Original Research Paper

Volume-9 | Issue-7 | July - 2019 | PRINT ISSN No. 2249 - 555X

Anaesthesiology

EFFECT OF DEXMEDETOMIDINE ON CAPILLARY BLOOD GLUCOSE AND SEVOFLURANE REQUIREMENT DURING LAPAROSCOPY IN DIABETIC PATIENT

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ABSTRACT

BACKGROUND: Dexmedetomidine has been shown to blunt the stress response to surgery. Hence a study was designed to evaluate the effect of intravenous (IV) dexmedetomidine infusion during general anaesthesia for abdominal surgeries on blood glucose levels and on sevoflurane requirements during anaesthesia.

MATERIALS AND METHODS: Thirty four patients scheduled for laparoscopic surgery under general anaesthesia were divided into dexmedetomidine (D) group and Placebo (P) group of 17 each. Group D received a loading dose of dexmedetomidine at 1 µg/kg/10 min diluted to 20 mL, followed by maintenance with 0.5 µg/kg/h., till the end of surgery. Group P received similar volume of IV normal saline. Anaesthesia was maintained with nitrous oxide in oxygen and sevoflurane keeping BIS between 40 and 60. Data were analyzed using students t test, chi square test and Fisher Exact test as applicable.

RESULTS: 90min after intubation, dexmedetomidine group showed blood glucose levels of 127.24 ± 6.14 mg/dL, compared to placebo group which was 146.88± 3.56mg/dL and it was statistically significant (P< 0.05). After 60min sevoflurane requirement in Group D was 12.65 ± 2.06 mL, compared to 19.82 ± 1.77 mL in placebo group. In peri-operative period, the heart rate and MAP were stable.

CONCLUSION: Intravenous Dexmedetomidine was effective in blunting stress response to surgical trauma as indicated by lower blood glucose levels, and reduced Sevoflurane requirements during BIS guided general anaesthesia for laparoscopy surgery.

KEYWORDS : dexmedetomidine, sevoflurane, strews response, glucose, hemodynamic requirement

INTRODUCTION

Dexmedetomidine being a very potent alpha 2 receptor anatagonist gradually developed as an anaesthetic premedication with the goal of attenuating the sympathetic responses to perioperative stress such as laryngoscopy and intubation[1] .The metabolic stress response to surgical trauma is characterized by increased serum level of catecholamines and other steroid hormones.[2] If this stress response is of prolonged duration ,the hypermetabolic state ,reflected by increased blood sugar,can lead on to decreased immunty, delayed ambulation and increased morbidity and mortality4[3].Hence monitoring blood glucose level can reflect the metabolic stress response to surgery and the effect of dexmeditomidine in blunting this stress response. Dexmedetomidine reduced stress response to major surgeries as indicated by clinically and statistically significant reduction in blood glucose, interleukin-6, and cortisol levels.[4] Several studies have indicated that administration of intravenous dexmedetomidine during general anesthesia can decrease the minimum alveolar anesthetic concentration (MAC) of sevoflurane. The aim of the present study was to observe the effect of intravenous (IV) dexmedetomidine on levels of blood glucose, which is one among several stress response markers and sevoflurane requirements under General Anaesthesia (GA). The secondary goals were to maintain intra- operative hemodynamic stability.

MATERIALS AND METHODS:

After obtaining approval from institutional ethical committee, a randomized, prospective, double blind, clinical study was formulated.34 diabetic patients scheduled for laparoscopy under general anesthesia were included in the study after obtaining informed written consent and divided into Dexmedetomidine(D) and placebo(P) group.

