

## Comparison of Dexmedetomidine and Magnesium Sulphate to assess neuroendocrine response using blood glucose as a marker in laparoscopic Cholecystectomy

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**Abstract:** Anaesthesia and surgery induced stress response can be modulated by premedication drugs. This study was done to assess the extent of stress attenuation by using dexmedetomidine and magnesium sulphate premedication by analyzing perioperative variation in blood glucose level during laparoscopic cholecystectomy under general anaesthesia. In a prospective blind study, 90 ASA I patients who were posted for elective laparoscopic cholecystectomy under general anaesthesia were divided into three groups. Group D patients (n = 30) were given intravenous dexmedetomidine 1 µg/kg, Group M patients (n = 30) received magnesium sulphate 30 mg/kg, Group C patients (n = 30) were given normal saline over a 10 min period, before induction of anaesthesia. Hemodynamic parameters like heart rate, MAP were assessed. Anaesthesia and surgical techniques were standardized. Perioperative blood glucose values were assessed preoperatively, 30 min and 1 hour after beginning of surgery. Both premedicants attenuated hemodynamic and neuroendocrine stress response of pneumoperitoneum and general anaesthesia. The dexmedetomidine group showed better intraoperative stability and blood glucose control on comparison to magnesium sulphate group. During laparoscopic cholecystectomy, dexmedetomidine and magnesium sulphate have effectively modulated neuroendocrine stress response of general anaesthesia as analyzed by blood glucose variation, but dexmedetomidine was better.

**Keywords:**  $\alpha_2$  receptor agonists, blood glucose, dexmedetomidine, magnesium sulphate, laparoscopic cholecystectomy, neuroendocrine stress response.

### I. Introduction

Patients subjected to surgery are anxious and under tremendous stress. Surgical stimuli initiate a complex metabolic, neuroendocrine and inflammatory stress response. This neuroendocrine response varies according to severity, intensity and duration of stimulus. Neuroendocrine stress response results in secretion of many anabolic and catabolic hormones resulting in an increased metabolic state. Blood glucose concentration shows an increase during surgery due to increase in hepatic glycogenolysis and gluconeogenesis facilitated by stress hormones. The physiological mechanisms that maintain glucose homeostasis are of less effect in perioperative period and a state of hyperglycemia persists.

Stress attenuation is of high relevance to anaesthesiologist. Stress response can be attenuated by various premedications and anaesthetic techniques. Pharmacological agents are used to improve outcome and decrease surgical stress. Dexmedetomidine, a  $\alpha_2$  adrenergic agonist is being used widely for stress attenuation because of its sympatholytic, hypnotic, sedative, anxiolytic, analgesic and anaesthetic sparing effect. Magnesium sulphate blocks release of catecholamines from both adrenal gland and adrenergic nerve terminal. It causes vasodilatation by directly acting on blood vessels and by attenuating vasopressin stimulated vasoconstriction. In 1987, Philippe Mouret performed the first laparoscopic cholecystectomy. Carbon dioxide is used to create pneumoperitoneum (PP) for laparoscopic surgeries. Cardiovascular changes like elevated arterial pressure, raised systemic vascular resistance and low cardiac output can occur mainly due to carbon dioxide and pneumoperitoneum. Normotensive patients can also have increased sympathetic response intraoperatively due to hypercapnia. This drastic increase in mean arterial pressure and heart rate is harmful to patients. Attenuation of this stress response is done by various pharmacological agents like opioids, vasodilators, beta blockers and alpha-2 agonist.

The objective of this study is to compare the influence of dexmedetomidine and magnesium sulphate premedication on stress attenuation during laparoscopic cholecystectomy done under general anaesthesia by analyzing perioperative blood glucose level variations. Blood glucose estimation is used as an indirect assessment of stress attenuation, as "stress induced hyperglycemia" is also prevented by usage of these premedication drugs. The advantage of blood glucose estimation is that it can be easily performed using a glucometer, less time consuming and cost effective compared to other investigations like serum cortisol estimation, estimation of cytokines and interleukins.

## **II. Aim**

Anaesthesia and surgery induced stress response can be modulated by premedication drugs. This study was done to assess the extent of stress attenuation by using dexmedetomidine and magnesium sulphate premedication by analyzing perioperative variation in blood glucose level during laparoscopic cholecystectomy under general anaesthesia.

