

Original research article

Hemodynamic effects of two different doses of dexmedetomidine in laparoscopic gynaecological surgeries under general anaesthesia

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Abstract

Introduction: Dexmedetomidine, a highly selective α_2 agonist is a well-known anaesthetic adjuvant. As it has sedative, sympatholytic and analgesic properties, it is an ideal adjuvant in laparoscopic surgeries as well. The aim of this study was to evaluate the effect of two different doses of dexmedetomidine infusion on hemodynamic response to critical incidences such as laryngoscopy, endotracheal intubation, creation of pneumoperitoneum and extubation in patients undergoing elective laparoscopic gynecological surgeries.

Methods: Sixty patients of American Society of Anesthesiologists (ASA) physical grades I and II undergoing elective laparoscopic gynecological surgeries were randomly allocated into two groups of 30 patients each. Group D1 patients received loading dexmedetomidine infusion at 0.6 mcg/kg for 15 min before induction, group D2 received loading dexmedetomidine infusion at 1 mcg/kg for 15 min before induction. In both the groups, maintenance infusion at a rate of 0.3 mcg/kg/hr was given till the end of surgery. Heart rate and mean arterial pressure (MAP) were noted preoperative, after bolus drug administration, 1 min after induction, 1 min after intubation, and after pneumoperitoneum at 15 min interval till the end of pneumoperitoneum and postoperative period. SPSS 17.0 version software was used for statistical analysis.

Results: In both groups, attenuation of hemodynamic stress response was seen following laryngoscopy, tracheal intubation, creation of pneumoperitoneum and extubation.

Conclusion: Dexmedetomidine, even in lesser loading dose of 0.6 mcg/kg,

Effectively attenuates hemodynamic stress response during laparoscopic surgery as compared to loading dose of 1 mcg/kg. So, Dexmedetomidine is an efficient preanaesthetic medication and intraoperative adjunct in laparoscopic gynecological surgeries.

Keywords: Dexmedetomidine, hemodynamics, laparoscopic gynecological surgeries.

Introduction

Laparoscopic surgery is emerging as the first choice for surgical management of various indications, especially with the well-trained laparoscopic surgeon. The benefits of minimal access techniques include less pain, early mobilization, shorter hospital stay, and better cosmetic results, which have further increased its applications [1, 2]. During general anesthesia, laryngoscopy, tracheal intubation and extubation are the critical events provoking transient but marked sympathoadrenal response manifesting by hypertension and tachycardia. In addition, in laparoscopic surgery, CO₂ is routinely used to create pneumoperitoneum, which causes increased plasma level of catecholamine and vasopressin.

Elevation of intra-abdominal pressure with raised diaphragm causes various adverse effects on the cardiovascular system such as decreased cardiac output, elevated arterial pressure, and increased systemic and pulmonary vascular resistance leading to hypertension and tachycardia [3, 4]. Severe increases in arterial pressure can be a risk factor in patients with preexisting hypertension, ischaemic heart disease, or increased intracranial pressure. Opioids, alpha-2-adrenergic agonists, beta-blocking agents, or vasodilators are often used to avoid circulatory response to pneumoperitoneum [5].

Dexmedetomidine is an alpha-2-adrenergic agonist; it has properties of analgesia, sympatholytic effect, and sedation without respiratory depression. It decreases opioid requirements and stress response to surgery ensuring a stable hemodynamic state. Its distribution half-life is around six min, so it can be used to attenuate the stress response to laryngoscopy [8-10].

The aim of this study was to evaluate the effect of two different doses of dexmedetomidine on hemodynamic response to critical incidences such as laryngoscopy, endotracheal intubation, creation of

pneumoperitoneum and extubation in patients undergoing laparoscopic gynecological surgeries.