All patients were premedicated with tab. alprazolam 0.5 mg oral, the night before surgery and a minimum fasting state of 6 h before anesthesia was ensured in all patients. The standard monitoring consisted of electrocardiography (ECG), pulse oximetry (SpO2), noninvasive blood pressure (NIBP), BIS, capnography ,temparature. The BIS was measured with a plug in DRAGER FABIUS PLUS WORK STATION. All patients were preoxygenated with 100% oxygen for 3 min and midazolam 0.05 mg/kg IV, glycopyrrolate 0.01 mg/kg IV, fentanyl 2 µg/kg IV were administered. Group D patients were given an initial dose of dexmedetomidine 1 µg/kg IV made to 20 mL with normal saline, over 10 min. Group placebo P patients received similar volume of normal saline over 10 min. The study drug and placebo infusions were prepared by an anaesthesiologist who was not involved in the study and the anaesthesiologist recording the details was unaware of the type of infusion patients received. Anaesthesia was induced in all the patients with. propofol until BIS dropped to 50, and confirmed with loss of response to verbal commands. In both the groups, atracurium 0.5 mg/kg IV was administered, and trachea was intubated after 4min. A maintenance dose of dexmedetomidine infusion at 0.5 µg/kg/hour made to 20 ml with normal saline was administered in group D patients and a similar volume of normal saline was administered in Group P, till the end of surgery. Anaesthesia was continued with sevoflurane and 60% nitrous oxide in oxygen 18 and ventilated to maintain end-tidal CO2(EtCO2) between 35 and 40 mmHg. Sevoflurane dial concentration was adjusted to ensure adequate depth of general anesthesia to maintain BIS levels between 40 and 60 and also to maintain clinical variables like HR, NIBP, mean arterial pressure (MAP) within normal limits. Top up doses of atracurium were given at 20min interval . Infusion of dexmedetomidine was stopped 30 min prior to expected time of completion of surgery. sevoflurane administration was turned off at the beginning of skin suturing. At the end of the surgery, residual neuromuscular blockade was reversed with neostigmine 0.5 mg/kg and glycopyrrolate 0.005 mg/kg and trachea extubated after satisfactory recovery and presence of response to oral commands. All patients were administered only IV normal saline during study period. The age, gender, body weight, duration of surgery (minutes), duration of anaesthesia (minutes) were recorded. Serial blood glucose levels from fresh capillary whole blood using glucose test strips were estimated at following points – just before induction, 30minutes, 60minutes and 90minutes after surgical incision End tidal concentration of sevoflurane: 60 minutes, 90minutes after surgical incision The usage of sevoflurane during anesthesia can be calculated as follows.22 Dion's Formula: Usage of volatile anesthetic (mL) = [Dialed concentration × Total fresh gas flow × Duration at that concentration × Molecular weight]/[2412 × Density]. Statistical analysis was conducted with statistical package for social sciences (SPSS) Version 20 (IL Chicago) for windows statistical package. All the parametric data are presented as mean ± SD and non-parametric data in tables. Parametric data were assessed with independent sample ttest. Bonferroni's correction was applied as appropriate. Non-parametric data with Chi square test and Fischer exact test as appropriate. P value of less than 0.05 was considered as statistically significant.

RESULTS and ANALYSIS :

The two groups were comparable regarding age, height, weight and gender proportion

On analysis of the CBG at the end of 30 min, 60 min and 90 min among the two groups by t-test, the P value of 0.000 (two sided) indicated significant difference among Group D and Group P (Table 1,Figure1).

Table 1: Table showing the CBG analysis of the two groups

CBG	Group	Mean±sd	Stastistical Test	P Value	Signficance
At the end of 30min	D	109.00±10.51	t-test	0.000	Significant
	P	126.53±6.65			
At the end of 60 min	D	117.41±8.75	t-test	0.000	Significant
	P	137.06±4.49			
At the end of 90min	D	127.24±6.14	t-test	0.000	Significant
	P	146.88±3.56			

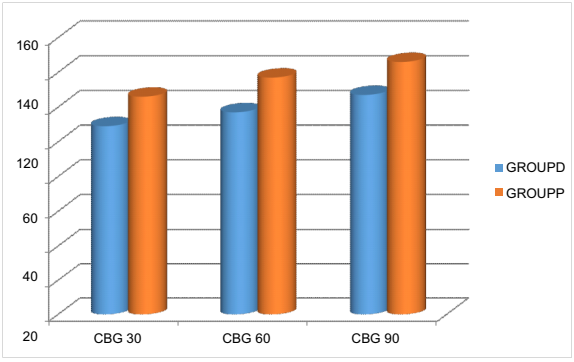

Fig-1: Column Chart showing CBG comparison of the Patients

On analysis of the hourly sevoflurane requirement at the end of 60 min(1sthr)and 90 min(2ndhr) among the two groups by t-test, the P value of 0.000 (two sided) indicated significant difference among Group D and Group P (Table 4,Figure 2).

