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CONTENTS

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Editorial

INTENSIVE CARE UNIT: BANGLADESH PERSPECTIVE

The care of critically ill patients in Intensive Care Unit (ICU) is primary component of modern medicine. ICU is a highly specialized unit in a hospital where life support is given to and invasive monitoring is done for the critically ill patients. This level of life support and monitoring is not possible to provide in ward or any other place in a hospital. The practice of intensive care medicine, which originated in the 1940's with anesthesiologists providing life support to patients with polio, has undergone revolutionary changes with the development of equipments, procedures and medications. In the past decade, another revolution has taken place with the introduction of evidence -based medicine into ICU practice.

In Bangladesh, concept of ICU is a relatively new one in both public and private sector. The first ICU in public sector was established in 1985 in Dhaka Medical College Hospital with the initiative of Professor Shahjahan Nurus Samad Chowdhury. After that no ICU was established in any of the government medical college hospital for 20 years. In Feb'2005 second ICU was established in Chittagong Medical College Hospital. Government has taken plan to establish ICU in every medical college hospital throughout the country. The cost of establishing and maintaining an ICU is very high, and is very difficult to run an ICU in both public and private sector. In poor countries, like us planning should be made appropriately so that it is cost effective and with good outcome. In all developed countries where separate ICUs exist e.g. medical ICU, neurosurgical ICU, neonatal ICU and so on. In our country all the existing ICUs are multidisciplinary. It is very difficult to manage different group of patients in same ICU. Among the patients admitted in ICU neurological and neurosurgical patients comprise a major group (46 of first 100 patients admitted in ICU of Chittagong Medical College Hospital) . Neurocritical care is an evolving subspecialty that just begin to reach maturity which focuses on the care of critically ill patients with traumatic brain injury, intracranial hemorrhage and complications of subarachnoid hemorrhage, including vasospasm, elevated intracranial pressure and the cardiopulmonary complications of brain injury[2]. Care in the specialized care unit (neuro ICU) is of higher quality than general units because it focuses on the special needs of a specific group of patients population and is provided by a multidisciplinary team whose training emphasizes the unique aspects of the disease processes in that population. With this knowledge we can think of establishing separate neuro ICU at least in Dhaka and Chittagong Medical College Hospital where ICU facilities already exist.

Overnight Intensive Recovery (OIR) is a new concept, which defines, identified recovery beds that are able to offer up to level 3 critical care for any post surgical patients for a period of 24 h[3]. The key to the defining the concept lies within the term OIR: duration of stay should be short, management is intensive and level 3 care in a recovery unit. The first OIR facility was opened in the general recovery ward at St. Thomas Hospital (UK) in 1988 and made this practice safe and successful alternative to the ICU for the short-term postoperative critical care. This concept may be applied to all hospitals in both public and private sector in our country where ICUs do not exist but there is a recovery area. Just identifying 2-3 beds, providing artificial ventilators, monitoring devices and appropriate manpower, life support can be provided for short-term basis. If long-term support is required patients may be transferred in own or nearest ICU. This type of critical care support was provided in Chittagong Medical College Hospital from 1996 before establishment of ICU and still exists for overnight support for post surgical patients.

Death rates, complications, length of ICU stay and cost of care measure the performance of an ICU. In our country where resources are limited, available resources should be utilized in a planned way. To get maximum output from limited facilities, stringent criteria for which patients get admitted to the ICU is to be set up. Only the patients likely to recover from critical illness

should be admitted in ICU. The poor outcome in our ICUs is mainly due to failure to follow the admission criteria. Another reason for poor outcome is absence of intensive care team, which should include intensivists, nurses, respiratory therapists, physiotherapists and others. Surveys of outcome of ICUs concluded that established protocols for management of specific critical illnesses contribute to the improve results. So we should have to develop detailed complete protocols by application of evidence-based practice and customize the protocols to fit resources available e.g. weaning protocol, infection control and antimicrobial therapy policy, sedation and glycemic control.

Advances in the medical science have led to increased expectations for favorable outcomes of episodes of chronic illness, even when the patient has severe co-existing chronic disease. A clinical course that runs counter to the family's hopes and expectations is extraordinally stressful and important contributor to ICU-related post-traumatic stress disorder (PTSD) among families[4]. A better understanding of how intensive care clinicians can support families as they make transition from a goal of cure to one of comfort and acceptance of death is clearly needed. Curtis and colleagues have described some of the components of a system of communication that is being increasingly recognized as an effective means of promoting harmony between critical care providers and families[5]. This five-part system, known by the mnemonic VALUE, includes the following elements: valuing and appreciating what the family members communicate, acknowledging their emotions by using reflective summary statements, listening to family members, understanding who the patient is as a person by asking open-ended questions and listening carefully to the responses, and eliciting questions from the family more effectively than by simply asking, "Any questions?" A key skill is listening more and talking less[6]. Structured, proactive multidisciplinary communication processes that are supported by ethics, consultation and palliative care teams are the foundations for improving end-of-life care for patients and interactions with their families[7].

The cost of providing intensive care is very high and care must be directed towards the patients who are most likely to benefit from it. In poor countries like us maintenance of an ICU is difficult both in public and private sector. But without an ICU a hospital is not standard, training is not complete and many lives can't be saved.

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Original Article

GLUCOSE, C-PEPTIDE AND CORTISOL RESPONSE TO SURGERY UNDER GENERAL ANESTHESIA IN DIABETIC SUBJECTS WITH TREATMENT VARIABILITY

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ABSTRACT

Diabetic patients are considered to be at increased risk of perioperative morbidity and mortality because of the involvement of their vital organs and the autonomic nervous system in the natural course of the disease. Various aspects of anesthesia and surgery cause stress induced hemodynamic, endocrine and metabolic changes in type 2 diabetic subjects. The present study was designed to investigate the surgical stress response difference between the patients groups those who are treated with only insulin and with insulin-oral hypoglycaemic drugs combination before surgery. Stress response was measured with the changes of blood glucose, C-peptide and cortisol.

A total number of 30 subjects who were admitted in BIRDEM hospital in fit physical condition (ASA Class I & II) were selected for the present study. Among them 15 patients were treated with only insulin and 15 patients were treated with insulin-OHA combination before surgery. All of the subjects were received total abdominal hysterectomy under general anesthesia. Three samples were collected from each subject. The first sample (control, PT_0) was collected just before anesthesia; second sample (PT_1) collected 10 minutes after incision and third sample (PT_2) collected 10 minutes after extubation. Plasma glucose was measured by glucose oxidase method, serum C-peptide and cortisol by chemiluminescent based ELISA technique.

The mean±SD age and BMI were 44±6 years and 24.4±3.0 kg/m^2 respectively. In insulin treated group, the plasma glucose level was significantly higher in PT_2 and it was about 147% whereas in insulin-OHA group, the plasma glucose level was significantly higher in both PT_1 (111%) and PT_2 (196%). The serum C-peptide values were decreasing tendency but not significant in both groups. The serum cortisol level was increased gradually and significantly higher in PT_2 in both groups.

The data suggest that a) insulin treatment alone is more effective than insulin-OHA combination to control blood glucose in type 2 diabetic subjects undergoing surgery under general anesthesia, b) lower abdominal surgery under general anesthesia in well controlled type 2 diabetic subjects is accompanied by a hyperglycemic response which results from rise of insulin antagonists like cortisol rather than fall of insulin secretion, but the two treatment modalities lead to similar cortisol response.

Key words: General anesthesia, Serum glucose, cortisol, Total abdominal hysterectomy

INTRODUCTION

Diabetes mellitus is one of the major chronic diseases affecting mankind all over the world and it has been declared as an epidemic in developing countries by both the World Health Organization and International Diabetes Federation. Epidemiological evidences suggest that fifty percent of all diabetic patients present for surgery during their life time[1]. Inevitably, diabetic patients presenting for incidental surgery, or surgery related to their disease, will place an increasing burden on anesthetic services. Perioperative morbidity and mortality are greater in diabetic than in nondiabetic patients[1]. This is due to the pathophysiology that is more and more complicated in diabetic than in nondiabetic subjects. Stress response to surgery and anesthesia, counter regulatory hormones, preoperative fasting states, dehydration and insulin deficiency complicate the

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situation. These lead to abnormal metabolism of carbohydrate, protein and fat as well as electrolyte imbalance. In response to stress during surgery and anesthesia- the biochemical parameters like stress hormone (cortisol, epinephrine, glucagon and growth hormone), plasma glucose, ketone bodies, blood urea nitrogen, lactate, free alanine, pyruvate, C-peptide and electrolytes being altered[2,3,4]. The stress response leads to secretion of many anabolic and catabolic hormones and if the stress response is prolonged, the continuous hypermetabolic state may result in exhaustion of essential components of the body e.g. glucose, fat, protein and minerals causing increased morbidity and mortality[5]. The stress response leads to secretion of many anabolic and catabolic hormones and if the stress response is prolonged, the continuous hypermetabolic state may result in exhaustion of essential components of the body e.g. glucose, fat, protein, minerals, causing loss of weight, fatigue, decreased resistance, delayed ambulation and increased morbidity and mortality[6]. The plasma concentration of insulin during stress has been noted to be biphasic, characterized by the suppression of insulin secretion followed by a normal secretion, which has been termed as the phase of physiologic insulin resistance. Insulin is short lived in comparison to C-peptide. It can be measured indirectly from C-peptide because, during the course of insulin synthesis, C-peptide is cleaved from proinsulin, stored in secretory granules, and eventually released into the bloodstream in amounts equimolar with those of insulin[7].

Diabetic patients are usually treated with three methods: diet control alone, diet control with oral hypoglycaemic agents and diet control with insulin[8]. According to recent guideline for management of diabetes, diabetologists of BIRDEM prescribe insulin and OHA combination for some patients.

The present study was designed to investigate the stress response difference between the patients groups those who are treated with only insulin and with insulin-oral hypoglycaemic drugs combination before surgery. Stress response was measured with the changes of blood glucose, C-peptide and cortisol.

SUBJECTS AND METHODS

Thirty subjects who were admitted in BIRDEM hospital in fit physical condition (ASA Class I & II) and received total abdominal hysterectomy under general anesthesia were studied. Among them 15 patients were treated with only insulin and 15 patients were treated with insulin-OHA combination before surgery. First blood sample of each subject were served as a control. Patients taking steroid or analgesics drugs, and obese or malnourish subjects were not included in the study.

DESIGN OF GENERAL ANESTHESIA

Thiopental, halothane, fentanyl, vecuronium, nitrous oxide with oxygen.

PREPARATION OF THE SUBJECTS

Patients were recruited 1 week before surgery while undergoing preoperative evaluation and testing in the hospital. First of all the purpose of the study was explained in details to each subjects. The evaluation consisted of nursing and anesthesia functional health evaluation, provision of information regarding the surgery and obtaining appropriate laboratory testing. After recruitment into the study, informed written consent and demographic data were obtained. Weight and height of individual were recorded accordingly. All the patients took 7.5 mg medazolam at bed time the night before surgery. Patients were fasted for 6-8 hours prior to surgery and morning dose of antidiabetic therapy was omitted.