Materials and Methods

The study was conducted in Vijayanagar Institute of Medical Sciences, Ballari between January 2019 and December 2020 after obtaining approval from the Institutional Ethics Committee and written informed consent from the patients, it is a double blinded randomised control study

Inclusion criteria

- 60 ASA grade I and II patients,
- Aged 30-50 years,
- Undergoing elective laparoscopic gynecological surgeries

Exclusion criteria

1. Patients belonging to ASA grade III, IV and V.
2. Patient refusal.
3. Liver and renal dysfunction.
4. Patients with cardiac dysrhythmias.
5. Weight >120 kg.
6. Allergy to drugs.

Patients were randomly assigned to two different groups, 30 each using a computer-generated random table.

Group D1 received loading dose of dexmedetomidine 0.6 mcg/kg and group D2 received 1 mcg/kg. Both groups received maintenance infusion of dexmedetomidine 0.3 µg/kg/hr. Infusion was prepared separately for each group by a separate person.

To prepare the infusion, dexmedetomidine 1 mL containing 100 µg of the drug was withdrawn in a 10-mL syringe and was diluted up to 10 mL with normal saline resulting in the final concentration of 10 mcg/mL. Dexmedetomidine infusion was given through a syringe infusion pump. Targeted infusion rate was delivered, depending on the weight and allotted group of the patient. All the patients underwent thorough pre-anesthetic evaluation on the day prior to surgery. Basic laboratory investigations were conducted including hemogram, urine analysis, chest X-ray, electrocardiogram, blood sugar, serum creatinine, blood urea, serum electrolytes and coagulation profile. Patients were alleviated of their anxiety.

All the patients were kept fasting overnight. On arrival at the operation theater, patient's pulse oximeter, noninvasive blood pressure monitor and three lead ECG monitoring were done. Intravenous access was secured with 18 G cannula. All patients received inj. *Ondansetron* 4 mg intravenously and inj. *Midazolam* 2 mg. The patients received loading dexmedetomidine infusion at 0.6 mcg/kg and 1 mcg/kg for 15 min before induction as per their groups, followed by maintenance infusion at a rate of 0.3 mcg/kg/hr continued till the end of surgery.

Patients were induced after 15 min of infusion of study drug with *Fentanyl* 1 mcg/kg intravenously and *Propofol* 2 mg/kg, given 20 mg every 5 sec. Endotracheal intubation was facilitated by muscle relaxant *Succinylcholine* 1.5 mg/kg. Anesthesia was maintained with O₂ in N₂O (50:50), intermittent bolus dose of fentanyl citrate 0.5 µg/kg and vecuronium 0.02 mg/kg. CO₂ insufflation into the peritoneal cavity (at a rate of 2 L/min) was done to create pneumoperitoneum. Intraabdominal pressure was maintained at 12 mmHg throughout the laparoscopic procedure. The patients were mechanically ventilated to keep ET/CO₂ between 35 and 40 mmHg.

At the end of the operation, the infusion of study medication was stopped. Residual neuromuscular block was reversed by appropriate dose of *Neostigmine* and *Glycopyrrolate* and tracheal extubation was performed. Heart rate and mean arterial pressure were monitored preoperative, after bolus drug administration, 1 min after induction, 1 min after intubation, and after pneumoperitoneum at 15 min interval till the end of pneumoperitoneum and postoperative period.

Mean arterial pressure was maintained within ± 25% of baseline. Hypotension (MAP < 25% of baseline on two consecutive readings within 2-3 min) treated with fluid bolus and ephedrine 3 mg intravenous boluses. Infusion of study medication was discontinued if hypotension persisted for >2 min. Upon return of MAP to ± 25% of baseline, the study medication was resumed at 50% of initial infusion rate. Hypertension (MAP > 25% of baseline on two consecutive readings within 2-3min) and/or tachycardia (HR > 25% of baseline for >2min) treated with *Metoprolol* 1 mg intravenous boluses. Bradycardia (HR < 45 for more than 2 min) treated with *Atropine* 0.5 mg intravenous boluses.

