

**EFFECT OF EPIDURAL NEOSTIGMINE WITH BUPIVACAINE ON HEMODYNAMIC AND STRESS RESPONSE IN TOTAL ABDOMINAL HYSTERECTOMY****Dr. Sahin Sultana Chowdhury\*<sup>1</sup>, Dr. Debabrata Banik<sup>2</sup>, Dr. Mohammad Abdul Hannan<sup>3</sup>, Dr. Md Abdus Salam<sup>4</sup>, Dr. Rahnuma Tasnim<sup>5</sup> and Dr. Abul Ishrat<sup>6</sup>**

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**ABSTRACT**

**Background:** Regional anesthesia techniques are not only performed for adequate anesthesia in the lower abdominal surgical procedures. They have also other advantages including excellent postoperative pain control, reduced side effects, decreased blood loss, and shortened stay in the postanesthesia care unit (PACU). Epidural administration of neostigmine has been suggested to reduce the stress response on major total abdominal hysterectomy. Epidural neostigmine used as an adjunct to epidural anesthesia. The purpose of this study was to determine whether a combination of low-dose neostigmine reduce the stress responses in patients undergoing total abdominal hysterectomy. **Objective:** To evaluate the effect of epidural neostigmine with bupivacaine on haemodynamics and stress response for total abdominal hysterectomy. **Method:** It was a prospective randomized study conducted in the dept. of Anasthesiology, BSMMU. A total 70 patients aged 40- 55 years, posted for total abdominal hysterectomy procedures was included in the study. Assessment of physical status of the patients was tested by American Society of Anaesthesiology (ASA) (Physical status ASA I, ASA II, ASA III and ASA IV). The intervertebral space at L3-4 was identify. The epidural neostigmine dose was 2 g/kg body weight, delivered via the epidural catheter with 0.5 % bupivacaine as a local anesthetic. Assessment of the stress response was done by monitoring and recording of haemodynamic variables, blood sugar level and cortisol level peri-operatively. Procedure details was recorded on specifically designed proforma. **Result:** All the demographic and haemodynamic variables of both groups were almost alike between two groups. Regarding the hemodynamic variables like heart rate and mean arterial blood pressure, preoperatively there was no significant difference between this two groups of people ( $p>0.05$ ). In the periopeartive period the heart rate and mean arterial pressure were more stable in Group B study population. Preoperatively in the cortisol level and the blood sugar level there were no significant differences between two groups of population. In intraoperative period the cortisol level and the capillary blood sugar level was significantly low in group B study population. **Conclusion:** Use of epidural neostigmine with bupivacaine significantly reduce the stress response in total abdominal hysterectomy operation.

**KEYWORDS:** Bupivacaine, haemodynamics, epidural anaesthesia, analgesia.

**INTRODUCTION**

Epidural anaesthesia is used in different type of surgey. Among them it is more popular in lower abdominal surgery, as it reduces mortality and morbidity, and provides a good way for postoperative pain control. There are many factors which influences the stress

during the total procedure of surgery, among them the most important factors determining the level of stress response are the patient, the type of anesthesia and the surgical procedures. The magnitude of the response is broadly related to the affected site (greater in regions with visceral pain afferents such as abdomen and thorax)

and the extent of the trauma. Integral to the stress responses are the effects of nociceptive afferent stimuli on systemic and pulmonary vascular resistance, heart rate, and blood pressure, which are a combination of efferent autonomic response and catecholamine release via the adrenal medulla.<sup>[1]</sup> The changes in pituitary secretion have secondary effects on hormone secretion from target organs like- ACTH, growth hormone from pituitary, cortisol and aldosterone from adrenal cortex and glucagon from pancreas etc.<sup>[2]</sup>

Anesthesia can modify the stress response via afferent blockage (local anesthesia), central modulation (general anesthesia), and peripheral interaction with the endocrine system (etomidate). (Adams et al.1991; Huiku M et al.2007).<sup>[3,4]</sup> Central neuroaxial block is a choice of anesthetic technique which can reduce the stress response in perioperative period.

As epidural anesthesia has the benefits of providing excellent surgical anesthesia and analgesia during perioperative period. (Myles et al. 2002).<sup>[5]</sup>

Inhibition of stress response is greatest with neural block. That's the reason why attenuation has focused largely on the effects of regional anesthetics and analgesic regimens, particularly epidural blockade with local anesthetic agents and its adjuncts. (J.P.Desborough. 2000).<sup>[6]</sup> Epidural analgesia with a local anaesthetics and opioid is one of the recommended techniques for control of postoperative pain (*Anaesthesia, Ronald D Miller*).