CONDUCTION OF ANESTHESIA

On arrival at preoperative room an 18G vasofix intravenous cannula was inserted into right anticubital vein for obtaining blood sample and another one was inserted into the left cephalic vein near to wrist for administration of fluid and other medications. The patients were next brought to the operating room where they underwent anesthesia and surgery. The anesthetic protocol was strictly maintained in all patients and consisted of an intravenous induction using thiopental sodium 5 mg/kg body weight, vecuronium 0.1 mg/kg body weight and fentanyl 1.5 μg/kg body weight. Once intubated with an endotracheal tube, anesthesia was maintained with inhaled O_2/N_2O (1:2) and appropriate dialing of halothane. Anesthesia is maintained with halothane as required to ensure adequate depth of anesthesia assessed by pulse, BP, tearing and sweating. Vecuronium 0.02 mg/kg body weight every 20 minutes and fentanyl 0.5 μg/kg body weight every

30 minutes is continued until 20 minutes before the anticipated end of surgery. Pulse, BP, SpO_2, continuous ECG, temperature, sweating and tearing is monitored every 5 minutely and recorded with corresponding sample. Temperature was maintained within normal limit. The patients were received ringer's lactate solution with appropriate volume as per 4-2-1 rule. After operation the patients were extubated with intravenous Neostigmine 0.05 mg/kg body weight and Atropine 0.02 mg/kg body weight. The time of introduction of anesthesia, incision, end of surgery and extubation was recorded properly.

SAMPLE COLLECTION

Three samples (8-10 ml) were collected through right handed cannula with all precautions. The first blood sample was drawn just before anesthesia, 2nd sample 10 minutes after incision and 3rd sample 10 minutes after extubation. Two ml of blood from each sample was kept in a test tube containing sodium fluoride and potassium oxalate in 1:3 ratios to prevent glycolysis and coagulation and remaining blood was taken in a plain test tube. Both of them were immediately placed into iced water and brought to Research division, BIRDEM. The samples were centrifuged at 3000 rpm for 15 minutes immediately and serum was stored at -40^0C until further analysis.

ANALYTICAL METHOD

Plasma glucose was measured by glucose-oxidase method (Randox, UK). Serum creatinine, urea, SGPT, uric acid was measured by colorimetric method. Total Cholesterol and TG was measured by enzymatic method. Serum electrolytes were measured by Dry Chemistry method (DT-60, USA). Serum C-peptide was measured by chemiluminescence based EIA method (Immulite, USA).

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS (Statistical Package for Social Science) software for Windows version 10 (SPSS Inc., Chicago, Illinois, USA).

RESULTS

All subjects were fit for general anesthesia in preoperative anesthetic assessment and values were within normal limit. The mean±SD age and BMI were 44±6 years and 24.4±3.0 kg/m^2 respectively, systolic and diastolic blood pressure were 140±15 mmHg and 85±10 mmHg respectively; pulse was 84±14 per minute and duration of surgery was 81±15 minutes (Table 1). The median (range), triglyceride and cholesterol were 131 (55-302) mg/dl and 190 (105-293) mg/dl respectively. The mean±SD, serum creatinine, SGPT, serum urea and uric acid were 1.0±0.12 mg/dl, 13.85±7.27 U/l, 20.42±6.50 mg/dl and 3.23±1.21mg/dl respectively. All the values within normal limit (Table 1).

Table-I

Clinical and biochemical characteristics of the study subjects (n=30)

Age (yrs)	44±6
BMI (kg/m^2)	24.4±3.0
Systolic BP (mmHg)	140±15
Diastolic BP (mmHg)	85±10
Pulse (per minute)	84±14
Duration of surgery (minutes)	81±15
TG (mg/dl)	131 (55-302)
Cholesterol (mg/dl)	190 (105-293)
Creatinine (mg/dl)	1.0±0.12
SGPT (U/l)	14±7
Urea (mg/dl)	20.4±6.5
Uric acid (mg/dl)	3.23±1.21

The mean±SD values of plasma glucose in PT_0, PT_1 and PT_2 were 6.38±2.62, 6.33±2.26 and 8.81±2.15 mmol/l and the serum C-peptide values were 1.73±0.90, 1.82±0.98 and 1.65±1.12 ng/ml respectively for insulin group. The plasma glucose level was significantly higher in PT_2 comparison to PT_0 (PT_0 vs PT_2, p=0.003)and PT_1 (PT_1 vs PT_2, p=0.003) whereas serum C-peptide values were almost similar in all samples (Table 2). The mean±SD values of plasma glucose in PT_0, PT_1 and PT_2 were 5.98±1.74, 6.66±1.78 and 11.16±2.70 mmol/l and the serum C-peptide values were 2.19±0.80, 1.92±0.85 and 1.85±0.75 ng/ml respectively for insulin-OHA combined group. The plasma glucose level was significantly higher in PT_1 (111%) than PT_0 it was also higher in PT_2 (196%) over PT_0 and PT_1 (PT_1 vs PT_2, p=0.0001) whereas serum C-peptide values were decreasing tendency but not significant (Table-II).

Table-II

Perioperative glycemic and insulinemic status of insulin and insulin-OHA treated subjects

Treatment group	Glucose (mmol/l)			C-Peptide(ng/ml)		
	PT_o	PT_1	PT_2	PT_o	PT_1	PT_2
Insulin	6.38±2.62[a]	6.33±2.26[a]	8.81±2.15[b]	1.73±0.90	1.82±0.98	1.65±1.12
(n=15)	(100%)	(99%)	(147%)			
Insulin-OHA	5.98±1.74[a]	6.66±1.78[b]	11.16±2.70[c]	2.19±0.80	1.92±0.85	1.85±0.75
(n=15)	(100%)	(111%)	(196%)			

Results are expressed as M±SD. PT_0= Preoperative (before anesthesia), PT_1= Peroperative (10 minutes after incision), PT_2= Postoperative (10 minutes after extubation). Values in rows with different superscripts are significantly different each other when using student paired 't' test.

Table-III

Perioperative serum cortisol status of insulin and insulin-OHA treated subjects

Treatment group	Cortisol (ng/ml)		
	PT_o	PT_1	PT_2
Insulin (n=15)	11.28±6.0[a100%]	12.77±7.17[a113.21%]	31.48±11.27[b279.08%]
Insulin-OHA (n=15)	11.91±3.30[a100%]	14.58±5.19[a122.42%]	34.84±5.87[b292.53%]

Results are expressed as M±SD. PT_0= Preoperative (before anesthesia), PT_1= Peroperative (10 minutes after incision), PT_2= Postoperative (10 minutes after extubation). Values in rows with different superscripts are significantly different each other when using student paired 't' test.

The mean±SD values of serum cortisol in PT_0, PT_1 and PT_2 were 11.28±6.00, 12.77±7.17 and 31.48±11.27 ng/ml respectively for insulin group. The serum cortisol level was increased gradually and significantly higher in PT_2 (Table 3). The mean±SD values of serum cortisol in PT_0, PT_1 and PT_2 were 11.91±3.30, 14.58±5.19 and 34.84±5.87 ng/ml respectively for combined group. The serum cortisol level was increased gradually and significantly higher in PT_2 (PT_0 vs PT_2, p=0.0001; PT_1 vs PT_2, p=0.0001) (Table 3).

DISCUSSION

Seshiah (2006) showed that surgery causes a considerable metabolic stress in the non-diabetic and more so in a diabetic subject[9]. The stress response to surgery is mediated by neuroendocrine system essentially by stimulating the adreno-medullary axis. The neuroendocrine system comes into play to maintain fuel requirements by glycogenolysis and gluconeogenesis through stress hormones like catecholamines, glucagon, cortisol and growth hormone. In a non-diabetic there is enough insulin secretion to utilize the fuel produced by the stress hormones and thus glucose homeostasis is maintained. This compensatory role of insulin is less possible in type 2 diabetic subjects.

Rothenberg and Loh-Trivedi (2006) documented that surgery elicits a stress response that is directly proportional to the degree of tissue trauma[10]. A recent study (Adams, 2000) suggests that the principal mechanism lies with the elevation of sympathetic tone with a consequent release of cortisol and catecholamines during surgery[11]. These hormones, in turn, lead to relative insulin hyposecretion, insulin resistance, and increased protein catabolism. Anesthesia also principally affects glucose metabolism through the modulation of sympathetic tone; however, *in vitro* evidence exists that insulin secretion is suppressed by inhalational agents with consequent increase in serum glucose level.

The perioperative stress response between insulin and combined insulin-OHA treated groups of type 2 diabetic patients are not well studied. The subjects those who are treated with insulin, only the PT_2 (147%) value of plasma glucose is

significantly high. But those who are treated with insulin with OHA combination shows both PT_1 (111%) and PT_2 (196%) values are significantly high (Table 2). It indicates that the type 2 diabetic subjects those who are treated with only insulin show better glycemic control when they undergo surgery under general anesthesia.

The C-peptide concentration in insulin treated group is slightly increased in PT_1, then it decreases in PT_2; but the change is not significant. In combined insulin-OHA group, C-peptide values decrease gradually in PT_1 and PT_2, but the difference is not statistically significant. Demirbilek *et al*. (2004) demonstrated a similar effect of remifentanil and alfentanil based intravenous anesthesia on endocrine response during total abdominal hysterectomy[12]. Sing (2003) reported that the plasma concentration of insulin during stress is biphasic, characterized by suppression of insulin secretion followed by a normal secretion, which has been termed as the phase of physiologic insulin resistance[13].

Carli (1993) reported that total abdominal hysterectomy with halothane or isoflurane anesthesia leads to two fold reduction in serum cortisol level[14]. But with the onset of surgery, serum cortisol concentration increased rapidly. Mizutani *et al*. (1996) showed that cortisol concentration during medazolam/fentanyl/oxygen/air anesthesia combined with epidural anesthesia in patients undergoing total abdominal hysterectomy and also compared with another group of patients sevoflurane/nitrous oxide/oxygen anesthesia combined with epidural anesthesia[15]. Castillo *et al*. (1997) reported that serum cortisol and other hormonal levels are significantly higher during intravenous anesthesia than during balanced anesthesia[16].

The present study shows serum cortisol level that is significantly higher in PT_2 in both groups. These were in good agreement with published data. When the patients are treated with only insulin cortisol, level raised by 279% after operation. But when they are treated with insulin with OHA, cortisol raised by 293%. It indicates that only insulin treated group gives better result regarding cortisol but it is not studied well.

CONCLUSIONS

a) Insulin treatment alone is more effective than insulin-OHA combination to control blood glucose in type 2 diabetic subjects undergoing surgery under general anesthesia

b) Surgery under general anesthesia in well controlled type 2 diabetic subjects is accompanied by a hyperglycemic response which results from rise of insulin antagonists like cortisol rather than fall of insulin secretion.

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Original Article

INTERVENTION AND THERAPIES ASSOCIATED MORTALITY IN INTENSIVE CARE UNIT OF BSMMU, DHAKA

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SUMMARY:

In the general ICU of BSMMU, Dhaka. 157 critically ill patients were studied for association between mortality and interventions/therapies. Among the patients 123 received mechanical ventilation (major interventions) and 100 of them expired which is very highly significant (P< 0.001). Among the patients who got minor interventions (urinary catheterization, nasogastric tube insertion, central venous line, tracheostomy)-none was significant. The patients who received therapies (fresh frozen plasma, whole blood, ionotropes/vassopressor drugs, platelet rich plasma)-no parameter was significant except the patients who got ionotropes /vassopressor therapy (P<0.05). From our study it is apparent that mortality is more associated with major interventions like mechanical ventilation and mortality associated with minor interventions are non-significant. Mortality associated with ionotropes /vassopressor therapy was significant.

INTRODUCTION:

While the majority critically ill patients require admission in ICU for a short period, some have particularly complicated courses of illness requiring admission for prolonged periods, as commonly defined by lengths of ICU stay for 2 to 3 weeks[1]. ICU length of stay is clearly influenced by a number of variables including the presence of intermediate care units and availability of ward beds and associated with increased risk for infection related complications, adverse outcomes, and consumption of a considerable amount of ICU resources[1,2]. Sixteen percent of the Dutch patients had an ICU-acquired infection in a European prevalence survey participated by 78 ICUs in Netherland[3]. Nosocomial infections lead to suffering of patients and cost burden of family as well. Majority infections at the ICU are device associated[4,5]. The effects of critical illness or treatments received in ICU contribute to mortality is poorly understood[6].