## **III. Materials And Methods**

In a prospective blind study, 90 ASA1 patients who were posted for elective laparoscopic cholecystectomy under general anaesthesia were divided into three groups. Group D patients (n =30) were given intravenous dexmedetomidine 1µgm/kg, Group M patients (n =30) received magnesium sulphate 30mgm/kg, Group C patients (n =30) were given normal saline over a 10 min period, before induction of anaesthesia. Hemodynamic parameters like heartrate, MAP were assessed. Anaesthesia and surgical techniques were standardized. Perioperative blood glucose values were assessed preoperatively, 30 min and 1 hour after beginning of surgery.

## **IV. Results**

The results obtained from this study are presented in tabulated manner. The results are expressed in Mean ±Standard Deviation. Comparison was performed with Kruskal –Wallis one way Anova by Ranks or Fisher's exact test for small samples with 5% risk. Mann Whitney Wilcoxon tests were performed when tests of normal distribution failed. P <0.05 was considered to be significant. Age distribution is comparable in the three groups and distribution of patients in age group 31 - 50 years is more. There was no significant difference in heartrate preoperatively and before pneumoperitoneum between the groups. Heart rate was significantly lower in Group D (p<0.05) throughout pneumoperitoneum, after release of pneumoperitoneum, after extubation when compared to Group M and Group C. There was no significant difference in MAP recorded preoperatively and before pneumoperitoneum between the groups. MAP was significantly lower in both Group D and Group M (p value <0.05), throughout pneumoperitoneum, after release of pneumoperitoneum and after extubation in comparison to Group C. There was no statistically significant difference regarding preoperative blood sugar values between the three groups of patients. Blood glucose concentration when measured 30 min after beginning of surgery showed a statistically significant (p <0.05) decrease in Group D and Group M when compared to Group C. Blood glucose concentration when measured 60 min after beginning of surgery showed a statistically significant decrease in group D and group M on comparison to Group C.

## **V. Discussion**

Stress response can be detrimental to patients and modulation or attenuation of stress is better than complete elimination as beneficial effects of stress response such as maintenance of blood pressure by catecholamines during hypovolemia or cytokine production for immunological enhancement will be retained. In our study 90 ASA 1 patients who underwent elective laparoscopic cholecystectomy under general anaesthesia were divided into 3 groups, each with 30 patients. Group D was given a premedication of injection dexmedetomidine 1µgm/kg, Group M was given a premedication of injection magnesium sulphate 30mg/kg, Group C was given normal saline before induction of general anaesthesia. Blood glucose concentration was measured preoperatively using glucometer. Elective laparoscopic cholecystectomy was done under general anaesthesia with thiopentone induction, nitrous oxide, oxygen, opioid (fentanyl) maintenance. Laparoscopic cholecystectomy was performed after abdominal insufflation by carbondioxide and intraabdominal pressure was maintained between 12 and 15 mm of Hg. Heartrate, systolic blood pressure, diastolic blood pressure, mean arterial pressure were measured preoperatively, after induction, before pneumoperitoneum, every 5 min interval after pneumoperitoneum till end of surgery. Blood glucose concentration was measured preoperatively, 30 min and 60 min after beginning of surgery. In our study, Group D patients, Dexmedetomidine group were observed to have better hemodynamic stability than Group M and control group patients. In their study, Sulaiman et al described the effect of dexmedetomidine infusion given in a dosage of 0.5µgm/kg as a 10 min infusion prior to induction for patients undergoing off pump coronary artery bypass surgery. They concluded that dexmedetomidine infusion caused an attenuation of sympathetic response to laryngoscopy and intubation as observed by a reduction in heartrate and arterial blood pressure.

In the study by Chiruvella et al, where injection dexmedetomidine (Group D) and injection clonidine (Group C) were given as premedication over a period of 15 min before induction and observed a significant decrease in mean heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure in dexmedetomidine group compared to clonidine group. Srivastava et al, in journal of clinical and diagnostic research have compared the efficacy of dexmedetomidine and esmolol on hemodynamic responses during laparoscopic cholecystectomy in ASA 1 and 2 patients where Group D received a loading dose of dexmedetomidine of 1 µgm/kg over a period of 15 min and maintenance of 0.5µgm/kg/hr throughout

pneumoperitoneum. Group E received esmolol loading dose of 1mg/kg over 5 min and maintenance dose of 0.5 mg/kg/hr throughout pneumoperitoneum. Group C received same volume of normal saline. Hemodynamic parameters like heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure were measured. In patients treated with dexmedetomidine there was a significant decrease in hemodynamic parameters on comparison with other group of patients.