Results were presented as mean ± standard deviation. SPSS 17.0 version software was used for statistical analysis. Chi-square test was used for non-parametric data (age, sex, weight and duration of surgery). Heart rate and mean arterial pressure were compared within the group against baseline values using paired t-test. ANOVA test was used for three group comparisons of continuous variables. If ANOVA was found significant, Tuckey post-hoc test was used for comparing two groups. P value < 0.05 was

considered significant and highly significant if <0.001.

Results

Both groups under study were comparable to each other in reference to the baseline PR. In both groups, after starting the infusion, the PR decreased highly significantly below the preoperative value. No further significant changes were observed immediately after induction. After intubation and extubation, the PR increased above the preoperative value in both groups, though this increase was not significant (P >0.05). Pneumoperitoneum did not result in a significant effect in both the groups.

	Group D1	Group D2	P value
Preoperative	80.0± 6.0	78.5±8.5	P >0.05
Preinduction after bolus	72+10.5	70.5±11.5	P >0.05
Post intubation	82.0±9.0	80.0± 14.5	P >0.05
1minute after intubation	81±12.0	78.5±16.5	P >0.05
After pneumoperitoneum	80.5±13.5	77.5±18.5	P >0.05
15minutes	85.5±10.0	83.5±18.0	P >0.05
30minutes	88.5±10.5	85.0±15.0	P >0.05
45 minutes	90.0±9.5	88.5±16.5	P >0.05
60minutes	95.5±10.0	93.5±16.0	P >0.05
End of pneumoperitoneum	97.5±9.0	95.5±12.0	P >0.05
Post-operative			
1 hour	82.5±10.5	81.5±15.0	P >0.05

	Group D1	Group D2	P value
Preoperative	104.5±14.5	104.0±14.0	P >0.05
Preinduction after bolus	88.5±13.5	87.5±11.5	P >0.05
Post intubation	82.0±9.0	81.0± 14.5	P >0.05
1minute after intubation	81±12.0	81.5±16.5	P >0.05
After pneumoperitoneum	80.5±13.5	79.5±18.5	P >0.05
15minutes	85.5±10.0	84.5±18.0	P >0.05
30minutes	88.5±10.5	87.0±15.0	P >0.05
45 minutes	90.0±9.5	89.5±16.5	P >0.05
60minutes	95.5±10.0	95±16.0	P >0.05
End of pneumoperitoneum	97.5±9.0	96±12.0	P >0.05
Post-operative			
1 hour	82.5±10.5	81.5±15.0	P >0.05

Discussion

We studied effects of dexmedetomidine on hemodynamic stability in patients undergoing laparoscopic gynecological surgeries. Dexmedetomidine is a highly selective alpha 2 adrenergic agonist with sedative, anxiolytic, analgesic, sympatholytic and antihypertensive effects.¹ Dexmedetomidine, alpha 2 adrenoreceptor agonist shows a biphasic, dose dependent, blood pressure effect. At low dose the dominant action is a reduction in sympathetic tone mediated by reduction of norepinephrine release at the neuroeffector junction and inhibition of neurotransmission in sympathetic nerves. The net effect of dex is a significant reduction in circulating catecholamines with a slight decrease in blood pressure and moderate reduction in heart rate.

When dex is administered as a continuous infusion, is associated with an expected and stable hemodynamic response. With continuous infusion for 24 hr, distribution half-life of 6 min elimination half-life of 2 hrs, availability of antagonistic agent Atipamezole, dexmedetomidine is an ideal drug for continuous infusion in the ICU, operation theatre and other areas.⁵ When labour epidural analgesia could not work, in such cases intravenous dexmedetomidine infusion with systemic opioids has been successfully used^[6,7].