Intensive care unit is expensive and scarce in worldwide including Bangladesh[7]. Total number of ICU beds in Bangladesh is about 190 for 150 million peoples. Therefore admission to the intensive care unit (ICU) should be restricted, so that patients likely to benefit from ICU care[8]. This restriction excludes patients whose death is inevitable as well as those patients who should survive and do well without the need for intensive care. The working practices and outcomes from intensive care units are poorly documented in our country. The patients were admitted in the Intensive care unit from different discipline of Bangabandhu Sheikh Medical University hospital and also referred from other hospitals.

This study was instituted to investigate retrospective review of stored data from the archive. Demographic details, length of stay in ICU, any new diagnosis or any complications, usage of invasive devices and therapies associated with outcome were recorded to provide data for future development of Intensive Care Facilities.

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METHODS:

We studied retrospectively of 157 patients admitted in General Intensive care unit of Bangabandhu Sheikh Mujib Medical University Hospital in the year 2007 from January to June. Ethical clearance was taken from the departmental Ethical Committee of the Department of Anaesthesia, Analgesia and Intensive Care Medicine, BSMMU. Patients were admitted from the general medicine and surgical wards and emergency department. Patients developing a medical problem following surgery and patients admitted under the care of surgical specialties and did not need any surgery were also included in the study.

In accordance of criteria for analysis, a structured questionnaire was used and data were obtained from admission register, patient follow-up sheets, mortality record books and also from patients admission files. We observed admission diagnosis, co-morbidities, length of stay, different procedures and overall outcomes. We divided the total patients in different age groups, observed relationship of mortality with interventions performed in ICU and categorized the patients as recovery and death and their relation with different procedures and therapies.

Summary statistics are given as means for normally distributed data. Association in distribution was examined using Chi-square test. A p-value of d"0.05 was considered statistically significant. SPSS 11.5 was used for data entry and analysis and Endnote X for creating reference library.

RESULTS:

A total of 157 admissions with complete records were available. It was observed that the highest concentration of the population was in age group 61-70 years which was 20.4% of total ICU admission and second highest was in age group 51-60 years which was 19.7%.

Among 157 patients, 60 were found female which was 38.2 % and 97 were male, 61.8 in percentage. It is not exactly same distribution of national average of sex.Hospitalization in ICU was highest for the first 5 days and 66 patients hospitalized which were 42.0 in percentage.

Consultants outside ICU gave their valuable opinion in patient's treatment. Single consultant visited 39 patients and two consultants visited 16 patients and seven consultants visited 1 patient only. 88 patients out of 157 patients were treated under consultation of intensivists only. From 157 admitted patients 46 new diagnosis or complication were noted by reviewing the medical records of the patients. Among those, septicemia, acute renal failure were notable.

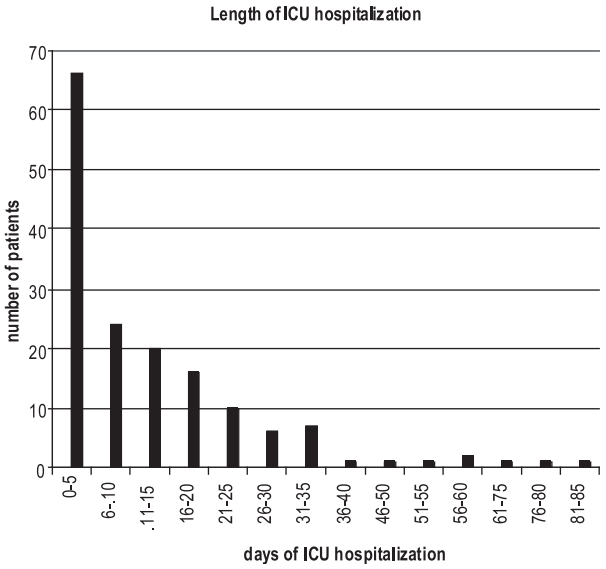

Fig.-1: *ICU length of stay*

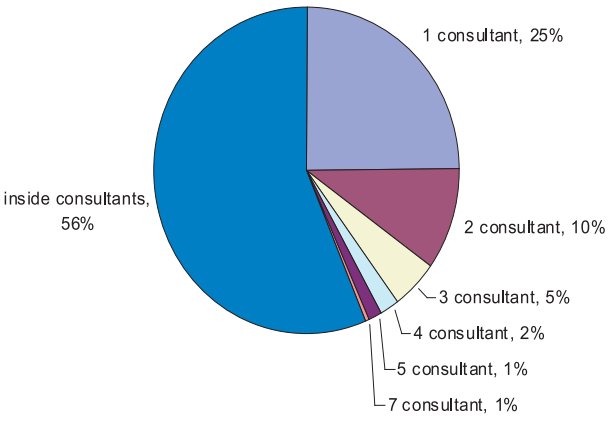

Fig.-2: *Number of Consultants per Patient*

Table - I

Relationship with interventions and outcome

Procedures or interventions		Recovery	Death	Total	Chi-square (P-value)
Mechanical ventilation	N (%)	23 (18.7)	100 (81.3)	123(100.0)	34.674(0.001)***
Urinary catherization	N (%)	37 (27.8)	96 (72.2)	133 (100.0)	0.302 (0.582)NS
Nasograstic tube insertion	N (%)	35(26.7)	96 (73.3)	131 (100.0)	1.463 (0.226) NS
Central venous line	N (%)	3 (37.5)	5 (62.5)	8 (100.0)	0.322 (0.570) NS
Tracheostomy	N (%)	0 (0.0)	1 (100.0)	1 (100.0)	0.404 (0.525) NS
Fresh frozen plasma	N (%)	3 (18.8)	13 (81.3)	16 (100.0)	0.856 (0.355) NS
Whole blood	N (%)	5 (18.5)	22 (81.5)	27 (100.0)	1.641 (0.200) NS
Ionotropic / vasopressor drugs	N (%)	9 (17.6)	42 (82.4)	51 (100.0)	4.483 (0.034)*
Platelet riched Plasma	N (%)	2 (18.2)	9 (81.8)	11 (100.0)	0.635 (0.425) NS

*** Very highly significant ($P < 0.001$)

* Significant ($P < 0.05$)

NS – Not significant.

N- Number

Urinary catheterization was done in 133 patients and 96 of them died. Nasograstic tube was inserted in 131 patients and 96 of them died. Central venous line was inserted to 8 patients 5 of them died. Tracheostomy was done in one patient and died none of them alone mortality relations was significant fresh frozen plaszma was given in 16 patients and 13 patients died. Whole blood was transfused to 27 patients and 22 patients died. Ionotropic/Vasopressor drugs were administered in 51 patients and 42 of them died which is significant ($P< 0.05$). Platelet riched plasma was given to 11 patients and 9 patients died.

DISCUSSION:

Our analysis was based on total number of ICU admission for the time period of six months. The data were gathered as a collaborative clinical ICU survey. The method of data collection, training and data validation was designed to minimize errors. However, the information was likely to be most accurate for objective information, such as ICU length of stay, therapies and invasive procedures and mortality rates, which were used to support the main themes of this article.

In our country, by the time patients reach the ICU, it may be possible to identify those with a high risk of death but it may be too late to do much to influence the outcome of those who die within the first day or two of admission. Such patients include those patients with brain damage after trauma or anoxia, with terminal cancer, and end stage respiratory failure. Many of these patients had underlying pathology and physiology too deranged to respond to a short period of intensive care therapy. Much intensive care research is focused on treatments directed at sepsis, adult respiratory distress syndrome, and multiple organ failure, problems that occur primarily in the long stay ICU patient. To appreciably decrease early ICU mortality, it may be necessary to intervene before ICU admission.

In our study in first 5 days, 66 patients hospitalized which were 42.0 in percentage. Among 46 new diagnoses or complication, septicemia and acute renal failure were notable. Major intervention (Mechanical ventilation) had strong association with outcomes (P value < 0.001). Eighty-one percent of patient died with Mechanical ventilation may be due to their moribund status, terminal stage of illness, lacking of proper knowledge of primary health care provider to deal with the primary illness, late referral of patients along with irreversible patho-physiological changes. On the

other hand, there is no significant association with minor intervention, which may be due to least nosocomial infections among the patients received medical therapies mortality is significant who received Ionotropic / vasopressors which is due to moribund status of patients.

The small proportion of patients with a longer ICU stay has the highest utilization of resources whereas ICU length of stay is the most important determinant of ICU cost and resource use[9]. Fourty-four percent patients were admitted for less than 2 days, 31% were admitted for 2 to 3 days, 21% were admitted for 4 to 13 days and 4% had a prolonged more than 14 days of admission to the ICU which is consistent with our study. The distribution of primary admission diagnosis was significantly (p £ 0.001) different among the patients who had intermediate (from 2 to 13 days) as compared to prolonged (³ 14 days) ICU admissions[1]. We have found more frequent usage of ventilation and indwelling catheter in comparison to a study whereas overall 58% of patients were mechanically ventilated, 61% had a CVC, and 86% had an indwelling catheter[4]. The incidence densities of patients at risk of developing an infection according to the duration of device they used. Patients with a device-associated infection had significantly longer ICU stays. When all patients were considered, developing nosocomial sepsis or two or more nosocomial infections independently increased mortality[4].

We enrolled all the patients during our study period, therefore, selection bias was minimized. Additional strength of our study was that we did not have such study before. A limitation of observational studies is that not all confounding variables can be taken into account. There is no explicit clinical diagnosis rule; therefore independent intensivists may classify a similar patient differently. As an analysis of a previous established database, we had limited clinical details of the course of illness. We did not have standard laboratory diagnosis for all patients and could not define a possible earlier infection of another type. We could not assess long-term outcome with follow-up.

Further study is needed to better define the determinants and clinical outcomes associated with prolonged admission to the ICU. Prevention of cross transmission of microorganisms may be more effective in patients housed in single rooms or cubicles.

Now ICU hospitals can use specific regular active surveillance systems, which take more treatment specific risk factors into account and may better support the critical care policy on the ICU.

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Review Article

ANESTHESIA CONSIDERATIONS IN LIVER TRANSPLANTATION

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INTRODUCTION

Liver transplantation has emerged as an increasingly successful treatment for patients with end-stage liver disease (ESLD).It is now a routine procedure performed in numerous medical centers throughout the world. Currently, about 250 liver transplants are performed in the United States every month. One year survival rates >80-85% & five years survival rates 50-60%.

Orthotopic liver transplantation (OLT) is the replacement of a diseased liver with a healthy liver in the normal anatomic position. The operative procedure is extensive, complex, and technically challenging with multiple vascular transections and anastomoses. In addition, the liver is an extremely vascular organ and extensive bleeding can occur in patients with portal hypertension due to ESLD.

The main indications for orthotopic liver transplantation (OLT) in adults are *alcoholic cirrhosis, chronic cirrhosis due to non-A, non-B hepatitis and hepatitis C, primary biliary cirrhosis, cryptogenic cirrhosis, and primary sclerosing cholangitis*. Only a minority of recipients are transplanted for cirrhosis due to hepatitis B, fulminant hepatic failure, malignancy, autoimmune cirrhosis, and a variety of inborn errors of metabolism.[1] The most common indication for OLT in pediatric patients is biliary atresia, followed by metabolic disorders, fulminant hepatic failure, cryptogenic cirrhosis, neonatal hepatitis, and malignancy.

Factors contributing to the recent success in liver transplantation[2]

1). Use of immunosuppressant therapy with cyclosporin & tacrolimus (FK-506)
2). Greater understanding and experience with liver transplantation.
3). Introduction of rapid infusion devices that allow transfusion up to 2 L/min of warmed blood.
4). Safe use of venovenous bypass.

