Int. J. Pharm. Sci. Rev. Res., 39(1), July – August 2016; Article No. 33, Pages: 167-172 ISSN 0976 – 044X

Research Article

A Study of Changes in Stress Factors during Elective Upper Abdominal Surgery Using Different Anaesthetic Techniques

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Accepted on: 12-05-2016; **Finalized on:** 30-06-2016.

ABSTRACT

Surgical procedures are associated with a complex stress response leading to morbidity as well as mortality. Stress response to surgery activates hypothalamic-pituitary-adrenal axis and the sympathetic nervous system with increase concentration of various stress hormones such as serum cortisol and norepinephrine. During surgery there is a decrease response to insulin action which leads to rise in blood glucose level. It has been suggested that administration of ideal anaesthetic techniques may alleviate the operative stress. Considering the above facts, present study was undertaken to evaluate any role of different anaesthetic techniques, altering the stress factors during upper abdominal surgery. This study was conducted on 120 patients, planned for elective upper abdominal surgery, divided randomly into three demographically identical study groups (A, B and C having 40 patients each). Different anaesthetic techniques such as epidural, general and a combination of both were administered to group A, B and C respectively. It was found that a significant rise ($p< 0.05$) in serum norepinephrine, cortisol and plasma glucose level at $TIME_{In}$ (15 minutes after skin incision is given) and $TIME_{END}$ (at the end of surgery) as compared to $TIME_{BL}$ (baseline value before induction of anaesthesia) among these three groups. Rise in mean serum norepinephrine, cortisol and plasma glucose level both at $TIME_{In}$ and $TIME_{END}$ of group B patients were found highly significant ($p< 0.001$) as compared to group C. Similarly these above parameters of group A at $TIME_{In}$ and $TIME_{END}$ when compared with group C were raised significantly ($p< 0.05$). So it can be concluded that combination of epidural and general anaesthesia may be considered as best choice in reducing the stress factors in elective upper abdominal surgery.

Keywords: hypothalamic-pituitary-adrenal axis, cortisol, norepinephrine.

INTRODUCTION

The key factor in the development of modern anaesthesia and surgery is the safe outcome. The anesthetic drugs, complicated surgical procedures and the patient's condition due to co-existing medical diseases increase the risk. The most important development in recently is, understanding the series of physiological changes (stress response) due to anesthesia and surgery[1]. The general stress response is broadly divided into acute phase and flow (hyperdynamic) phase. They involve wide spread endocrinal, metabolic and biochemical reactions throughout the body resulting changes in cardio-vascular, metabolic, fluid and electrolytes etc. and directly affects the condition of patients and increases the risk. It has been shown that the magnitude of stress response is directly related to the magnitude of injury[2], total operating time[3], and the amount of intraoperative blood loss[4] as well as to the degree of postoperative pain[5].

Surgery and associated infection stimulate the production of a variety of endogenous mediators, and these mediators initiate alterations in various organs that are integral to the response of the host to injury[6]. Among these stress responses, activation of hypothalamic-pituitary-adrenal (HPA) axis and resultant stimulation of glucocorticoid secretion seem to be of extreme importance[7,8]. The metabolic effects of cortisol are directed to overcome the stressful state. Nociceptive stimuli arising from the site of tissue damage produce responses of different intensity that reflect the severity of the injury. Cytokines- several classes of polypeptide mediator, such as IL-1, IL-6 and TNF-α produced by immune cells play important roles as the afferent signal to the neuroendocrine system. Cytokine production reflects the degree of tissue trauma, with lowest release in least invasive and traumatic procedures such as laparoscopic surgery and largest rise after major surgical procedures.

Cytokines also have central hormonal modulating effects causing release of ACTH, CRF and marginal increase in catecholamnes[1,9]. Anaesthesia has little effect on the cytokine response to surgery as it cannot influence tissue trauma. Regional anaesthesia has no significant effect on cytokine production where as combined general and regional anesthetic regimens showed a small decline in IL-6 concentrations and the acute phase response[9].

The stress response leads to secretion of many anabolic and catabolic hormones resulting in hypermetabolism, with the acceleration of most of the biochemical reactions[10] resulted from decrease in insulin secretion and increase resistance. This results in catabolism of proteins, lipids and rise in blood glucose level. This may be beneficial in early state but when prolonged, may be detrimental to the patients. Increase plasma glucose concentrations are related to the intensity of the surgical injury; and follow closely with the increase in serum catecholamines. The changes are less marked with minor surgery. In upper abdominal surgery plasma glucose concentrations can increase up to 140—200mg/dl and remain elevated for >24 hours after surgery. The stress response to surgery initiates a predictable cascade of physiologic and metabolic events through direct activation of the sympathetic and somatic nervous system. The response begins with the initiation of anaesthesia and lasts 3 to 4 days postoperatively[1,2]. Other key factors induced by stress response are prostaglandins, serotonin, kinins and heat shock protein etc. Currently three main methods are available for modifying the response. 1. Spinal/ epidural anaesthesia for neuronal blockage. 2. Intravenous administration of large doses of potent opiate analgesics to block hypothalamic-pituitary function. 3. Use of agents to inhibit the secretion or action of the catabolic hormones, or by the infusion of anabolic hormones such as insulin.

