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Original Research Paper

Anesthesiology

COMPARISON BETWEEN TWO DOSES OF DEXMEDETOMIDINE ON HEMODYNAMIC STRESS RESPONSE TO LARYNGOSCOPY PNEUMOPERITONEUM, SEDATION AND POST OPERATIVE ANALGESIA WHEN USED AS PREMEDICANT IN PATIENTS UNDERGOING LAPAROSCOPIC SURGERIES.

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ABSTRACT

Background:The benefits of laparoscopic surgeries include less pain,early mobilization,shorter hospital stay which have further increased its applications.But during laparoscopic surgeries, CO2 is routinely used to create pneumoperitoneum,which causes increased plasma levels of catecholamine and vasopressin.Elevation of intraabdominal pressure with raised diaphragm causes adverse effects on cardiovascular system such as decreased cardiac output,elevated arterial pressure and elevated systemic vascular resistence leading to hypertension and tachycardia.Hence drug which can blunt hemodynamic response to laryngoscopy,intubation and pneumoperitoneum without any adverse side effect is required for this purpose.Dexmedetomidine is a alpha 2 adrenergic agonist which has properties of sedation,sympatholysis and analgesia without having any adverse side effects..

AIM: PRIMARY OBJECTIVES:

1)To compare two doses of dexmedetomidine(0.50mcg/kg and 0.75mcg/kg) in attenuatuating stress response during laryngoscopy and intubation in patients undergoing laparoscopic surgeries.

2)To compare the effects of two doses of dexmedetomidine in attenuating intraoperative hemodynamic changes during laparoscopic surgeries.

3)To compare reduction in intraoperative analgesic requirements with two doses of dexmedetomidine used as premedicants.

SECONDARY OJECTIVES:

1)To study and compare the sedation score and duration of post operative analgesia with two different doses of dexmedetomidine.

2)To study the side effects and complications related to dexmedetomidine if any.

Material and Method: It was a randomized, prospective, double blinded, comparative hospital based study at Department of Anaesthesiology, Gandhi Medical College, Bhopal. 60 ASA Grade I-II patients, age ranging from 18-60 years of either sex, scheduled for laparoscopic surgeries were randomly allocated into three groups of 20 patients each:

- Group P(n=20): received 20 ml of normal saline as placebo over 10 minutes prior to induction.
- Group D(n=20): received i/v dexmedetomidine 0.5mcg/kg diluted upto 20ml with normal saline slowly over 10 minutes prior to indution.
- Group M(n=20): received i/v dexmedetomidine 0.75mcg/kg diluted upto 20 ml with normal saline slowly over 10 minutes.

Results: There was significant decrease in mean HR and MAP in group M as compared to saline group and group D (Dxm=0.50mcg/kg) through-out the surgery (P< 0.05) which shows that dexmedetomidine (0.75 mcg/kg/h) was effective in reduction of HR and BP due to stress response of laparoscopic surgery and endotracheal intubation.

The duration of analgesia was significantly higher in the patients belonging to the Group M. Likewise, the average number of rescue analgesic doses received by Group D patients were more compared to patients in Group M.

Conclusion: From our study we conclude that Dexmedetomidine 0.75µg/kg is significantly superior to Dexmedetomidine 0.50µg/kg in attenuating hemodynamic respose to laryngoscopy ,pneumoperitoneum,sedation and postoperative analgesia when used as premedicant in patients undergoing laparoscopic surgeries.

KEYWORDS : Dexmedetomidine, General Anesthesia ,hemodynamic effects, Laparoscopic surgeries.

Introduction

- Laparoscopic surgery has considerable advantage over open surgery in reducing post operative morbidity and hospital stay.It produces less pain however the major limitation are due to intraoperative physiological complication like hemodynamic instability caused by CO2 pneumoperitoneum[1].co2 pneumoperitoneum causes significant hemodynamic changes such as increase mean arterial B.P.,SVR and reduced cardiac output necessitating preloading or other appropriate therapeutic intervention[2,3].Trendelenberg position given intraoperatively; increases intraabdominal pressure which in turn reduces venous return and cardiac output leading to cardiac dysfunction.
- Dexmedetomidine is highly selective α2 agonist and has significant sympatholytic property. It causes dose dependent reduction in heart rate and blood pressure.
- Furthermore Laryngoscopy and endotracheal intubation are noxious stimuli capable of producing a huge spectrum of stress response[4] such as tachycardia and hypertension ,laryngospasm ,bronchospasm and raised ICT and IOP.
- Thus various drug regimes have been used for obtunding stress response.[5].α2 agonist mediate their action through α2a receptor located in locus ceruleus; the predominant nor adrenergic nuclei of upper brainstem[6].
- Dexmedetomidine attenuates stress response to intubation by decreasing central sympathetic outflow;thereby decreasing the epinephrine and norepinephrin levels[7].
- Dexmedetomidine serve as useful anesthetic adjuvant to control hemodynamic stress response to intubation, pneumoperitoneum and during extubation.It also provides sedation and reduce intra operative and post operative analgesic requirements.
- The dexmedetomidine therefore is used as premedicant in this study in infusion form[8] to assess its effects on hemodynamic response in patients undergoing laparoscopic surgeries.