Problems complicating the anesthesia for liver transplantation

1). Multisystem nature of cirrhosis
2). Massive blood loss throughout the procedure.
3). Haemodynamic consequences of clamping and unclamping the IVC and portal vein.
4). Metabolic consequences of the anhepatic phase.
5). Risks of air embolism and hyperkalemia when circulation to the new liver is fully established.

Pre-anesthetic evaluation

Preoperative evaluation is performed in two stages. In the first-stage all liver transplant candidates are examined by anesthesiologist. The later, second-stage evaluation is performed immediately before surgery.

Organization of preparation phase

Use of resources is the prime consideration during preparation for transplant. One should plan for an operating room time of 8 to 20 hours[3], with an average total time of 8.5 hours for anesthesia, 7 hours of which are devoted to surgery. The minimum anesthesia staff should be a 3:2 ratio of physician to certified registered nurse anesthetists or technicians to deal with simultaneous administration of anesthesia and operation of the rapid infusion system (RIS) device and the thromboelastrograph (TEG). A courier, responsible solely for the transport of specimens and blood products, is indispensable.

Anesthetic Technique

Because of the possibility of delayed gastric emptying, a routine rapid sequence induction should be performed. Induction with thiopental or

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ketamine with succinylcholine or vecuronium are techniques that work well. Maintenance of anesthesia with isoflurane in an air-oxygen mixture supplemented with sufentanil and vecuronium provides optimal conditions. Vecuronium is used so that the function of the new liver graft may be evaluated. The time for the return of a train-of-four (TOF) mode with a nerve stimulator correlates well with the function of the new graft[4]. Positioning and padding of the patient requires particular care be use the procedure may take many hours. The incidence of postoperative neuropathies is significant[5].

Typical transfusion requirements consist of

1. 15-30 Units of FFP.
2. 15-25 Units of platelets.
3. 15-30 Units of red blood cells.
4. 10-20 Units of cryoprecipitates.

Blood salvaging techniques (cell saver) can be extremely useful in reducing donor red cell transfusion. Aprotinin or EACA infusion may significantly reduce blood loss.

Several lines required

1) Two arterial lines, one radial & one femoral. 2) One large bore peripheral intravenous catheter in the antecubetal vein. 3) One large bore external or internal jugular catheter. 4) A Swan-Ganz catheter.

Monitoring

Liver transplantation requires the management of a) Severe coagulopathy b) Metabolic derangements c) Massive fluid shift & blood loss d) Temperature derangement e) Haemodynamic instability and Renal dysfunction.

Full invasive monitoring is mandatory with

Direct arterial pressure, Central venous pressure and Pulmonary artery pressure sensors. So that haemodynamic profiles can be calculated and appropriately managed. The presence of a *'stat lab'* in the immediate operating suite area allows rapid analysis of haemostasis profiles, electrolytes, and glucose and blood gases.

Coagulation status monitored by prothrombin time, APTT, platelet count, fibrinogen level, D-dimer or TEG.

Thromboelastography (TEG)

TEG has proved extremely valuable for relatively fast interpretation and understanding of the dynamic and complex coagulopathy pattern inherent in this procedure, thus guiding effective clinical therapy.Clinically useful information available within 30 minutes.

Transplant surgery can be divided into 3 phases:-

1. *Preanhepatic phase*. Through a wide subcostal incision, the liver is dissected so that it remains attached only by the inferior vena cava, portal vein, hepatic artery and common bile duct.
2. *Anhepatic phase*: This stage includes the hepatectomy and ends when vascular anastomosis of the IVC and portal vein is complete; the intrahepatic IVC anastomosis is prepared but not completed until late in this stage.
3. *Neohepatic phase* (Reperfusion and biliary reconstruction).the donor liver is incorporated into the recipient circulatory system by releasing, in sequence,clumps from the portal vein, the infrahepatic IVC and suprahepatic IVC. The portal artery anaestomosis is then perfomed and after adequate hemostasis the bile duct is reconstructed.

Each phase requires careful consideration by the anaesthesiologist.

Preanhepatic phase

At the beginning of surgery high filling pressure due to fluid overload, ascites, plural effusion, pulmonary hypertension, hyperdynamic circulation. Major fluid shift occurs due to drainage of liters of ascitic fluid, transection of large varices , surgical manipulation of liver & major vessels. These lead to decreased venous return & hypotension.Aggressive correction of coagulapathy is not necessary unless bleeding is excessive.

Packed red cells, FFP, platelets & cryoprecipitates are given according to coagulation status.

Anhepatic phase

Total hepatectomy is performed. Significant changes in haemodynamic indices with decreased venous return & fall of cardiac output , increased splancnic & lower caval pressure , decreased renal purfusion pressure, decreased systemic arterial pressure

Venovenous bypass (VVB)

Technique is used in patients identified at increased risk with venacava clamping. This technique involves cannulating the IVC and portal vein and diverting their blood flow (1-3 L/min) away from the liver and back to the heart, usually via an axillary vein. VVP is suggested for venous decompression, improve hemodynamic stability, and decreased intraoperative blood loss[6].

Neohepatic phase

This phase of surgery is marked by the release of portal blood flow through the graft. Severe haemodynamic instability known as the postperfusion syndrome may follow within a few minutes with severe hypotension, decreased heart rate, decreased SVR, increased pulmonary arterial pressure.

Hypotension is treated by strong vasopressors like, dopamine, epinephrine, phenylephrine & norepinephrine[7].

Coagulopathies should be corrected during this stage to obtain excellent haemostasis. Fibrinolysis if detected by TEG , reversed with aminocaproic acid & tranexemic acid

Hyperkalaemia & systemic acidosis may occur due to sudden influx of a cold, acidic, hyperkalemic fluid into the circulation. It is corrected by NaHCO3 (50mEq) just before unclamping & CaCl2 (500mg) exactly simultaneous with portal unclamping.

Fluid & metabolic consideration

Maintenance with IV fluid that does not contain lactate is a prudent choice.Infusion of crystalloid guided by renal function & haemodynamic parameter.Urine output is optimized by fluid challenge, osmotic & loop diuretics, dopamine infusion[8]. Ionised calcium levels should be monitored closely.

Postoperative management

If the new liver is functioning well, the patient can be extubated within two hours and transferred out of the intensive care unit within 24 hours. Marginal grafts may respond to continued infusions of PGE1 and careful management of fluid, electrolyte, and coagulation status. Postoperative bleeding requires early surgical intervention. Postoperative pain can be well controlled with the use of a patient-controlled analgesia pump.

New immunosuppressive drugs - Cyclosporin is the most commonly used maintenance immunosuppressive drug. Ster-oids are almost invariably added[9]. Azathioprine may be used as a third agent to reduce the dose of cyclosporine and, in some cases, may replace cyclosporine altogether when the latter is contraindicated or can no longer be used because of adverse side effects.

Anti-lymphocyte globulin preparations, including the mono-clonal antibody OKT-3[10], have been given prophylactically and for specific indications to prevent rejection. OKT-3 reacts against all mature T lymphocytes.

Other new drugs have been developed and tested in multicenter trials in the last decade. The most prominent is tacrolimus (FK506), which became an established immuno-suppressant agent for primary and rescue therapy in patients with liver, kidney and pancreas transplants.

Summary

Liver transplantation is no longer experimental and has become an acceptable therapy for chronic liver failure. Good anesthetic support is an essential element of a liver transplantation service.Anesthesia consideration for liver transplantation include the management of severely deranged physiology, pharmacology and biochemistry as all organ systems may be affected adversely by the failing liver. A close working relationship between all members of the operating team is necessary for the success of the program. The development of such teams in major transplant centers has resulted in a marked reduction in the morbidity and mortality of this procedure and a concomitant reduction in the cost.

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Case Report

HYPERSENSITIVITY REACTION AFTER INFUSION OF HARTMAN SOLUTION: IMMEDIATE DETECTION AND MANAGEMENT

Hasina Begum[1], Yameen Hossain[1], UH Shahera Khatun[2]

SUMMARY:

Although uncommon, hypersensitivity(allergy) and idiosyncratic reactions are potentially disastrous without early recognition and effective management. A 16 years old male patient suffering from stricture urethra (post traumatic) scheduled for urethro plasty under SAB(Subarachnoid block). But during preloading with intravenous fluid patient suddenly developed dyspnea, wheezing and rash which was managed immediately with steroid , antihistamine and bronchodilator and diagnosed as febrile reaction and surgery posponded. After 6 months he was again scheduled for surgery and at that time no adverse reaction was revealed after IV infusion for 15 minutes but suddenly developed severe respiratory distress and cardiac arrest and diagnosed as anaphylactic reaction which was managed with inj. adrenaline, cardiac massage, intubation & ventilation with 100% O2. And patient became completely stable within minute.

INTRODUCTION:

The risk of an adverse reaction increases in a non-linear fashion with the number of drugs given to a patient. Therefore, as polypharmacy is usual during anaesthesia, there is a substantial risk of drug reaction. The incidence of perioperative drug hypersensitivity in anaesthetic practice is about 1 in 11,000.[1] Most reactions during general anaesthesia follow intravenous drug adminstration.

Hypersensitivity reaction may be either anaphylactic or anaphylactoid. These reaction differ from direct drug induced histamine release which does not have an immunological basis.[2]

When an immune response results in exaggerated or inappropriate reactions harmful to the host, the term hypersensitivity or allergy is used.[3] The immune responses that may result from exogenous antigens take a variety of forms, ranging from annoying but trivial discomforts such as itching of skin to potentially fatal disease.[4]

Immediate hypersensitivity or anaphylaxis is an antibody-mediated reaction to an antigen characterized by a sudden, life threatening, generalized patho-physiological response involving the cutaneous, respiratory and cardiovascular systems. Primary antigen exposure stimulates the production of specific IgE antibodies which binds to mast cells. Re-exposure with antigen bridging of these IgE antibodies stimulates mast cell degranulation and systemic release of the mediators of anaphylaxis. Mediators are primary like histamine, adenosine, eosinophil chemotactic factors, poteases, heparins and secondary like leukotrienes, postaglandines, platelet activating factors, cytokines etc.[5]

Most important agents responsible for systemic anaphylaxis in anaesthetic practice includes I.V induction agents, muscle relaxents, opoids, ester local anaesthetic agents, colloid solutions, antibiotics like penicillin, blood products, hormones, enzymes, polysaccharides etc[6].

As the cause is unpredictable and as mortality increases with the delay in treatment, so early recognition and effective measures are essential.

CASE REPORT:

A 16 years old male patient of 48 kg with ASA physical status 1 was admitted to Dhaka Medical College Hospital with stricture urethra and had a plan to do urothroplasty under sub-arachnoid block(SAB). All physiological parameters, chest X-ray and laboratory findings were normal.

6 years back, he experienced RTA and developed ruptured urethra and subsequently stricture urethra and was operated under SAB without any

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anaesthetic complication[for 4 times]. But due to operative complication, he was scheduled for reconstruction operation[5th time] under SAB. During preloading with Hartman solution (iv fluid) for SAB patient suddenly developed dyspnea, wheeze and skin rash on OT table and treated with inj. hydrocortisone, inj. oradexen and inj. phanargan assuming a case of febrile reaction?, patient then become alright and surgery postponded. After 3 months patient again sent to OT for reconstruction under SAB. As patient previously developed saline reaction, preloading done slowly with Hartman solution and closely observed for 15 mins.and then prepared for intrathecal block.Suddenly patient developed severe respiratory distress and cardiac arrest. He was then immediately diagnosed as anaphylactic reaction and managed with CPR i.e inj. adenaline, intubation and ventilation with 100% O2. Patient became completely stable after few minutes. Now the patient is completely alright and waiting for operation.