Furthermore, it has been shown that the choice of anaesthetic technique may modulate the extent of such response[11,12]. Decreasing the stress response to surgery and trauma is of high relevance to the anaesthesiologist, since it may allow complex operations in high risk patients. In upper abdominal surgery it is not possible to prevent pituitary and adrenal hormone response completely even with extensive neuraxial blockade[13]. Clinical evidence shows that general anaesthesia plus epidural analgesia certainly reduces neuro-endocrine stress responses by stimulating, inhibiting or modulating the pathophysiological pathways which induce neurohumoral and immunologic alterations[6,13].

MATERIALS AND METHODS

The present study was undertaken in the V.S.S. Medical College Hospital, Odisha. The cases were chosen from the admitted patients in the surgery indoor wards scheduled for various types of elective upper abdominal surgical procedures. After obtaining approval from institutional ethical committee, the study was done under guidance of the senior faculties of the Department of Anaesthesiology.

Selection of Cases

120 adult patients (A.S.A Grade I and II) of either sex, between 22 to 60 years of age, weighing between 32 to 64 kg scheduled for elective upper abdominal surgeries were selected as simple random sampling by computer generated random number from indoor admittance. The patients selected were randomized into three demographically identical study groups of A, B and C (with respect to age, weight, sex).

They were assessed preoperatively and suitable cases were prepared for the operation and study. Patients with obesity (BMI >30 kg/m^2) and any history of hypertension, cardiovascular disorder, renal or hepatic dysfunction, endocrine or autonomic dysfunction neuromuscular or neurological disorder, bleeding disorder, drugs or alcohol abuse, use of medication that affects hormonal or sympathetic response and previous spine surgery were excluded from the study.

The purpose and procedure of the study was explained to all patients and written, informed consent for anaesthesia and the procedure was obtained.

Procedure

On arrival in the operating room, pulse, non-invasive blood pressure, oxygen saturation (SpO_2) and the electrocardiogram (ECG) were monitored. Intravenous access was secured with an 18G cannula and an infusion of Ringer's solution was started. Ryle's tube aspiration was done in all GA cases. All operations began between 9.00 a.m. and 9:30 a.m. to minimize variability in the secretion of hormones such as cortisol, which is dependent on circadian rhythm. All patients received anaesthesia according to the following protocol:

- Group A patients (n=40) were positioned in the right lateral position, administered regional (epidural) anesthesia only. They received 12-20 ml of 0.5% bupivacaine epidurally, at T6-8 intervertebral space by a thoracic epidural catheter (18G). Position of catheter was tested by standard methods.
- Group B (n=40) patients were administered general anesthesia (ISOFLURANE) only. These patients were given isoflurane gas, opioid analgesic, oxygen, nitrous oxide and muscle relaxant.
- Group C (n=40) patients received a combination of general and regional (epidural anesthesia).

5 ml venous samples were collected peripherally (from an antecubital vein of the arm contralateral to the I.V. infusion) as follows: $TIME_{BL}$ in the operating room before any premedication or anaesthesia is given. $TIME_{In}$, fifteen minutes after the skin incision is given, which is generally given 30 minutes after endotracheal intubation in group B and C to prevent any fallacy rise due to laryngoscopy and endotracheal intubation. $TIME_{END}$ when all the skin sutures are completed, at the end of surgery. Serum norepinephrine, cortisol and plasma glucose samples were centrifuged at 2500 rpm for 10 minutes and analysed in department of Biochemistry as follows.

- Serum concentration of norepinephrine (NE) and cortisol were estimated by chemiluminescence immunoassay (CLIA) method using Cobas e411 fully autoanalyzer.
- Plasma glucose level was estimated by hexokinase method by using Cobas 400 plus fully auto analyzer.

Statistical analysis was done with MANOVA and independent t-test. All the analyses were done using statistical software SPSS 20.0. The associations were considered statistically significant if the p value < 0.05.

RESULTS

120 patients of A.S.A Grade I and II scheduled for elective surgery under anaesthesia were included in our study.