With the introduction of multimodality approach to pain management, wherein two or more drugs with different mechanisms of action are used, newer adjuvants like clonidine, ketamine, tramadol, fentanyl, midazolam, neostigmine etc. have been all tried as adjuvants to local anaesthetic agents with varying success rates.<sup>[7]</sup>

The degree to which analgesia and these side effects can be separated after epidural neostigmine administration will depend on the amount of tonic release of acetylcholine at each of these sites.<sup>[8]</sup>

There are various study wherein neostigmine is added to compound anaesthetic mixtures of local anaesthetic agents for epidural analgesia, but no study yet documented wherein neostigmine is added to see the surgical stress response. This study is designed to evaluate the effects of neostigmine on stress response bupivacaine for epidural analgesia for lower abdominal surgeries.

## OBJECTIVES

### General Objective

Evaluation of effectiveness of epidural neostigmine with bupivacaine in stabilizing haemodynamics and reducing stress response in total abdominal hysterectomy.

### Specific Objectives

1. To assess the effect of epidural neostigmine on haemodynamics
2. To measure the preoperative & intraoperative blood sugar level
3. To measure the preoperative & intraoperative cortisol level
4. To see the intraoperative side effects of epidural neostigmine in total abdominal hysterectomy.

## METHODOLOGY

**Study design:** Randomized control trial.

**Place of study:** Department of Anesthesiology, BSMMU.

**Study population:** This study was conducted on patients who were undergoing total abdominal hysterectomy surgeries at the department of Anesthesiology, BSMMU, Dhaka.

**Period of study:** 9 months.

**Screening Method:** The preliminary screening panel for each patient was included the complete history, physical examination and the necessary laboratory test.

**Sampling method:** The sample was collected by computer generated random sampling method.

**Sample Size:** A total of 70 patients will be selected for this study. 35 patients was taken in each group.

### Sample Selection Criteria

#### Inclusion Criteria

After obtaining the approval of Institutional ethics committee and written informed consent, 70 adult female patients of ASA physical status I & II were enrolled in this clinical study.

- Aged 40 to 55 years
- Posted for lower abdominal hysterectomy
- ASA Physical status I & II

#### Exclusion Criteria

- Patients with the absolute contraindication for regional anesthesia were excluded.
- Patients who are non-cooperative
- Patients who have had hypersensitivity to local anaesthetics and neostigmine
- Morbidly obese
- ASA physical status 3 and 4
- Block failure
- Patients getting systemic steroid due to any cause
- Patients with diabetes melitus

### Methodology of data collection:

A prospective randomized study was conducted after obtaining approval from the Institution Ethical Committee and informed written consent, 70 patients of aged 40 to 55 years of female, posted for total abdominal

hysterectomy procedures was included in the study. Assessment of physical status of the patients was done by American Society of Anaesthesiology (ASA) grading. All patients was monitored by using standard monitoring like ECG, NIBP, pulse oximeter. Intravenous line with 18 g cannula was secured and a preload with Ringer's lactate solution was done to every patient according to bodyweight before start of operation. The patients was supported in sitting posture on a horizontal table, by an assistant. The lumbar area was prepared aseptically and draped. The intervertebral space at L3-4 was identified. The prick point was infiltrated with 2 ml of 1% lignocaine.

### Statistical Analysis of Data

All the relevant collected data was compiled on a master chart first. Then organized by using scientific calculator and standard statistical formula. Statistical analyses were carried out by using the Statistical package for social sciences (SPSS) version 22.0 for windows (SPSS INC.,

Chicago, Illinois, USA). Qualitative variables of this study had been expressed as percentage and were derived from chi square test. Quantitative variables were expressed as mean±sd. Student unpaired t-test was used for quantitative variables like MAP and HR at different intervals. A "p" value <0.05 was considered as significant. Fisher exact test also used in analysis of some variable.

### RESULTS

In my study the sample size is 70 and they were selected as simple random sampling technique. The following parameters of my study are statistically analyzed.

### Demographic data of my study people are as follows

Measures of statistical significance between two groups. p-value was calculated by unpaired t-test. No significant difference was found between two groups regarding their age.

**Table 1: Comparison of two groups according to age.**

	Group A (n=35)	Group B (n=35)	P value
Age in years	45±7.7	46.3±9.9	0.57

Data were analysis using fisher exact test.

Hormonal level can be different in between sedentary worker and hard working people.

labour and 54.3% were housewife. The difference was statistically not significant between two groups (P> 0.05).

Table shows 45.7% were service holder, 11.4% were day labour and 42.9% were housewife in group A. On the other hand 28.6% were service holder, 17.1% were day

**Table 2: Distribution of occupation of the study subjects. (n=70)**

	Group A (n=35)		Group B (n=35)		P value
	No	%	No	%	
Service	16	45.7	10	28.6	0.324
Day labour	4	11.4	6	17.1	
House wife	15	42.9	19	54.3	
Total	35	100	35	100	

Data were analysis using chi-square test.