Table 2: Table showing the sevoflurane requirement of the two groups

Parameters	Group	Mean±sd	Statistical Test	P Value	Signifcance
Sevoflurane at the end of 60 min(1sthr)	D	12.65±2.06	t-test	0.000	Significant
	P	19.82±1.77			
Sevoflurane at the end of 90 min(2ndhr)	D	3.47±0.63	t-test	0.000	Significant
	P	5.35±0.70			

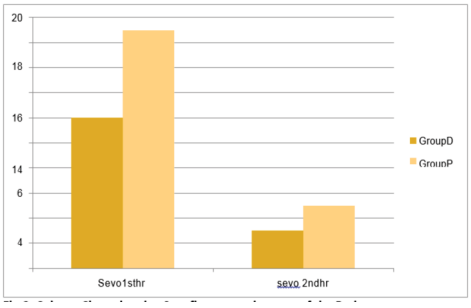

Fig-2: Column Chart showing Sevoflurane equirement of the Patient

Comparison of hemodynamic parameters which included non-invasive mean arterial blood pressure, heart rate revealed no significant difference among the two groups.(Table 5, Fig 3; Table 6, Fig 4)

Table 3: Comparison of MAP of two Groups

PARAMETERS	GROUP	MEAN±SD	P value	SIGNIFCANCE
MBP0	D	95.59±9.49	0.621	NO
	P	97.65±8.25	0.621	
MBP30	D	88.53A±7.62	0.876	NO
	P	99.18±7.86	0.876	
MBP60	D	89.06±6.63	0.234	NO
	P	98.82±7.28	0.234	
MBP90	D	90.65±8.89	0.129	NO
	P	99.47±9.40	0.129	

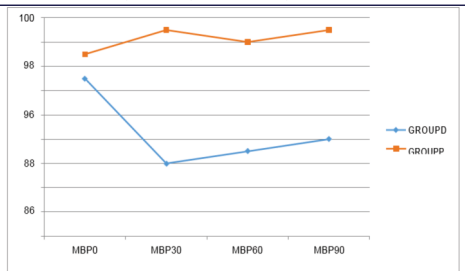

Fig 4: Line Diagram showing Comparison of MAP of two Groups

Table 4: Comparison of Heart Rate of two Groups

PARAMETERS	GROUP	MEAN±SD	P value	SIGNIFCANCE
HR0	D	92.00±7.08	0.112	NO
	P	90.35±5.88	0.112	
HR30	D	81.41±10.64	0.321	NO
	P	92.00±6.58	0.321	
HR60	D	74.94±7.97	0.678	NO
	P	89.35±4.19	0.678	
HR90	D	70.88±8.61	0.789	NO
	P	90.76±3.36	0.789	

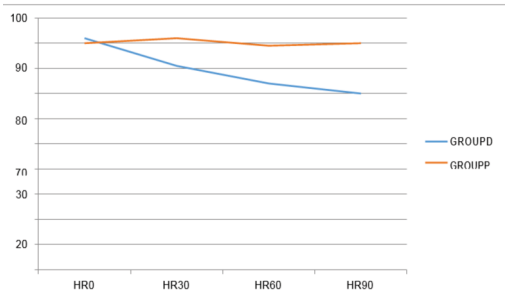

Fig 5:Line Diagram showing Comparison of Heart Rate of two Groups

DISCUSSION

Dexmedetomidine, a highly selective α2-adrenergic receptor agonist has generated lot of interest for its sedative, analgesic, perioperative sympatholytic, anesthetic-sparing, and hemodynamic- stabilizing properties with a relatively high ratio of α2/α1 activity (1620:1).[5]The hypnotic and supraspinal analgesic effects of dexmedetomidine are mediated by suppression of neuronal firing in the locus coeruleus, resulting in inhibition of norepinephrine release and activity in the descending medullo-spinal noradrenergic pathway.[6,7]The stress response manifests clinically and metabolically with a wide range of endocrinal, immunological and hematological effects which include insulin resistance and hyperglycemia.

Blood glucose concentrations increase after surgical incision. The cortisol and catecholamines facilitate glucose production as a result of increased hepatic glycogenolysis and gluconeogenesis. In addition, peripheral use of glucose is decreased due to insulin resistance. The blood glucose concentrations are related to the intensity of the surgical injury; the changes follow closely the increases in catecholamines. In diabetic subjects, poor glycemic control is associated with an increase in diabetic complications, which can be avoided with tight control of blood glucose.[8]

An increased incidence of wound infection and mediastinitis was found in diabetics and non-diabetics in whom blood glucose concentrations were >200 mg dl^{-1}after cardiacsurgery.