DISCUSSION:

Richet & portier[8] were attempting to immunize dogs against toxins of the sea – anemone and noted that animal that had survived a sub lethal injection to toxins were unduly sensitive to a second injection – so sensitive indeed that quite small doses produced a severe reaction, often resulting in death. At first the phenomenon was explained on the basis of the toxic nature of the extract, but further works showed that other antigenic proteins could produce the same effects even though they were not in themselves toxic. Richet called the reaction anaphylaxis because it seemed to represent the antithesis of immunity (Gr. ana – against & phylaxis – protection). It was later demonstrated that anaphylaxis wad mediated by 'reagenic antibody' and finally that reagin was IgE[9].

The typical reaction is sometimes caused by the injection of drugs or forign proteins or by the bite of an insect. Systemic anaphylaxis may occure by polysaccharides[10].

In typical anaphylaxis antigen exposure has occured previously, leading to significant quantities of IgE being fixed to basophiles and mast cells. On a subsequent encounter with antigen a severe reaction ensures due to sudden release of mediators especially histamine.

In this case, the patient was operated several times (4 times) before these two episodes, when infusion of Hartman solution given all the times during operation without any reaction. But after that patient developed typical allergic reaction like itching, mild respiratory distress (wheeze) and skin rash. Unfortunately he was diagnosed as a case of febrile reaction and managed with steroids and antihistamines as hypersensitivity to polysaccharides are very rare.

Keeping in mind of saline reaction infusion of Hartman solution was introduced very slowly and observed for 15-20 minutes but there was no reaction. After that during preparation for SAB, patient suddenly developed severe respiratory distress and cardiac arrest. Advanced life support started immediately and patient became stable.

In case of systemic anaphylaxis Rachet & Portier shown that very small dose of offending antigen produced severe reaction in subsequent injection. But unusually the reaction occured after 15-20 minutes in this case, though the clinical features were typical of systemic anaphylaxis and managed accordingly. And the boy became completely stable after few hours. So prompt diagnosis and management can save some valuable life in anaesthetic practice.

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Original Article

NUTRITIONAL SUPPORT TO CRITICALLY ILL PATIENTS - A COMPARATIVE STUDY BETWEEN BRANDED AND HOMEMADE PREPARATIONS

Kazi Ashkar Lateef[1], Abdullah Al Maruf[1], Iqbal Hossain Chowdhury[2], Sayeed Mahmud Ali Reza[3], AKM Shafiqur Rahman[4]

ABSTRACT:

We have evaluated the effectiveness of nutritional support to critically ill patients undergoing treatment in ICU. We provided commercially prepared branded food in one group and compared this, with those of homemade preparations. Fifty adult critically ill patients getting treatment in ICU aged between 20 to 60 years having no diabetes, hypertension, ischaemic heart disease and chronic renal failure, were scheduled for providing enterai nutritional support. They were randomly allocated into two groups. Group A (n=25) received commercially prepared branded food containing balanced food consisting of protein, fat, and carbohydrate in calculated proportion. The aim was to provide 2500 Kcal of energy per day for an average adult in his/her critical state. Group B (n=25) received homemade food preparations in proper proportion of those of group A and of equal calories. The purpose of the study was to assess, formulate and compare the efficacy, tolerability and cost effectiveness of homemade prepared food with commercially formulated branded food in maintaining nutritional status of critically ill patient in ICU. Patient's nutritional assessment was done before the commencement of nutritional support, Nutritional assessment was repeated weekly for successive two weeks. Group A showed better result than Group B, significant improvement has been observed also in group B and the differences between two groups are statistically not significant Both the methods of nutritional support were adequate and effective in maintaining the nutritional status. Considering the poor socio-economic environment in an under developed country like Bangladesh, a less costly homemade preparation can be an effective alternative over the branded food.

INTRODUCTION:

Nutrition is defined as science of food and its relationship to health. It is not a single science but a duster of sciences related to the production and utilization of food.' Critical illness evoke a constellation of metabolic changes in the host inducting a transitory "ebb" phase followed by a hyper metabolic 'flow' phase. Magnitude of the change is proportional to the extent of insult or illness. Those changes require an extra amount of energy in addition to basic metabolic requirement to maintain the nutritional status of the host if this basic and extra amount of energy cannot be provided, the patient may show diverse systemic functional impairments. It is dear that nutrients are needed for protein synthesis, for organ function and to sustain life[2].

It is common for patient requiring intensive care to need nutritional support. It must follow the same rules as any other form of treatment with careful appraisal in each patient of the likely benefit or harm to be expected from it[3]. Critical illness is usually accompanied by anorexia or inability to eat because of impaired consciousness, sedation or incubations through upper airway. They are also metabolically stressed by the severity of their illness, injury or major surgery. So without nutritional support there is rapid loss of body weight and muscle mass Hence provision of adequate nutritional support in such patient is must requirement in Bangladesh, here may be two types of enteral food available for critical patient one commercially prepared branded food and another is homemade preparation maintaining proper nutrition, and equal calories.

This prospective randomized study was designed to assess, formulate and compare the efficacy, tolerability and cost effectiveness of homemade prepared food with commercially formulated

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branded food in maintaining nutritional status of critically ill patient in ICU.

MATERIALS AND METHODS:

We performed a randomized study on fifty critically ill patients of both sex, aged between 20-60 years in intensive care unit requiring nutritional support along with treatment. The study was performed at BSMMU, Dhaka in one calendar year. Patients with having hypersensitivity to artificial food, who can continue oral food intake, chronic renal failure, diabetes mellitus, ischemic heart disease and hypertension, were excluded from the study. Feeding was given through nasogastric tube. Total feeding procedure was explained to patient or their relatives and written consent were taken from them.

Nutritional assessment of each patient was done before commencing the nutritional support. It was done by taking dietary history-dietary habit, recent omission or inclusion of any food item, recent development of excessive vomiting, diarrhoea or any other form of gastric upset. Patient's nutritional requirement was assessed basing on their bodyweight and age, also considering the increasing requirement of calorie for the hypercatabolic state due to critical illness. As such and average requirement of an adult of average body weight was considered to 2000 Kcal using the Harris Benedict's equation. Another 500 Kcal was allotted for their hypercatabolic state. Patients were randomly allocated into two groups. Group A contained 25 patients, was considefed to be control group, who had fed Revit R' (a branded food). The amount of food powder was taken to achieve 2500 Kcal and preparation of the feed was done according to the instruction provided. Group B contained 25 patients was considered to be case or study group. The energy requirement was calculated like control group. Composition of homemade preparation was advised by the did nutritionist of BSMMU, selecting cheap, easily available food items in our country. Selection of food items such as chicken, beef, mutton, pulse, egg white etc. as protein source, rice powder, glucose, sugar as carbohydrate source and soyabean oil, mustard oil, butter etc. as fat source were done.. A feed composition was designed to provide a same caloric value as that of control group (2500 kcal). There were no fixed food composition and had relaxation of change depending on the availability, and patient's financial condition. But the food composition was always containing essential nutrients in all the cases. Both the groups were fed 10 times (feeds) per day roughly 200-250 ml/feed through easily accessible nasogastric tube.

Nutritional assessment of all the patients was done before commencing the study. Every patient was gone under thorough clinical examination. About body weight ,a clinical assessment of bodyweight which was correlated with the patient's expected bodyweight depending on his/her age and height. Other anthropometric parameters like triceps skin fold thickness, mid arm circumference and mid leg circumference were observed and recorded in both groups at the start of feeding and for successive two weeks in each subsequent follow up. Laboratory investigations like Hb%, lymphocyte count, serum total protein and serum albumin were also observed and recorded at the start of nutritional support and for successive two weeks in each subsequent follow up. Complications during nutritional support like, vomiting, diarrhoea and constipation also observed and recorded in both groups. The daily average cost of both feeding regimens in both groups were also calculated and recorded.

RESULTS:

Patient's demographics were similar and fairly comparable in both groups and the differences were statistically of significant (Table-1). Monitoring of patients nutritional status or the improvement of the status could be better comparable if the patients were of same disease. In this study it had been seen that the type of the cases studied was tried to be almost similar, brain tumour (operated) and head injury got the priority (Table-n).

Pre support arthropometric measurements lice triceps skin fold thickness, mid arm circumference and mid leg circumference were seen to in the lower limit in both groups and the differences between two groups were statistically not significant *(Table-111).* Pre support laboratory investigations like Hb%, lymphocyte count, serum total protein and serum albumin in both groups were observed near lower limit Differences of these laboratory values between two groups were statistically not significant (Table-III).

Table-I

Demographic data

Parameters	Group A (N=25)	Group B (N=25)
Age	36.92 ± 1.98	36.34 ±2.1
Sex (Male / Female)	21/4	20/5
Height	157.0 ±1.52	156.5 t 1.76
Expected Body Weight (Kg)	56.3 ± 1.48	532 ±1.51

Values are mean ± SEM

No significant differences between groups.

Table- II

Types of cases studied

Name of disease studied	Group A	Group B	Total
Brain tumour OP effective of (ICSOL)	7	7	14
Head Injury	6	5	11
Chronic obstructive pulmonary disease(COPD)	3	4	7
Guillain Barre Syndrome (GBS)	2	2	4
Bronchial carcinoma	1	1	2
Cerebral malaria	1	1	2
Viral encephalitis	1	1	2
Meningitis	1	1	2
Oral malignancy	1	1	2
Hydrocephalus	1	1	2
Disseminated intravascular coagulation (DIC)	1	1	2

Table –III

Comparison of pre support parameters of patient between two groups

Groups	Triceps skin fold thickness (mm)	Mid arm circumference (cm)	Midleg circumference (cm)	Hb% (gm/dl)	Lymphocyte count(%)	Serum total protein (gm/dl)	Serum albumin (gm/dl)
Group A	12.58 t 0.04	26.32 ±1.96	36.42 t 2.2	8.8 ±0.4	12.2t2.3	5.1 t0.22	2.6t0.02
Group B	12.6 t 0.05	26.28	± 2.20	36.38	± 2.5	8.6	± 0.3
ResultStudents	NS	NS	NS	NS	NS	NS	NS

Values are mean ± SEM

NS - No significant difference

Table –IV

Comparison of pre and post support parameters of patient after completion of nutritional] support in group A

Groups	Triceps skin fold thickness (mm)	Mid arm circumference (cm)	Midleg circumference (cm)	Hb% (gm/dl)	Lymphocyte count(%)	Serum total protein (gm/dl)	Serum albumin (gm/dl)
Presupport	12.58± 0.04	26.32 ±1.26	36.42 t 2.2	8.8 ± 0.4	12.2t2.3	5.1 t0.22	2.6t0.02
Postsupport	12.6t0.05	26.80	36.81 t2.02	10.0 t0.7	21.5t1.2	6.2t0.21	3.2t0.02
15 After days							
Result							
Students 't'test(unpaired)	P<0.01	P<0.01	P<0.01	P<0.01	P<0.01	P<0.01	P<0.01

Values are mean ± SEM

P<0.01 - Statistically significant

P<0.001 - Statistically highly significant

Table -V

Comparison of pie and post support parameters of patient after completion of nutritional support in group B

Groups	Triceps skin fold thickness (mm)	Mid arm circumference (cm)	Midleg circumference (cm)	Hb% (gm/dl)	Lymphocyte count(%)	Serum total protein (gm/dl)	Serum albumin (gm/dl)
Pre support	12.6±0.05	26.28±2.2	36.38±2.5	8.6±0.3	11.8±2.1	5.2±1.89	2.7±0.01
Post support after 15 days							
Students 't' (unpaired)	P<0.01	P<0.01	P<0.01	P<0.01	P<0.01	P<0.01	P<0.01

Values are mean ± SEM

P<0.01 - Statistically significant

P<0.001 - Statistically highly significant

Table -VI

Comparison of post support parameters of patient after 15 days between two groups

Groups	Triceps skin fold thickness (mm)	Mid arm circumference (cm)	Midleg circumference (cm)	Hb% (gm/dl)	Lymphocyte count(%)	Serum total protein (gm/dl)	Serum albumin (gm/dl)
Group A	12.6±0.05	26.8±2.28	36.81 +2.02	10.0 ± 0.7	21.5+1.2	6.2 ± 0.21	3.2 ±0.02
Group B	12.63±0.03	26.68±2.22	36.68±2.4	9.9 ± 0.5	20.6 ± 1.2	6.3 ± 0.18	3.3 ± 0.04
Result Students 't' test(unpaired)	NS	NS	NS	NS	NS	NS	NS
Values are mean ± SEM							

NS- No significant difference

In control group A, branded food was fed and the results were recorded (Table-IV). Values of biceps skin fold thickness, mid arm circumference and mid leg circumference showed significant (P<0.01) improvement after 2nd week from pre support values. Laboratory investigations -Hb% and lymphocyte count showed improvement from pie support recordings to recordings *after* 2nd week and improvements were statistically highly significant (P<0.001). Serum total protein and serum albumin showed improvement and the difference between pre support values and values after 2nd week were statistically Significant (P<0 01).