AIMS AND OBJECTIVES:

- **PRIMARY OBJECTIVES:**

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2) To compare the effects of two doses of dexmedetomidine in attenuating intraoperative hemodynamic changes during laparoscopic surgeries.
3) To compare reduction in intraoperative analgesic requirements with two doses of dexmedetomidine used as premedicants.

- **SECONDARY OJECTIVES:**

1) To study and compare the sedation score and duration of post

operative analgesia with two different doses of dexmedetomidine.

2) To study the side effects and complications related to dexmedetomidine if any.

Material and Methods

The present study was conducted in department of Anesthesia; GMC Bhopal and associated Hamidia Hospital in patients posted for elective laproscopic surgeries under general anaesthesia.After approval by institutional ethical committee and written informed consent;60 patients of ASA grade 1 and 2 posted for elective laproscopic surgeries; age ranging from 18-60 years were taken.

Patients were randomnly divided into 3 groups of 20 patients

- Group P(n=20): received 20 ml of normal saline as placebo over 10 minutes prior to induction.
- Group D(n=20): received i/v dexmedetomidine 0.5mcg/kg diluted upto 20ml with normal saline slowly over 10 minutes prior to indution.
- Group M(n=20): received i/v dexmedetomidine 0.75mcg/kg diluted upto 20 ml with normal saline slowly over 10 minutes.
- In the operation theatre, intravenous line, pulse oximeter, electrocardiograph and a non invasive blood pressure monitor was attached.Baseline parameters HR, SBP, DBP, MAP, SpO2 and ECG were noted.

Patients were premedicated with Inj. ondansetron 0.08mg/kg, Inj glycopyrrolate 0.01mg/kg, Inj midazolam 0.05mg/kg, Inj fentanyl 1mcg /kg given intravenously. Group D received i.v. dexmedetomidine 0.5mcg/kg diluted up to 20 ml with normal saline and infused over 10 minutes. Group M received i.v. dexmedetomidine 0.75mcg/kg diluted up to 20 ml with normal saline and infused over 10 minutes. After completion of dexmedetomidine infusion; HR, SBP, DBP, MAP, Spo2 were again noted and sedation was assessed using Ramsay sedation score at 2min, 5min and 10 minutes.

The Ramsay Scale

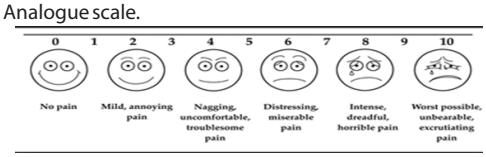
Scale	Description
1	Anxious and agitated or restless, or both
2	Cooperative, oriented, and tranquil
3	Response to commands only
4	Brisk response to light glabellar tap or loud auditory stimulus
5	Sluggish response to light glabellar tap or loud auditory stimulus
6	No response to light glabellar tap or loud auditory stimulus

Pre oxygenation was done and patient was taken into General Anesthesia.Following laryngoscopy and intubation; the H.R., SBP; DBP and MAP were recorded at 1min, 3 min and 5minutes after intubation.

The number of intubation attempts and the duration of intubation was also noted. HR, SBP, DBP, MAP, SpO2 and ECG was noted further at 10 min,20 min;30 min; 40 min and till end of surgery.

On completion of surgery,the neuromuscular blockade was reversed with 0.05mg/kg neostigimine and 0.01mg/kg of Glycopyrrolate.

Duration of postoperative analgesia was assessed according to the Visual Analogue scale.



Statistical Analysis

The data was compiled and subjected to stastical analysis.

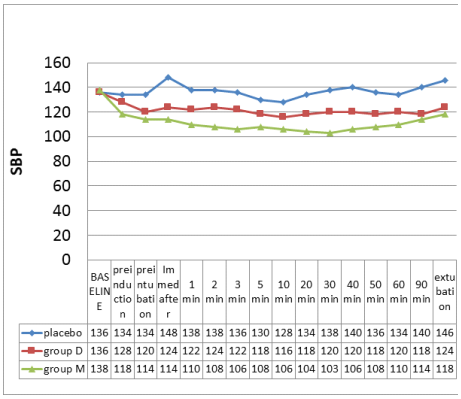
Results are tabulated and analyzed using spss software. ANOVA test is used for continuous variables and Chi square test for discrete variables is applied. Results are expressed as Mean±SD. P value<0.05 will be considered significant and p value<0.01 will be considered highly significant.