They were equally divided randomly into age and sex matched three different groups such as A, B and C, each comprises of 40 patients. Table 1 shows the mean age of group A, B and C were 42±11.3, 38±11.2 and 41±11.6 years respectively. Among group A patients, 21(52.5%) were male and 19 (47.5%) female while in group B, 22 (55%) male and 18 (45%) female and in group C, 20 (50%) were male and 20 (50%) were female. The mean age belongs to A, B and C were 50±9.3, 49±8.8 and 48 ±9.1 kg respectively.

Table 1: Distribution of Age, Sex and Weight in Different Study Groups

Age (Years)	Weight (kg)	Group A (n=40)		Group B (n=40)		Group C (n=40)	
		M	F	M	F	M	F
21 – 30	31- 40	6	5	4	6	5	4
31 - 40	41 – 50	5	4	6	6	5	6
41 - 50	51 – 60	6	7	5	6	6	7
51 – 60	61 – 70	4	3	3	4	4	3
Total		21	19	18	22	20	20
Age (mean± SD)		42±11.3		38±11.2		41±11.6	
Range of age		22 – 58		22 – 58		22 – 60	
Wt. (mean±SD)		50± 9.3		49 ± 8.8		48 ±9.1	
Range		35 – 64		32 – 64		32 – 64	

Table 2 shows different type of elective upper abdominal surgeries conducted in different study groups

Table 2: Type of Surgery in Different Groups

Type of Surgery	Group A	Group B	Group C
Partial gastrectomy	9 (22.5%)	10 (25%)	9 (22.5%)
Cholesystectomy	8 (20%)	9 (22.5%)	10 (25%)
Truncal Vagotomy + Gastrojejunostomy	10 (25%)	9 (22.5%)	8 (20%)
Ventral Hernia repair	6 (15%)	5 (12.5%)	7 (17.5%)
Splenectomy	7 (17.5%)	7 (17.5%)	6 (15%)
Total	40	40	40

Table 3: Study of Total Duration of Surgery, MAP and HR in Different Study Groups

	Group A mean± S.D	Group B mean± S.D	Group C mean± S.D
Total duration of Surgery (min)	129.2±10.0	134± 6.8	132.8± 8.8
Mean arterial pressure (mm of Hg) Base line values	92.3± 4.9	91.6± 4.0	92.4± 4.2
Heart rate (bpm) Base line values	81.1± 6.9	80.4± 7.4	80.7± 7.3

(P < 0.05 is considered to be significant)

Table 4 Study of Mean Serum NE, Cortisol and Plasma Glucose Level in Different Study Groups

Serum Norepinephrine level (pg/ml) – MEAN ± S.D			
Group	$TIME_{BL}$ Base line value	$TIME_{IN}$ After skin incision is given	$TIME_{END}$ At the end of surgery
Group A	336.2 ± 19.3	464.3 ± 19.4	537.9 ± 20.8
Group B	338.2 ± 17.7	492.3 ± 16.1	605.3 ± 14.4
Group C	339.5 ± 17.8	430.9 ± 13.8	466.2 ± 15.1
Serum Cortisol level (µg/dl) – MEAN ± S.D			
Group A	22.9 ± 1.9	28.6 ± 1.9	30.9 ± 1.8
Group B	22.6 ± 1.9	30.1 ± 1.8	32.9 ± 1.4
Group C	22.2 ± 1.9	26.1 ± 1.5	28.2 ± 1.4
Plasma Glucose level (mg/dl) – MEAN ± S.D			
Group A	98.0 ± 5.7	132.8 ± 5.6	142.9 ± 5.7
Group B	97.8 ± 5.5	140.2 ± 5.3	151.1 ± 4.9
Group C	97.9 ± 5.8	124.3 ± 5.1	132.3 ± 4.9

(P < 0.05 is considered to be significant)

As in Table 3, the mean values of total duration of surgery belong to group A, B and C are 129.2±10.0, 134± 6.8 and 132.8± 8.8 minutes respectively.

Base line values of Mean arterial pressure (MAP) and heart rate in these above groups are 92.3± 4.9, 91.6± 4.0, 92.4± 4.2 mm Hg and 81.1± 6.9, 80.4± 7.4 beats per minute respectively.

Among these variables of different study groups, the multivariate test is not significant (P= 0.315). Tukey's post hoc analysis revealed the statistically significant difference in total duration of surgery in minutes between epidural and general anaesthesia group as evidenced by P value of 0.044, but overall there is no significant difference in the multivariate analysis.

Table 4, summarises that there is no significant change (P= 0.786) in mean serum level of norepinephrine, cortisol as well as plasma glucose level among these three study groups before the induction of anaesthesia ($TIME_{BL}$).

