom of the figure. Its noted that maximum numbers of table and figure 5/6 nos. No punctuation mark in caption of Tables and Figures.

Illustrations
All illustrations must be numbered and cited in the text. Print photograph, B2 size with good contrast (600 pixels) should be submitted. Figure number and name of the 1st author should be written on the back of each photograph marking the top edge. For case report only 3 photographs are allowed.

Abbreviations
Standard abbreviation should be used. The full form for which the abbreviation stands followed by the abbreviation in parenthesis should be preceded the use of the abbreviation in the text except the standard ones.

References
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Agarwall P, Datta S, Garg SK et al. Multiple dose pharmacokinetics of ciprofloxacin in preterm babies. Indian pediatr. 2004; 4:1001-1007.

Organization as Author
The TIME Investigator. Trial of invasive versus medical therapy in elderly patients with chronic symptomatic coronary artery diseases (TIME): A randomized trial. The Lancet. 2001; 358(9286):951-957.

No Issue and No Volume
Browell DA, Lennard TW. Immunologic status of the cancer patient and the effects of blood transfusion on antitumour responses. Curr Opin Gen Surg. 1993;325-333.

Journal Article on the Internet
Kafuko JM, Zirabumuzaale,C. Bagenda D.Rational drug use in rural health units of Uganda: Effect of National Standard Treatment guidelines on rational drug use (Unpublished report). 1994. available at http://archives.who.int/icium/icium1997/posters/2f3_text.html accessed on 27th September 2013.

References from Books and Monograph

Personal author
Haque M.M. abc of research methodology and biostatistics, Department of Biochemistry, 2009. BSMMU, Dhaka.

Editor (s) as author
Basmajian JV, Slonecker CE, editors. Grant's method of anatomy. A clinical problem-solving approach. 11th ed. New Delhi : BI Waverly Pvt Ltd. 1997;180-183.

Organization as author and publisher
World Health Organization. Revised 1990 estimates of maternal mortality : A new approach by WHO and UNICEF. Geneva: World Health Organization. 2003;132-151.

Chapter in a book
Ford HL, Sclafani RA, Degregori J. Cell cycle regulatory cascades. In: Stein GS, Pardee AB, editors. Cell cycle and growth control: Biomolecular regulation and cancer. 2nd ed. Hoboken (NJ): Wiley-Liss. 2004; 42-67.

Article from an encyclopedia: No author
Mental disorders and their treatment. In: The new encyclopaedia Britannica. 5th ed. Chicago (IL): Encyclopaedia Britannica. 1987;23:956-975.

Conference proceedings
Khalifa ME, Elmessiry HM, ElBahnasy KM, Ramadan HMM. Medical image registration using mutual information similarity measure. In: Lim CT, Goh JCH, editors. Icbme 2008: Proceedings of the 13th International Conference on Biomedical Engineering. 2008 Dec 3-6; Singapore.
Dordrecht: Springer. 2009;151-155.

Conference paper
Yamane Y. The effect of spirulina on nephrotoxicity in rats. Presented at Annual Symposium of the Pharmaceutical Society of Japan at Chiba University. 1988 April 15; Japan.

Reference from dissertation or thesis
Siddika AN. Does Antimicrobial Prescribing of BSMMU Hospital comply to its' Antibiotic Guideline? MPhil. Thesis, Dhaka: Bangabandhu Sheikh Mujib Medical University. 2012.

Newspaper Article
O'Leary C. Vitamin C does little to prevent winter cold. The West Australian. 2005 Jun 29.

Acknowledgements
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