Observation and Results

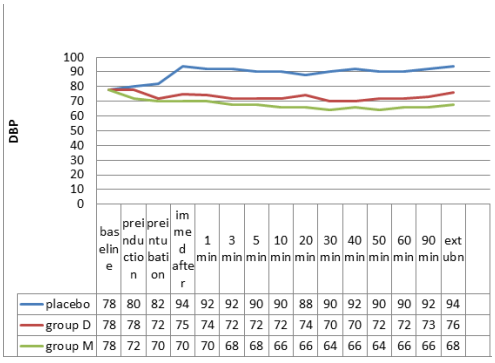
1) The mean age, weight and sex distribution in all groups were nearly same without any significant differences.

parameters	Group P (mean+sd)	Group D (mean+sd)	Group M (mean+sd)	P value
AGE	34.10+12	36.07+10	36.10+12	0.44
SEX(male) (female)	45% 55%	38% 62%	40% 60%	
WEIGHT	64.3+12.05	63.5+11.57	62.6+11.26	0.75
HEIGHT	162.6+9.2	164+8.7	162+9.4	
BMI	23.79+2.5	24.28+2.7	23.86+2.6	0.47
ASA 1 ASA 2	75% 25%	71% 2%	70% 30%	

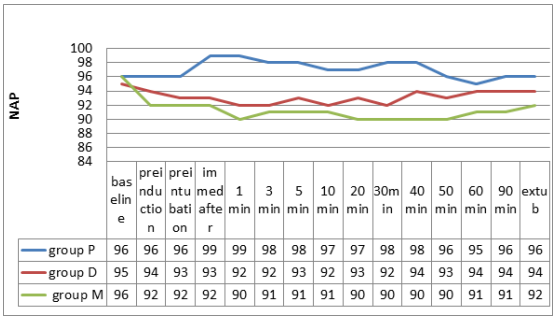
2) Comparison of systolic blood pressure between the two groups



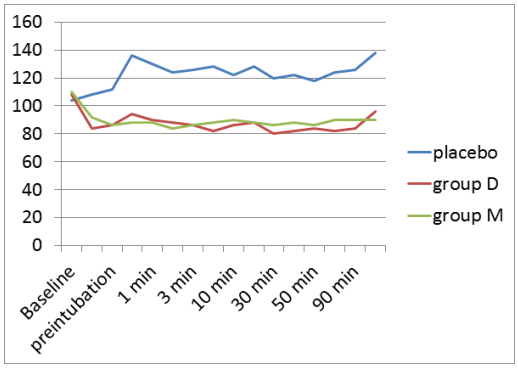
3) Comparison of diastolic blood pressure between the two group:



4)Comparison of mean arterial pressure between the groups:



5)Comparison of heart rate between the groups:



6)Comparison of sedation score between the groups:

	group P	group D	group M	p value
2min	1	3	4	0.005
5min	2	4	4	0.006
10 min	2	4	5	0.001

7)Comparison of VAS score between the groups:

VAS	Group P	%	VAS	Group D	%	VAS	Group M	%
0	0	0%	0	10	50%	0	14	70%
1	8	40%	1	6	30%	1	4	20%
2	12	60%	2	4	20%	2	2	10%
Total	20		P VALUE =0.01					

8)Time of first Rescue Analgesia:

Time for 1st rescue analgesia(min)	group P	Group D	Group M	P VALUE
Mean	10min	60min	125min	0.001
Median	12min	64min	132min	
SD	2.8	8.6	9.2	

Adverse effects:

2 patients from group D showed extreme hypertensive response following dxm infusion requiring nitroglycerine administration which was stastically insignificnt.

1 patient from group M developed bradycardia (HR=55/min) which was treated with inj atropine 0.6mg immediately.

Discussion

The groups were comparable with their demographic profile including age, sex, gender.

The baseline mean SBP were comparable in all three groups.After 10 min of Dxm administration the mean SBP in placebo group was significantly higher as compared to group D and group M.

Immediately after intubation the mean SBP rises significantly in placebo group while in group D rises mildly and in group M the mean SBP immediately after intubation in most of the cases remained similar to preinduction values.

Baseline MAP of group D was 95.24+6.34mmHg while in group M it was 96.28 ± 6.28 mmHg , which was not significant between two groups (P> 0.05). Significant decrease in MAP was found 10 min after dexmedetomidine , after intubation, after 20 min of pneumoperitoneum, after extubation, in group M compared to group D, (P =0.012). While in placebo group MAP increases by 30-40mm Hg to baseline values.