In study group B, homemade food was fed and pre support and post support (after 2 weeks) values were recorded (Table-V). Values of triceps skin fold thickness, mid arm circumference and mid leg circumference showed significant (P<0.01). improvement after 2nd week from pre support values. Laboratory investigations - Hb% and lymphocyte court showed improvement from pre support recordings to recordings after 2nd week and improvements were statistically highly significant (P0.001)- Serum total protein and serum albumin showed improvement and the difference between pre support values and values after 2nd week were statistically significant (P<0.01).

After 2nd week both groups showed improvement in patients by feeding regimens by increasing anthropometric parameters and laboratory findings. Values showed a better improvement in group A than group B but differences were statistically riot Signifcant (Table-VI).

Incidence of complications like vomiting, diarrhoea and constipation during nutritional support was less in both groups and differences between two

groups were statistically not significant. None of the patients of both groups showed any complications associated with tube insertion, tube itself or due to feed content. Cost status of feeding regimen in both groups were calculated, group A showed 750 taka/day and group 6 *showed* 150 taka/day. Statistics showed it was 5 tines costly in group A than group B.

DISCUSSION:

The accelerated catabolism associated with acute illness or injury may further exacerbate tissue loss superimposed upon weight loss. Malnourished persons are depressed and suffer from muscle wasting and respiratory muscles including diaphragm, impairing respiratory function and dear secretion. Malnutrition also reduces respiratory drive[3,4,] impaired immune functions and increased rate of infection[5,6,7]. Acute illness and malnutrition may impair the digestive and barrier function of the gut Both the functions may be protected by enteral feeding not by pererderal nutritional support[3,8], and more than 48 hours starvation may also impair vasoconstrictor responses to cold and reducing heat conseivation[9].

Nutritional support is an obvious life support for critically ill patients. The aim of nutrition al support for critically ill patient proposed by American Society for Perenteral and Enteral Nutrition has included[2,10] (1) detection and correction of preexisting malnutrition, (2) prevention of progressive protein energy malnutrition, (3) optimizing patient's metabolic state and, (4) reduction of morbidity and time of convalescence.

Method of support may vary considering the nature of critical illness. It should be done by a team which includes concerned physician, clinician nutritionist, dietetic and cook. The method of nutritional support to critically ill patients in different hospital of Bangladesh is in primitive state. We are running short of concerned specialist manpower, resources and lack of organized way of providing nutritional support. So, present trend is that either clinician prescribes a branded preparation or patient's party prepares a homemade food regimen at their own with proper calculation about patient's energy requirement Patient in ICU, stay is usually for a short time so total duration of nutritional support was considered to be 15 days in this study. Regarding selection of cases post operative neurosurgical patients and patients with head injury got priority.

Pre support parameters were thoroughly assessed obtaining details of the dietary history, physical examination, anthropometry and laboratory investigations. Amongst the anthropometric measurements, body weight was scheduled to be given due importance. But considering the clinical state of patient lying flat on the bed or on ventilator and non availability of the weighing bed it could not be done properly and monitoring of body weight was discontinued. Among other anthropometric parameters, triceps skin fold thickness mid arm circumference and mid leg circumference were observed. Triceps skin fold thickness representing the body fat", mid arm circumference, mid leg circumference represent skeletal muscle mass and fat. Considerable changes may occur with progress of disease, but nutritional support can improve the condition. In group A, significant improvement had occurred with the provision of nutritional support after IS days although no such changes were marked after initial 7 days. Similar changes were marked in group B, which confirmed the theoretical basis.

At the start of this study, laboratory findings showed significant deterioration of Hb%, lymphocyte court, serum total protein and serum albumin. Almost all the findings were below or near acceptable limit in respect to the patient's age and sex. Decrease in Hb%, serum total protein and serum albumin may be a reflection of the metabolic response to trauma and injury (increase protein catabolism). Reduction in lymphocyte count may be due to immunosuppressant factors. These deteriorations reflect critical illness. In group A highly significant improvement had occurred in Hb% and lymphocyte count with nutritional support. Similar highly significant improvement was observed in group B where nutritional support was provided with homemade preparations. Serum total protein and serum albumin were showed significant improvements in both groups after 15 days of nutritional support. Patients of both groups showed clinical improvements in respect to their muscle power and sense of well being which signified the adequacy and effectiveness in maintaining the nutritional status and these revealed homemade preparations are equally adequate and effective Iike branded food. So under developed country like Bangladesh, nutritional status can be maintained satisfactorily selecting

common, cheap, easily available food items, which can reduce the huge expenditure of the patient in ICU. The homemade preparation adopted in this study can be applicable to other cases in future. Some untoward incidences like diarrhoea, vomiting, constipation developed in both groups but they were not significant. Avoidance of complication could be possible with caution. Regarding cost effectiveness homemade preparation was less costly (5 times) than that of branded formula. In poor socio-economic country like Bangladesh cost of treatment is definitely a matter of consideration.

CONCLUSION:

Patients undergoing treatment in ICU remain in a critical state of their health where nutritional support can ensure a good organ function or can prevent their functional impairment. In this study nutritional support to critical patients was provided with branded food in one group and homemade preparation in another group. Both groups showed almost equal improvement in nutritional status. Both the methods were adequate and effective in maintaining nutritional support of the critically ill patients. Branded food items are costly and not easily available but easier to prepare. On the contrary homemade preparations were cheap, easily available and prepared from common food items. To bring out a successful outcome both the methods of nutritional support can be recommended but considering the poor socio-economy of Bangladesh homemade preparations can be preferred.

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Original Article

ROLE OF DEXAMETHASONE ON REDUCING POST TONSILLECTOMY MORBIDITIES

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SUMMARY

Pain, nausea, vomiting, oedema and poor oral intake are the most common morbidities after general anesthesia and surgery like tonsillectomy. This study was done to evaluate the effectiveness of intravenous dexamethasone (0.15mg/kg) at induction of anaesthesia on post tonsillectomy morbidities. In this prospective randomized double blind study, sixty children of age between 8-12 years, ASA I & II undergoing tonsillectomy under general anaesthesia were randomly assigned into two equal groups of 30 each. They received dexamethasone IV or saline (control) following induction of anaesthesia. Both anesthetic and surgical techniques were standardized. Post operative pain was assessed by visual analogue scale (VAS). Inj. Tramadol 1mg/kg in first 6 hrs and oral paracetamol 10mg/kg in next 24 hrs were administered as rescue analgesic. Incidence of nausea, vomiting, time and quantity of first oral intake were also noted. Patients receiving dexamethasone experienced significantly less pain, nausea and vomiting than control group throughout 24 hrs. Lesser patients required rescue analgesics (23.33% vs. 46.67%) in first 6 hrs. So, it is found that, single intravenous dose of dexamethasone (0.15mg/kg) provided significant analgesia, reduced nausea, vomiting and improved quality of oral intake in paediatric patients who underwent tonsillectomy.

INTRODUCTION

Following tonsillectomy in paediatric patient, pain, nausea, vomiting, oedema, poor oral intake are the most common morbidities which need medical attention. Association between pain and postoperative nausea, vomiting is also proved. [1] Postoperative pain in children is intense and short lasting, children with mild to moderate pain need analgesia only for 24 hrs.[2] Postoperative nausea, vomiting not only causes dehydration, electrolyte imbalance and delayed discharge, it can result in tension on suturelines, venous hypertension, increased bleeding under skin flap and pulmonary aspiration of vomitus.[3] There have been different reports of anti-inflammatory and antiemetic properties of corticosteroids used during different types of surgeries [4,5]. Tissue-injury induced acute inflammation is known to play a significant role in the genesis of surgical pain and dexamethasone is also known to have potent anti-inflammatory effect.[5] Aasbo etal [6] have demonstrated the effectiveness of steroid for hallux valgus and haemorhoidectomy surgery. Analgesic effect of corticosteroid has been observed by Baxendale etal [7] for extraction of third molar tooth. Dexamethasone has been used successfully as an enti-emetic for chemotherapy induced vomiting[7]. This study was undertaken to find out the effectiveness of a single intravenous dose of dexamethasone (0.15 mg/kg) on post tonsillectomy morbidities like pain, nausea, vomiting and oral intake.

MATERIALS AND METHODS

After taking informed consent and authority approval children aged between 8-12 years, ASA I & II undergoing tonsillectomy under general anaesthesia were recruited in this study. Patients with coagulopathy, diabetes, gastritis, peptic ulcer, cardiovascular, renal, hepatic diseases or on therapy with steroid, anti-emetics, anti-histamine or aspirin were excluded from the study. The patients were randomly assigned into two equal groups (dexamethasone and control groups) each with 30 members. The procedure of induction and maintenance of anaesthesia were the same for both groups. After preoxygenation with 100% oxygen for 3 mins, induction of anaesthesia was done with Inj. Fentanyl 1µg/kg and Thiopentone sodium 5mg/kg IV and tracheal intubation done after giving Inj Succinylcholine 1.5 mg/kg IV. General anaesthesia

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was maintained with 0.5-0.6 % halothane and 50% N_2O in oxygen and Inj. Atracurium besylate 0.5mg/kg. Before surgical incision one blinded anaesthesiologist administered either saline 2ml or dexamethasone 0.15mg/kg diluted in 2ml saline IV. Per- operatively D_5 0.225 NS fluid was infused at a rate of 5ml/kg/hr. Neuromuscular blockade was reversed with Inj. Neostigmine (0.05mg/kg) along with Inj. Atropine (0.02mg/kg) and tracheal extubation performed.

Another anaesthesiologist monitored the patient in post operative room for first 6 hrs and in the ward for 6 - 24 hrs. Pain was assessed by visual analogue scale (VAS – 0 to 100). Monitoring was done half hourly for the first 2 hrs, hourly for the next 4 hours and then at 8, 10, 12 & 24 hrs. If VAS > 40, rescue analgesic Inj. Tramadol 1mg/kg for first 6 hrs and orally paracetamol 10mg/kg for 6 – 24 hrs were administered.

Patients were divided into three pain groups for first 6 hrs and 6 – 24 hrs.

Moderate to severe pain	if,	VAS 40
Mild pain	if,	VAS < 40 > 20
No pain	if,	VAS < 20.