In the present study it was found that dexmedetomidine administration along with sevoflurane maintained CBG at much lower value compared to sevoflurane alone in diabetic subjects undergoing laparoscopic surgery.

HarsoorSS et al[9] did a study on 40 patients for abdominal surgery under general anaesthesia and concluded that intravenous dexmeditomidine was effective in blunting stress response to surgical trauma as indicated by lower blood glucose levels and reduce sevoflurane requirement during entropy guided general anesthesia without affecting time for extubation.

Hui Yun S, Suk Choi Y10studied in the year of 2016 on the effects of dexmedetomidine administration on postoperative blood glucose levels in diabetes mellitus patients undergoing spinal anaesthesia and came to conclusion that intraoperative dexmedetomidine infusion maintains blood glucose levels at a constant level relative to baseline in diabetic patients within 24 hourspostoperatively.

In the current study dexmedetomidine reduced significantly requirement of sevoflurane as assessed by BIS .

Edno Magalhães[11] did a study aimed at evaluating the effects of dexmedetomidine continuous infusion on end-tidal sevoflurane concentration (ETsevo) in general anaesthesia, monitored by EEG spectral index (BIS).They concluded that the association of dexmeditomodine continuous infusion to inhalational anesthesia with sevoflurane provided end-tidal sevoflurane concentration decrease while maintaining hemodynamic stability.

He L,Wang X ,Zhenq S[12] investigated in the year of 2014, the effects of two dexmedetomidine bolus and infusion combinations on the amount of sevoflurane required to produce 50% excellent tracheal intubation conditions (ED50 TI) and concluded that dexmedetomidine infusion produce a dose dependent decrease in the ED50 T1 of sevoflurane in children.

Na Young Kim, So Yeon Kim, HyeJin Yoon, and HaeKeum Kil13did a study in 2014 on Effect of Dexmedetomidine on Sevoflurane Requirements and Emergence Agitation in Children Undergoing Ambulatory Surgery.They came to the conclusion that end tidal sevoflurane of dexmedetomidine group was significantly reduced in compared to control group during surgery. Mean arterial pressure and heart rate were significantly lower in dexmedetomidine group duringsurgery.

Nunes RR , Cavalcante SL[14]. studied on influence of dexmedetomidine upon sevoflurane end-expiratory concentration in 2002. The conclusion was Dexmedetomidine was effective in decreasing sevoflurane end-expiratory concentration while maintaining hemodynamic stability without impairing time for hospitaldischarge.

Fragen RJ, Fitzgerald PC15. did a study in 1999 on Effect of dexmedetomidine on the minimum alveolar concentration (MAC) of sevoflurane in adults age 55 to 70 years. The conclusion was dexmedetomidine 0.7 ng/ml decreased the MAC of sevoflurane by 17%.

Lin Chung et al[16]conducted a study in2014 to observe the effects of different doses of dexmedetomidine on plasma cortisole and glucose during anesthesia in patients undergoing uvuloplasty under sevoflurane inhalation anesthesia and came to the conclusion that dexmedetomidine infusion maintains a stable hemodynamics, alleviates stress response and reduces consumption of sevoflurane.

In present study hemodynamic parameters like MAP, HR were comparable between the two groups.

Patel CR et[17] a did a study in 2012 on 60 patients and concluded that dexmedetomidine attenuates variousstress response during surgery and maintains the hemodynamic stability when used as an adjuvant in generalanesthesia. This study found significant hemodynamic difference with dexmedetomidine as this compared it with placebo.

Blood glucose levels are only a tip of iceberg in showcasing the stress response to surgery; assessment of cytokines and interleukins may be better markers for stress response to surgery.

Bekker A et al[18].in 2002 did a study on The effect of intraoperative infusion of dexmedetomidine on the quality of recovery after major spinal surgery.They hypothesized that the intraoperative administration of dexmedetomidine , a sympatholytic agent, would reduce the stress response and improve the quality of recovery in patients undergoing major surgery.They concluded that dexmedetomidine reduced plasma levels of cortisol and IL-10, stress response marker during surgery, in comparison with the controlgroup

CONCLUSION

Dexmedetomidine as a preanaesthetic medication and intraoperative infusion was effective in blunting metabolic stress response to major surgeries as indicated by stable blood glucose levels. It also decreased intraoperative anaesthetic requirement and had significant anaesthetic sparing property during BIS guided general anaesthesia. In addition, continuous intraoperative administration of dexmedetomidine does not affect intraoperative cardiovascular stability.

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