Table shows 42.9% were lower socioeconomic status and 57.1% were middle socioeconomic status in group A. On the other hand 40% were lower socioeconomic

status and 60% were middle socioeconomic status. The difference was statistically not significant between two groups (P> 0.05).

**Table 3: Distribution of socioeconomic status of the study subjects. (n=70)**

Socioeconomic status	Group A (n=35)		Group B (n=35)		P value
	No	%	No	%	
Low	15	42.9	14	40.0	0.808
Middle	20	57.1	21	60.0	
Total	35	100	35	100	

Data were analysis using chi-square test.

It was observed that ASA status were statistically no significant difference between two groups (P> 0.05).

**Table 4: Body mass index status of the study subjects. (n=70)**

	Group A (n=35)		Group B (n=35)		P value
	No	%	No	%	
Normal range	25	71.4	30	85.7	0.265
Over weight	4	11.4	1	2.9	
Obese	6	17.1	4	11.4	
Total	35	70	35	70	

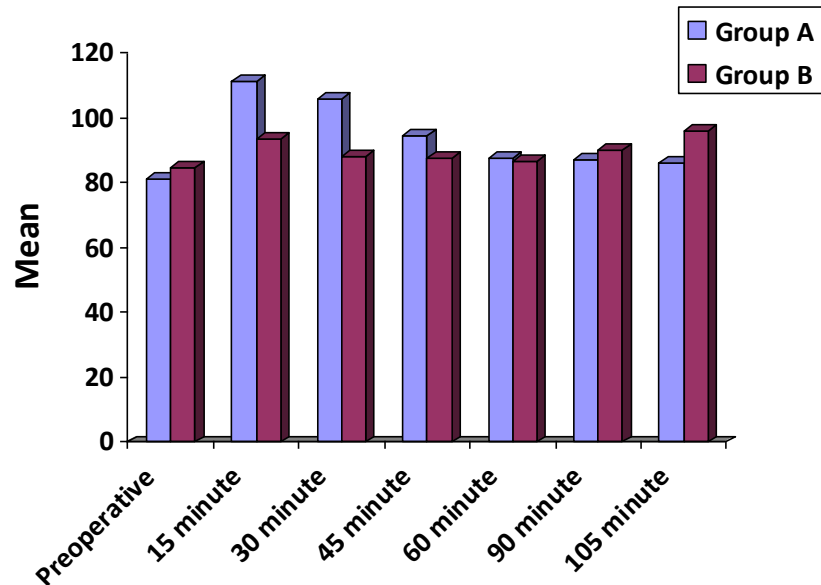
Data were analysis using student 't' test.

Table shows duration of surgery  $82.54 \pm 20.57$  in group A and  $87.00 \pm 11.95$  in group B. The difference was statistically significant between two groups ( $P > 0.05$ ).

**Table 5: Co-morbid status of the study subjects. (n=70)**

Co-morbid status	Group A (n=35)		Group B (n=35)		P value
	No	%	No	%	
COPD	2	5.7	00	0.0	0.388
Bronchial asthma	3	8.6	5	14.3	
Hypertension	11	31.4	12	34.3	
IHD	0	00	00	00	
Diabetes mellitus	16	45.7	12	34.3	
CKD	0	00	00	00	
Others	0	00	00	00	
None	8	22.9	12	34.3	

It was observed that co-morbid status were statistically no significant difference between two groups ( $P > 0.05$ ).

**Fig.1: Comparison of groups in term of heart rate.**

It was observed that preoperative period, 60 minutes and after 90 minutes no statistically significant difference between two groups ( $P > 0.05$ ) in term of heart rate. But others different follow up period were statistically

significant difference between two groups ( $P < 0.05$ ). Data were analysis using student 't' test.

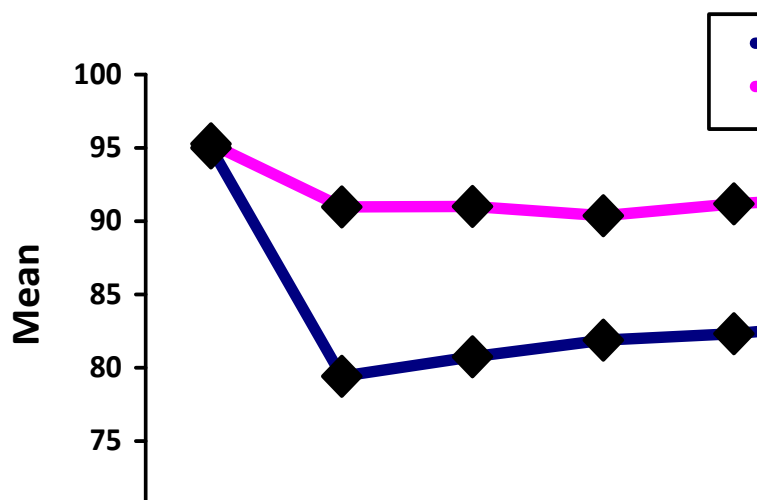


Fig 2: Comparison of groups in term of mean arterial pressure.