Chaitanya et al, compared injection dexmedetomidine 1µg/kg and injection magnesium sulphate 30 mg/kg given before intubation for attenuation of cardiovascular stress response during laryngoscopy and endotracheal intubation and concluded that both dexmedetomidine and magnesium sulphate were effective in attenuation of stress response during laryngoscopy and endotracheal intubation.

Hyperglycemia is common in surgical patients due to hypermetabolic stress response. Stress response increases glucose production with associated insulin resistance (Andra et al). Blood glucose estimation was used as an indirect measure of the extent of stress attenuation. (Gupta et al). In the study by Gupta et al, in patients undergoing laparoscopic cholecystectomy under general anaesthesia blood glucose estimation was used as an indirect measure of stress attenuation in patients given injection dexmedetomidine or injection fentanyl. They concluded that dexmedetomidine was effective in modulating stress response as analyzed by blood glucose estimation. Ahmed et al, observed in their study that intravenous infusion of dexmedetomidine caused a reduction in stress response to major surgeries as seen by a decrease in blood glucose, interleukin 6 and blood cortisol levels. Harsoor et al, studied influence of effect of dexmedetomidine as premedication (1µg/kg) followed by an infusion of dexmedetomidine (0.5µg/kg/hr) and found that dexmedetomidine infusion resulted in better hemodynamic stability and attenuation of stress response as evident by a significant decrease in blood glucose concentration. In our study, blood glucose concentration was significantly decreased in both dexmedetomidine and magnesium sulphate group on comparison to control group. There was also a significant decrease in blood glucose estimation in dexmedetomidine group on comparison to magnesium sulphate group. Thus stress attenuation was seen in patients treated with dexmedetomidine and magnesium sulphate as seen by hemodynamic stability and blood glucose estimation. The extent of stress attenuation was better with patients treated with dexmedetomidine premedication.

## VI. Conclusion

Both premedicants attenuated hemodynamic and neuroendocrine stress response of pneumoperitoneum and general anaesthesia. The dexmedetomidine group showed better intraoperative stability and blood glucose control on comparison to magnesium sulphate group. During laparoscopic cholecystectomy, dexmedetomidine and magnesium sulphate have effectively modulated neuroendocrine stress response of general anaesthesia as analyzed by blood glucose variation, but dexmedetomidine was better.

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**TABLE: CHARACTERISTICS OF STUDY PATIENTS**

	Control	Group D	Group M
<b>Age distribution</b>			
<30 yr	4	6	10
31 - 50	16	17	20
51 - 70	10	7	0
<b>Sex</b>			
Male	27	19	22
Female	3	11	8
<b>Changes in Heart rate</b>			
Preoperative	73±7.1	75±7.3	74.2±6.2
Before pneumoperitoneum	78.2±4.4	79.3±8.2	78.4±3.9
15 min after pneumoperitoneum	96.44±10.4	80.2±7.8	81.1±6.4
30 min after pneumoperitoneum	97.8±11.4	80.4±8.4	82.2±7.8
After release of pneumoperitoneum	94.6±7.9	79.4±5.6	81±6.2
After extubation	103.84±9.6	89.2±10.2	92±8.4
<b>Changes in mean arterial pressure</b>			
Preoperative	93.6±8.9	90.44±6.8	92.52±2.8
Before pneumoperitoneum	98.6±9.32	96.4±8.6	96.8±7.4
15 min after pneumoperitoneum	108±13.6	98.54±10.2	98.6±8.9
30 min after pneumoperitoneum	109±12.7	97.6±10.6	98.2±6.4
After release of pneumoperitoneum	101.8±12.4	92.5±8.4	96.2±8.4
After extubation	107.4±11.6	96.8 ±9.36	98.4±32
<b>Perioperative blood glucose concentration (mg/dl )</b>			
Preoperative	100.73	99.73	88.03
Intraoperative after 30 min	160.87	100.17	110.27
Intraoperative after 60 min	167.17	101.73	117.67

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