Nausea and vomiting if occurred, were recorded. Numbers of episodes of vomiting were also recorded. Inj. Ondansetron (0.1mg/kg) was used as rescue anti-emetic, if more than 2 episode of vomiting occurred in an hour.

Post tonsillectomy bleeding if occurred was noted. 4 hours after surgery patients were asked to take oral liquids. Quality of oral intake was graded as follows:

Excellent – when patient requested it, Good – patient accepts it when offered, Fair – patient accepts it on pressure, Poor – when patient refuses it.

If oral intake was delayed, time duration between the end of surgery and first acceptance of oral liquid noted.

Statistical Analysis

The data were compiled and analysed with the help of Chi-square test.Values were expressed as significant if $p< 0.05$ (confidence limit – 95%).

RESULTS

There was no significant difference between groups in ages, weight, height, ASA, type & duration of surgery. Regarding post operative pain, dexamethasone group had significantly lower VAS score than control group although 24 hrs. VAS of 27.4 ± 7.82 in control group versus 12.8±8.24 in dexamethasone group was noted ($p < 0.001$). In first 6 hrs incidence of moderate to severe pain was 73.33 % in control group versus 43.33 % in dexamethasone group ($p <0.05$). In 6 – 24 hrs 37 % of control group versus 90% of dexamethasone group were pain free ($p <0.001$). Through out 24 hrs analgesic requirement was less in dexamethasone group ($p <0.05$).

Rescue analgesics in control versus dexamethasone group was (46.67% vs. 23.33%) in first 6 hrs. and in 6 – 24 hrs. (20% vs. 3.33%).

Total no of vomiting episode were significantly higher in control (25) group compared to dexamethasone group (13), $p<0.01$. Six patients in control group versus two in dexamethasone group had two or more episodes of vomiting.

Table-I

Post Tonsillectomy Pain

Parameters	0-6 hours		6-24 hours	
Pain	Control	Dexamethasone	Control	Dexamethasone
Moderate/Severe	22(73.33)	13(43.33)*	10(33.33)	2(6.67)***
Mild	6(20)	11(36.66)*	9(30)	1(2.22)***
No Pain or pain free	2(6.67)	6(20)*	11(36.67)	27(90)***

* $p < 0.05$

*** $p < 0.001$

Table-II

Postoperative nausea, vomiting (PONV)

Parameters		Control	Dexamethasone	
Nausea	0-6 hrs	10 (33.33)	8 (26.67)	P>0.05
	6-24 hrs	4 (13.33)	0 (0)	P>0.05
Vomiting	0-6 hrs	8 (26.67)	6 (20)	P>0.05
	6-24 hrs	2 (6.67)	1 (3.33)	P>0.05
Pts. with multiple episodes of vomiting			6 (20)	2 (6.67)
Total number of episodes of vomiting			25	13

Oral intake was significantly delayed in control group (7.55 ± 1.91hrs) than dexamethasone group (5.77 ± 1.5 hrs) $p < 0.05$. In control group number of patients with excellent / good / fair and poor quality of intake was (2, 22, 5,1) and in dexamethasone group it was (8, 19, 3, 0) $p < 0.05$.

No patient had post tonsillectomy bleeding in dexamethasone group.

DISCUSSION

Tonsillectomy is a common operation performed in paediatric patients, but its post operative morbidities really need medical attention. Post tonsillectomy pain is caused by tissue injury induced acute inflammation, nerve irritation and spasm of exposed pharyngeal muscle. Oropharyngeal pain and irritation of gastric mucosa by swallowed blood are two main contributors of high incidence of PONV following tonsillectomy. Acute nociception at peripheral tissues leads to prostaglandin synthesis by induction of cyclo-oxygenase-2 and activation of phospholipase A2, resulting in a hyperalgesic state[8]. Corticosteroids are known to inhibit phospholipase and block both cyclo-oxygenase & lipo-oxygenase pathway, thus reducing prostaglandin synthesis[8] and thereby causing pain relief. In 1964, Smith injected a steroid penicillin- local anaesthetic mixture into the tonsiller fossa during surgery and observed a reduction in post operative pain and inflammation[9]. Corticosteroids have shown significant analgesia for extraction of third molar tooth, hallux valgus correction and haemorroidectomy [6,7]. The mechanism of dexamethasone induced anti emesis is not fully understood, but central inhibition of prostaglandin synthesis[10] and decrease in 5-HT turnover in the CNS[11] or changes in the permeability of blood CSF barrier to serum proteins may be involved[12]. Multiple studies have shown benefits with corticosteroid alone or as adjuvant for chemotherapy induced vomiting, gynaecological surgeries, thyroidectomy and opoid induced vomiting[13,14,15]. Local infiltration of steroids and oral 4 day course of steroids have shown promising results in tonsillectomy patients[16,17].

Our main aim was to evaluate the analgesic and anti-emetic effects of steroid on post-tonsillectomy paediatric patient.

Dexamethasone is highly potent and for its glucocorticoid activity has long half life (36-72 hours), so that the effect would remain even after the discharge of the patient. Single intravenous dose is devoid of side effects like gastritis, delayed healing in surgical patient, adrenal suppression etc[18]. Dexamethasone was given in intravenous route just before surgery to achieve peak effect in the early post operative period.

In our study the dose of dexamethasone selected was 0.15 mg/kg as doses ranging from 0.15 to 1mg/kg with maximum doses ranging from 8 to 25 mg have been used in the children. Splinter and Roberts[19] have used 0.15 mg/kg dexamethasone with good results. Doses used in adults are 8mg or 10mg, this also corresponds to 0.15mg/kg dose.

For evaluation of pain, we have used visual analogue scale, as we have selected children between 8 to 12 years of age. VAS score was lower in dexamethasone group throughout 24 hrs, this indicates prolonged analgesic effect of dexamethasone. Number of patients requiring rescue analgesic was less in dexamethasone group than control group.

In our study overall incidence of PONV was less (25%), compared to previous studies (40 – 70%). Splinter et al also showed reduction in PONV from 72% to 40% using 0.15 mg/kg dexamethasone.

We found better quality of oral intake in dexamethasone group, perhaps by decreasing pain and inflammation.Steward etal[20] found that children receiving dexamethasone were more likely to advance to a soft or solid diet in first tonsillectomy day.

CONCLUSION

In conclusion, we can say that a single intravenous dose of 0.15mg/kg dexamethasone, following induction of anaesthesia provided adequate and prolong analgesia, anti-emesis and earlier and better quality of oral intake without any complications in paediatric patients who underwent tonsillectomy.

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Original Article

COMPARISON OF PRE-EMPTIVE USE OF DICLOFENAC, KETOROLAC AND TRAMADOL FOR POST-OPERATIVE PAIN IN LAPAROSCOPIC CHOLECYSTECTOMY

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ABSTRACT:

Under treatment of postoperative pain has been the topic of several recent editorials[1]. The prevention, recognition, and management of postoperative pain in adults, as well as in children, have been receiving a great deal of interest. The poor outcome obtained with current regimens is primarily due to the inadequacies of drug administration techniques rather than the qualities of opioids themselves[2].

In this prospective study comparison of preemptive use of diclofenac, ketorolac and tramadol was done for postoperative pain in laparoscopic cholecystectomy.60 patients were divided into three groups. Group A received injection Diclofenac (3mg/kg) 75mg maximum at a time. Group B received injection Ketorolac (30 mg). And group C patients received injection Tramadol (100 mg). All drugs were given intravenous half an hour before induction. Analgesic efficacy was measured in VAS scale. In addition pulse, systolic blood pressure, diastolic blood pressure, mean blood pressure, total pethidine requirement and time of first pethidine requirement were recorded Patients received an increment of 10-20 mg of pethidine when pain score was 3-4.

In this study, total pethidine consumption in group A is 56.5±5.14, in group B is 46.75±4.65 and in group C is 49±5.42. It shows that group B and group C have same analgesic effectiveness and which is better than group A.

On the basis of present prospective clinical study postoperative pain can be managed by preemptive use of diclofenac, ketorolac and tramadol. The analgesic efficacy of ketorolac and tramadol is same and better than diclofenac.

Key Words: Pre-emptive analgesia, Laparoscopic cholecystectomy.

INTRODUCTION:

Under treatment of postoperative pain has been the topic of several recent editorials[1]. The prevention, recognition, and management of postoperative pain in adults, as well as in children, have been receiving a great deal of interest. The poor outcome obtained with current regimens is primarily due to the inadequacies of drug administration techniques rather than the qualities of opioids themselves[2].

The most common method of managing pain following surgery is the use of intramuscular (1M) opioids prescribed on demand basis [3]. Fluctuating blood levels of opioids may result in sedation or other adverse effects when the blood levels are high and inadequate analgesia when the levels are low before the next injection can be given. Another reason for inadequate pain relief by IM opioids is the excessive delay to administer the ordered injection[4]. Excessive concerns about side effects of opioids and addiction also result in the current undertreatment of postsurgical pain[5].

The importance of peripheral and central modulation in nociception has fostered the concept

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of "preemptive analgesia" in patients undergoing surgery. This type of management pharmacologically induces an effective analgesic state prior to the surgical trauma. This may involve infiltration of the wound with local anaesthetic, central neural blockade, or ketamine. Experimental evidence suggests that preemptive analgesia can effectively attenuate peripheral and central sensitization to pain. Although some studies have failed to demonstrate preemptive analgesia in human, other studies have reported significant reductions in postoperative analgesia requirements in patients receiving preemptive analgesia[6] Transmission of pain signals evoked by tissue damage leads to sensitization of the peripheral and central pain pathways. Pre-emptive analgesia is a treatment that is initiated before the surgical procedure in order to reduce this sensitization. Owing to this protective effect on the nociceptive system, pre-emptive analgesia has the potential to be more effective than a similar analgesic treatment initiated after surgery[7].

NSAIDs inhibit the cyclo-oxygenase enzymes, and decrease peripheral central prostaglandin production. In addition to reducing the inflammation that accompanies tissue injury, decreasing prostaglandin production attenuates the response of the peripheral and central components of the nervous system to noxious stimuli. Such a reduction in the response to pain can reduce the peripheral and central sensitization induced by noxious stimuli. These properties would seem to make NSAIDs ideal drugs to use in a pre-emptive fashion, where analgesics are administered prior to a noxious stimulus, such as surgery, with the expectation that reduction in peripheral and central sensitization will lead to a decrease of pain[8]. Tramadol has three fold of mode of action. It binds to and activates the opioid receptors with a 20-fold preference for μ receptor. This action is weak but is that of a full agonist. It also inhibits the neuronal reuptake of norepinephrine, potentiates the release of serotonin and causes descending inhibition of nociception[9]. In laparoscopic surgery there is decreased postoperative pain and consequent smoother recovery than after open operations. Pain after laparoscopy is caused by the stretching of the peritoneum, residual gas, the effect of surgery and the portholes or any skin incisions. Pain is treated optimally with local anaesthetic, paracetamol, NSAIDs and opioids if required[10].

This study was performed to compare the preemptive use of diclofenac, ketorolac and tramadol for postoperative pain in laparoscopic cholecystectomy.

SUBJECTS AND METHODS

Subjects**:**

It is a prospective comparative study of 60 patients scheduled for laparoscopic 1 cholecystectomy under general anesthesia. The purpose of the study was explained to each subject and recruited only after they gave their written consent. In this study patients for laparoscopic cholecystectomy were in ASA grades I&II and the age were in between 18-60 years. Patients who were unwilling to be included in the study, with the H/O allergy to drugs (under study), bleeding diathesis, COPD and lastly the renal disorder were excluded from this study.

Method:

A total of 60 cards, 20 in each group were prepared by another person who was blind about the study. After recruitment every patient was allowed to draw one card and grouped accordingly. Group A: These patients received injection diclofenac. It was given in a dose of 3 mg/kg, up to maximum of 75 mg.