Data were analysis using student 't' test. It was observed that preoperative period no statistically significant difference between two groups ( $P > 0.05$ ) in term of mean arterial pressure. But others different follow up period were statistically significant difference between two groups ( $P < 0.05$ ).

## DISCUSSION

Surgical stress is the systemic response to injury and is characterized by activation of the sympathetic nervous system, endocrine responses as well as immunological changes.<sup>[9,10,11]</sup> A lots of stress response related hormonal study is done in various types of surgery. Most of the study involve serum cortisol, epinephrine, nor-epinephrin CRP etc. Anesthetic technique greatly influences the perioperative stress response and the incidence of complications. It has been shown in various studies that combination of epidural anesthesia with general anesthesia attenuates surgical stress response and minimized the chances of perioperative morbidity.<sup>[12]</sup>

surgical procedures causes hypothalamic activation of the sympathetic autonomic nervous system results in increased secretion of catecholamines from the adrenal medulla and release of norepinephrine from presynaptic nerve terminals.<sup>[13]</sup>

In this present study it was observed that majority of the patient (43.8%) patients belongs to age  $> 40$  yrs and in the mean age between group A and group B has no significant difference with the range from 40-55 yrs.

A. Ahiskalioglu et al. 2015 showed the mean age group between group A and group B has no significant difference, which is comparable with my study. Their study used epidural levobupivacaine, and fentanyl as an adjuvant and they measured the cortisol, insulin, prolactin and blood sugar level to assess the stress response.<sup>[14]</sup>

Att eggo et al. (2011) showed the average age of the patient in both group A and group B was similar to my

study. In their study they compared the serum cortisol level in between general anesthesia and epidural anesthesia group.<sup>[15]</sup>

Hafiza sobia et al. (2017) in her study most of the study subjects were male in which stress response were measured by cortisol, IL-6 and TNF- $\alpha$  in patient scheduled for appendicectomy. As appendicitis is more common in male that's why most of the study subject were male here.<sup>[16]</sup>

In the study of P calvo soto et al. 2012 conducted a study in female patients who were scheduled for laparoscopic cholecystectomy and their stress response were measured by using cortisol, adrenain and nor-adrenalin level.<sup>17</sup> In this present study it is observed that the BMI of group A- 71.1% patients was with in normal range and in group B it was 85%.

Unase buyukkocak et al. 2005 was conducted to see the effects of general and spinal anaesthesia on stress response to haemorrhoidectomy and the BMI of the study subject were similar to the current study.<sup>[18]</sup>

In most of the previous study it has been observed that they didn't use BMI, instead of that they used used weight of the subjects, but we use BMI as it is more scientific to use BMI.

In this current study it is observed that mean heart rate between two groups were similar preoperatively (Fig.1). But the significant difference between two groups were found in 15 min, 30 min and 45 min after induction and it was more stable and near to base line in group-B.

At Aggo et.al 2011 in their study they compared the serum cortisol level in between general anesthesia and epidural anesthesia group and the heart rate was significantly more increased in GA group at 30 min of operation and also after skin closer.<sup>[19]</sup>

Hafiza Sobia Ramzan et al. in 2017 compared the epidural and general anesthesia group in patients undergoing appendectomy showed that heart rates in both groups remained lower than those at baseline, at all times during surgery. However, the heart rates of group GA patients remained significantly higher throughout surgery as compared to those of EGA group.

In this current study it is observed that pre-operatively there was no difference in the mean cortisol level between group A and group B.

During the intraoperative period the mean cortisol level is more raised in group A than group B, and p-value was 0.001 which indicates that the difference is significant between two groups of people.

Similarity was found in At Aggo et al. 2011 showed that in their study they compared the serum cortisol level in between general anesthesia and epidural anesthesia group at 30 min after skin incision and after skin closer and they found that significant difference in two groups which was significantly low in EA group.<sup>[19]</sup> In this current study it showed that the adverse effects between two groups of people is not significant statistically.

Manoj Chaurasia et al. in 2017 showed that only one patient (3.3%) had pruritus where they used neostigmine as an adjuvant with sufentanil, and that was comparable with the current study.<sup>[20]</sup>

## CONCLUSION

Epidural anesthesia with bupivacaine and neostigmine is effective and safe, reduces per operative stress response due to surgery and anesthesia and keeps the hemodynamic status more stable during the intraoperative period in patient undergoing total abdominal hysterectomy.

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