Baseline mean HR was not significant between two groups (P> 0.05) as mean HR of group D was 108+5.34 while in group M it was 110 + 6.86(p=0.021). There was a significant reduction in HR following the dexmedetomidine, after intubation, after 20 min of pneumoperitoneum, after extubation, in group M (P< 0.021) as compared to group D while in saline group heart rate increased significantly as compared to baseline value.

10 patients in group S (50.14%) required tramadol in the postoperative period for pain relief as compared to 6 patients in group D (30.71%) and 2 patients in group M(10%) which was statistically significant (P =0.03). Nine patient had sedation score slightly higher in group M as compared to group D and placebo group, but none of the patient had an undue sedation, so the values are not statistically significant.

In the present study, we found that premedication with dexmedetomidine 10 minutes prior to induction decreased hemodynamic responses to various noxious stimuli perioperatively in laparoscopic surgeries. Thus, there was significant decrease in mean HR and MAP in group M as compared to saline group and group D (Dxm=0.50mcg/kg) through-out the surgery (P< 0.05) which shows that dexmedetomidine (0.75 mcg/kg/h) was effective in reduction of HR and BP due to stress response of laparoscopic surgery.

In the present study, VAS score was less in group M relative to group P and group D and postoperative tramadol requirement was significantly less in group M relative to that in group P and group D. due to action of dexmedetomidine on postsynaptic alpha-2-adrenoceptor located in the locus cerulus.

Gourishankar et al [4] have used low dose infusion of dexmedetomidine at the rate of 0.4mcg/kg/h without any bolus dose, in patients undergoinlaparoscopic cholecystectomy. They found that the drug serves as a very useful anaesthetic adjuvant to control haemodynamic stress response to intubation , pneumoperitoneum and extubation. It also provides lighter sedation and reduces the postoperative analgesic requirements without any significant adverse effects [3, 4].

In a similar study,Vora et al have demonstrated that an infusion of dexmedetomidine (0.5mcg/kg/h) is also effective and safe for attenuation of increase in HR and BP due to stress response of laparoscopic surgery [9].

Review of literature suggests that infusion rates varying from 0.1 to 10 mcg/ kg/ h have been studied. However, with higher dose infusion of dexmedetomidine, high incidences of adverse cardiac effects have been observed [10].

Lawrence and De Lange have investigated the effect of a single pre-induction intravenous dose of dexmedetomidine 2µg/kg on anaesthetic requirements and peri-operative haemodynamic stability in patients undergoing minor orthopaedicand general surgery. They have found that the hypotension and bradycardia occurrence has been more frequently after dexmedetomidine [10]. Yildiz et al [11] have evaluated the effect of a single pre-induction intravenous dose of dexmedetomidine1mcg/kg on cardiovascular responseresulting from laryngoscopy and endotracheal intubation, need for anaesthetic agent and perioperative haemodynamic stability on patients undergoing minor surgeries under general anesthesia. In their study they have concluded that single dose of dexmedetomidine in preoperative period decreases blood pressure and heart rate during laryngoscopy, reduce opioid and anaesthetic requirements and enhances speed of recovery postoperatively.

Our results are also in line with their observations.We have observed that dexmedetomidine in a doseof 0.75µg/kg could effectively attenuate the vasopressor response of laryngoscopy, and intubation and the sympathoadrenal response occurring with pneumoperitoneum as compared to dexmedetomidine in the dose of 0.50 µg/kg.

Hall , Uhrich et al in their research have determined the safety and efficacy of two small dose

infusions (0.2 and 0.6mcg/kg) of dexmedetomidine by evaluating

sedation analgesia, cognition, and cardiorespiratoryfunction. Dexmedetomidine infusions have resulted in reversible sedation, mild analgesia, and memory impairement without cardiorespiratory compromise [12]. We have also found that dexmedetomidine significantly reduces the need of post operative analgesics. In our study, dexmedetomidine in a dose of 1 µg/ kg has provided better pain relief and sedation than at the dose of 0.7µg/kg without compromising safety.

Conclusion:

Thus from above study we concluded that among the two doses of dexmedetomidine(0.5mcg/kg) and (0.75mcg/kg), patients with dxm(o.75mcg/kg) showed better attenuation of stress response to laryngoscopy, better hemodynamic stability through out the perioperative period during laparoscopic surgeries and reduction in dose of intraoperatve and post operative analgesic requirement without any adverse effects as compared to patients with dxm(0.5mcg/kg).

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Conflicts of Interest: None

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