A significant rise (P<0.05) in mean value of above mentioned parameters was found at $TIME_{IN}$ (after skin incision is given) as compared to $TIME_{BL}$ and it continues to rise till it reaches its peak at the end of surgery ($TIME_{BL}$) in all the three groups.

The mean serum norepinephrine level in group C as compared to group B at $TIME_{In}$ and $TIME_{END}$ showed a highly significant difference (P<0.001). Similarly significant difference (P<0.05) in mean serum nor-epinephrine level in group C as compared to group A was observed at $TIME_{In}$ and $TIME_{END}$.

Significant difference (P<0.05) was observed in mean serum cortisol level of group C as compared to group A after skin incision was given and at the end of surgery.

The mean serum cortisol level in combined epidural and general anaesthesia group as compared to general anaesthesia group showed a highly significant difference (P<0.001) after skin incision was given and at the end of surgery.

The mean plasma glucose level in group C as compared to group B at $TIME_{In}$ and $TIME_{END}$ showed a highly significant difference (P<0.001). Significant difference (P<0.05) was observed in plasma glucose level of group C as compared to group A after skin incision was given and at the end of surgery.

DISCUSSION

There has been growing interest in the use of regional anaesthesia in combination with general anaesthesia for the management of high risk surgical patients scheduled for major abdominal or vascular surgery.[14,15]

Studies have shown that the advantages of combined general and epidural anaesthesia there is an overall reduction in morbidity, complications, lower incidence of cardiovascular failure, with less need for prolonged ventilator support, improved pulmonary function, postoperative analgesia and reduction in release of stress hormones[16].

There was significant rise in serum nor epinephrine level above the baseline i.e. (38%,47% & 26%) in A, B and C study groups samples taken just after the skin incision with higher level in general anaesthesia group (B) and lower level observed in combined general and epidural anaesthesia group (C).

Similarly samples taken after completion of surgery showed that all the stress factor markers values were well above the baseline values i.e. (59%,82%,& 37%), with highest level observed in general anaesthesia group (B) and lower level observed in combined general and epidural anaesthesia group (C).

Findings of our study were compatible with observation made by Goldmans[17] and Fant F.[18], who were of the view that the rise of catecholamine level was maximum in patients receiving general anaesthesia and least in patient receiving a combination of both general and epidural anaesthesia.

There was significant rise in serum cortisol level above the baseline i.e. (25%,33% & 17%) in A,B,C study group samples taken just after the skin incision with higher level in general anaesthesia group (B) and lower level observed in combined general and epidural anaesthesia group (C). Similarly samples taken after completion of surgery showed that values of serum cortisol were well above the baseline values i.e. (35%,46%,& 27%), with highest level observed in general anaesthesia group (B) and lower level observed in combined general and epidural anaesthesia group (C).

Liu XY[19] and Derya Acar[20] concluded that people receiving only general anaesthesia experienced a significant rise in serum cortisol after skin incision and throughout the intraoperative period whereas serum cortisol was minimally raised in patient receiving combined general anaesthesia and regional anaesthesia.

There was significant rise in plasma glucose above the preinduction baseline level in all the three groups i.e. (34%, 43%, 26%) after the skin incision was given and at the end of surgery it was increased by (46%, 54%, 34%) respectively in group A, B and C. the increase in plasma glucose level was maximum in group B and least in group C.

Our study was well supported by Yuhong[21] who had observed that combined general and epidural anaesthesia during upper abdominal surgery suppress stress response and thus glucose intolerance quite effectively, whereas only general anaesthesia was quite ineffective in attenuating the rise of plasma glucose. Ghodki PS[22] observed that combination of general and epidural anaesthesia reduce the surgical stress response during major upper abdominal surgery.

The mechanism probably involves the blockage of all nociceptive stimuli arising of the surgical tissue trauma at the spinal level with epidural anaesthesia. Regional anaesthesia blocks the sympathetic fibres and thus sympathetic response to surgical stimulus. Whereas general anaesthesia even though not interpreted by the brain it can exert its effect on the neurons in spinal levels[10,23].

CONCLUSION

The body reaction to surgery ranges from minor to massive both locally and generally. Neuro-endocrinal hormone system and inflammatory mediators are involved and this process is called “stress response”. Recognizing the factors precipitating the stress response and applying appropriate therapeutic methods to minimize these changes are vital.

The present study provides evidence for the usefulness of administrating combined epidural and general anaesthesia in upper abdominal surgery, would be more effective in blocking the nociceptive stimulus as well as sympathoadrenal response as compared to other anesthetic techniques. Therefore, based on the findings of this study, the clinical application of combined general and epidural anaesthesia is warranted in all abdominal surgeries attenuating the post operative catabolism and morbidity.

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Source of Support: Nil, **Conflict of Interest:** None.