Group B: Patients received injection ketorolac (30mg).

Group C: Patients received injection tramadol (100mg).

All drugs were diluted up to Sm1. After taking approval from the departmental ethical committee and informed consent from each

Patient during preoperative visit 24hours before operation was instructed for 6 hours of fasting and was prescribed tablet Ondansetron (8mg) I hour before operation with sips of water.

In the operation room an intravenous cannula (18G) was inserted and the patient received Ringers lactate solution. Pulse rate, blood pressure, rate of respiration, ECG was recorded before general anesthesia. Then study drug was injected as per group of the patient according to random assignment half an hour before induction. All patients were pre oxygenated/ for 3mins. Induction was done by Thiopental sodium 3-5mg/kg,

suxamethonium 1.5 mg/kg body weight for tracheal intubation and then vecuronium 0.08mg/kg body weight and then incrementally at 0.02mg/kg (when TOF returns at 25%) was used for maintenance of muscle relaxation.

Per operative monitoring was Pulse, Blood pressure oxygen saturation ($SP0_2$), electro cardiogram (ECG), Temperature every hourly for the first six hours, then 2hourly for three readings and then 3hourly for 4 readings.

Pain was evaluated postoperatively using a standard 10cm linear visual analog scale. 0 corresponding no pain and 10 the worst pain possible In addition heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, SP02, and ECG were monitored. This recording was performed immediately after operation and then hourly for 6 hours, then 2 hourly for 6 hours, then 3 hourly for 12 hours. The duration of time from the end of operation to the first requirement of analgesic was recorded. When pain score was 3-4, Pethidine 10-20mg I.V. was given. Total consumption of Pethidine in 24 hour was recorded.

RESULTS

Observation of the present study (Table I) was analyzed in the light of comparison among the subject groups (20 patients in each group). All results are expressed as mean ± standard error of mean (SEM) or in frequencies as applicable (Table I). The studied groups became statistically matched for age (p =0.720), weight (p =0.471), duration of surgery (p = 0.671), base line pulse rate (p = 0.121), base line systolic blood pressure (p = 0.939), base line diastolic blood pressure (p = 0.893) as well as base line mean blood pressure (p= 0.900).

There was no significant difference in pulse rate among the three groups. The decrease or increase of systolic blood pressure was not statistically significant. Statistically no significant difference was observed in diastolic blood pressure. The changes of mean blood pressure were not statistically significant. Intensity of pain at different time period was measured using 10 cm visual analogue scale (VAS). The mean-+SEM values of VAS in the POW of group A was 0.65±0.209, group B was 0.45±0.135 and group C was 0.45t0.135; (p = 0.000). (Figure.3) The values are not significant. The time of mean±SEM of 1st rescue dose of pethidine in diclofenac was 1.8±0.11 hour, in ketorolac was 2.2+0.12 hour and in tramadol was 2.3f0.10 hour.

Total pethidine consumption in the present study was measured in mg. The mean±SEM value of the total Pethidine consumption in group A was 56.50±5.14, in group B was 46.75±4.63 and in group C was 49.00±5.42.

Three fourth of the study population experienced no adverse effects. Rest of the patient complains incidence of non-serious adverse effects. No patient terminated the study prematurely because of these adverse events. Some patients of tramadol group complained of nausea & vomiting. Other adverse events such as hangover, urinary retention, itching, and headache were less frequent in all three groups.

Table-I

Demographic data:

	Group A	Groups B	Group C
Age (years)	38.45±192	37 50±1 88	39 60± 1.68
Weight (kg)	65.50±1.05	66.00±0.45	64.75±0.49
Duration (minutes)	70.90+5.08	68.05±6.56	76.00±7.22

Values are expressed as mean ±SEM. between groups analyses were done by ANOVA test. Values are expressed as significant if p<0.05 (CI-95%).

Table-II

Age Distribution:

Age (years)	Group A	Group B	Group C	Total
20-34	5(25%)	7(35%)	3(15%)	15(25%)
35-49	14(70%)	*11(55%)*	14(70%)	39(65%)
50-64	1(5%)	2(10%)	3 (15%)	6(10%)

Values are expressed as frequency. Within parenthesis are percentages over column total.

Table-III

Weight distribution.

Weight(kg)	Group A	Group B	Group C
55-61	3(75%)	0(0%)	l(5%)
62-68	12(60%)	19(95%)	19(95%)
69-75	5(25%)	1(5%)	0(0%)

Values are expressed as frequency. Within parenthesis are percentages over column total.

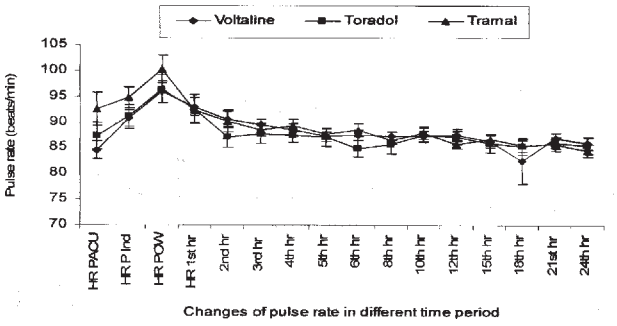

Fig.-1: *Changes of pulse rate in different time period (mean+SEM)*

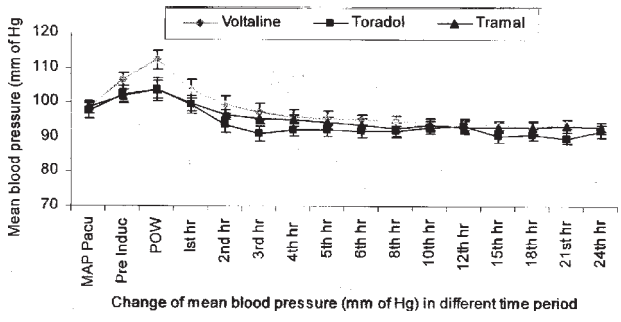

Fig.-2 : *Change of mean blood pressure (mm of Hg) in different time period*

DISCUSSION

Morphine and its derivatives have been extensively used to treat postoperative pain in spite of relatively high incidence of side effects11. The standard practice of injecting intramuscular opioids on demand gives poor result for several reasons. These include difficulty in quantifying pain, widely varying analgesic requirements and varying pharmacokinetics between individuals. The technique of infective IM opioids on demand represents familiar practice, generation of nurses have used this technique and therefore may be safe because of accumulated experience. However, too frequent adequate analgesia is not achieved by this approach [12]. Nevertheless better drugs for relief of postoperative pain are needed[13].

The mean±SEM of pulse rate per minute in group A was 84.55+1.67, in group B was 87.30±2.68 and in group C was 92.55±3.29. There was no significant difference in pulse rate among the three groups. This indicates that analgesia was ensured in three groups: the mean±SEM of systolic blood (SBP), diastolic blood pressure, and mean blood pressure were 110t significant. The mean±SEM of VAS in the POW were not significant. There was no significant difference in pain score among the three groups. The time of mean+SEM of 1st rescue dose of pethidine in diclofenac was 1.8±0.11 hour. in ketorolac was 2.2±0.12 hour and in tramadol was 2.3-0.10 hour.

The pain intensity was highest in 1st hour in all three groups and gradually declining as time passed which was similar to other study. M. A. Claeys et al., in his study showed that despite diclofenac infusion starting before surgery postoperative pain was present and was similar to that experienced with placebo during the first postoperative hour. This may be either some delay in the onset of effect of diclofenac or limited analgesic capacity of the drugs insufficient to obtund the severity of immediate postoperative pain[14]. In one study of tramadol infusion the pain was according to visual analogue scale between 42 in the 4th hour gradually decreasing up to 12 in 24 1h hour. But in our study it is different, as pain on tramadol group was 12±2.25 in the 4th hour and decline to 5.5±1.35 in 24t" hour. The VAS in the 1st hour is 12.5-+2.98, but in that study VAS in the 1st was not recorded". The difference was due to

rescue pethidine, as pethidine was given when VAS scale 3-4. There was another study where tramadol and ketorolac was compared for postoperative pain. This study showed that tramadol and ketorolac was similar in analgesic efficacy for postoperative pain[16]. Here preoperatively fentanyl was given 1 µgm/kg. In the postoperative period tramadol 100mg was given intramuscular 6 hourly, ketorolac 30 mg was given intramuscular 6 hourly, and in the control group pethidine 75 mg was given intramuscular 6 hourly. There was another study where tramadol and diclofenac infusion was used for postoperative pain, which showed the same result[17].

In this study, the mean±SEM of total pethidine consumption in group A was 56.5±5.14, in group B is 46.75±4.65 and in group C is 49±5.42. It showed that group B and group C had same analgesic effectiveness and which was better than group A. In another study showed that diclofenac and tramadol were compared for postoperative pain, it showed that analgesic efficacy was similar between these two drugs[18]. Here tramadol group received an initial intravenous bolus of 100 mg just after completion of operation and was followed by infusion of 15mg/hour through an infusion pump. Diclofenac group received an initial loading dose of 0.35 mg/kg, infused in the first 15 minutes followed by infusion of 90 µgm/min. Control group received injection pethidine 2mg/g up to a maximum dose of 100 mg 6 hourly intramuscularly.

Lack of changes in pulse rate, blood pressure and VAS scale in all three groups demonstrate that the analgesia were similar in all three groups. The effect of duration, sex, body weight and ASA grade can be ignored as these data were broadly similar in all groups.

From this study it may be said that both ketorolac and tramadol have same preemptive analgesic effect and which is better than diclofenac in the management of postoperative pain.

CONCLUSION:

On the basis of present prospective clinical study postoperative pain can be managed by preemptive use of diclofenac, ketorolac and tramadol for the 1st 24 hours with little or no supplementation of low dose intravenous pethidine. The analgesic efficacy of ketorolac and tramadol is same and better than diclofenac. There was no significant complication in using the drugs. The drugs are easily available, so they can be used preemptively for postoperative pain.

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Obituary

We informed with a great shock that our dearest Professor Moazzem Hossain Mostafa Sir passed away on 21st July, 2008 in BIRDEM Hospital. He was 73 years old. He had been working in the department of Anaesthesiology in BIRDEM Hospital as an honorary consultant till passing away. He left two sons & a number of well wishers. Bangladesh Society of Anaesthesiologists expresses deep mourn & pray to the Almighty for his ultimate happiness & expressess deep sympathy for mourning family.

He was born in 1935 in a Muslim family of Kustia. After graduation from Dhaka Medical College in 1961 he achieved Diploma in Anaesthesia in 1967 from Royal College of Physician and Surgeon.

He accomplished FFA in 1968 from Royal College of Surgeon, Ireland and Royal College of Surgeons, England.

During his famed working life, he worked as an anaesthestist in the Dhaka Medical College from 1963-1964 & as an assistant surgeon from 1964-1965. Then he joined as Senior house officer (Anaesthesiologist) in Royal Victoria Hospital in 1965. After that he worked in Glasgow Royal Infirmary Hospital, Farnham Hospital, Edgeware General Hospital and Redhill General Hospital till 1969 with very good reputation. Then he came back home and joined as an assistant professor in BSMMU in 1969. In 1970 he joined as a clinical assistant in Middlesex Hospital. Next on 1971 joined as a consultant in Kettering General Hospital. Then he worked in Law Hospital (Scotland), Enderclinic (Tripoli, Libya), Mafraq Hospital (UAE) up to 1987.

He came back to the country in 1988 & joined in BIRDEM Hospital as a senior consultant & Working here till his passing away. Bangladesh Society of Anaesthesiologists keeps in mind his contribution to the subject with appreciation.

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