At higher doses of dex produce and hypertensive action caused by activation of alpha 2 adrenoceptor located on vascular smooth muscle cells. Therefore rapid injection of dex is not advised. Dex produces analgesia effect by an action on alpha receptor within the locus ceruleus and the spinal cord. Dex is eight times more specific for alpha 2 receptors than clonidine (alpha2 alpha 1 ratio for dex is 1620:1 and that for clonidine is 220:1)^[8] When combined with alfentanil, dex enhances analgesia without causing further respiratory depression.

Because the primary site of action is the locus ceruleus, dex produce a different type of sedation compared with benzodiazepines and propofol. Central stimulation of parasympathetic outflow and inhibition of sympathetic outflow from the locus coeruleus in the brainstem plays a prominent role in the sedation and anxiolysis produced by dexmedetomidine. The unusual subcortical form of dex induced sedation is characterized by an easy and quick arousal, resembling natural sleep. With increasing dose of dex, profound anaesthetic action have been demonstrated and this advocates that Dex could be used as

total intravenous agent.

Few studies have reported use of Dexmedetomidine upto 7 days and case studies have reported use beyond 3 weeks, without any side effects. Low and high dose of Dexmedetomidine is reported to cause a 55% and 45% decrease in Isoflurane MAC respectively^[4, 9].

In our study, we observed that both group D1 and group D2(Dexmedetomidine + fentanyl) provided good hemo stability-intraoperatively.Similar findings studied by B. Tufango^[10]. Author used intra operative Dexmedetomidine infusion (0.2-0.8µg/Kg/hr) which decrease fentanyl requirement. P.E. Tanskanen also proved decreased intra operative opioid requirement. 8 According to Hassan S9, the intraoperative infusion of Dexmedetomidine decreased the total amount of propofol and fentanyl required to maintain anaesthesia with good hemodynamics stability and rapid recovery in morbidly obese patients undergoing laparoscopic gastric bypass.10 Research showed that Intraoperative Dex infusion is helpful in alleviation of post-operative shivering, nausea and vomiting in gynaec laparoscopic surgery^[13,14,15] We found that both groups provided better pressure attenuation response during direct laryngoscopy and intubation(Pvalue>0.05) FerdiMenda^[16] *et al.*, hypothesized that in fast track CABG, Fentanyl 5 µg/Kg and IV dex infusion started before endotracheal intubation provided attenuation response to intubation without hemodynamic compromise.

Even In hypertensive patients, administration of dexmedetomidine before anesthesia induction blunts the hemodynamic response to tracheal intubation and reduces the thiopental Dose^[17,18].

In the study done by Keniya VM^[19] *et al.*, dex infusion blunts the hypertensive and tachycardia response to endotracheal intubation. Systolic blood pressure was decreased in dex group as compare to control group (8% vs 40%). Similarly Heart rate was also decreased in dex group as compare to control group (7% vs 21%).Consumption of fentanyl, thiopentone and isoflurane was reduced with intraoperative dex infusion. Yildiz M20 *et al.* hypothesized that single dose of dex in preoperative period decreased blood pressure and heart rate during laryngoscopy, reduced opioid and anaesthetic requirements,rapid recovery postoperatively.

As shown in Table,with respect to Heart Rate and MAP, there is no much difference between 2 groups and also in comparison to preoperative value at various points of surgery.Similar Findings correlated with D.P.Bhattacharjee.^[21]

After discontinuation of infusion, rapid recovery was found in both groups.Hassan *et al.* studied same findings in morbidly obese patients^[12].

According to StaffanWahlender, Dex reduces the rescue analgesia Requirement in Post-operative thoracic patients along With low dose epidural bupivacaine(0.125%).23the activation of α2adrenoceptors, imidazoline-preferring receptors,or both in the ventrolateral medulla and especially in the solitarius nucleus tracked by dexmedetomidine causes bradycardia.

In our study we found 3 patients had episode of bradycardia. Treated with inj. Atropine 0.5 mg.similar findings have been made by carollo DS and Lawrence CJ24,^[9].The novel therapeutic uses of this α2-AR agonist can be put safely into practice after thorough evaluation by Randomized Controlled Trials.

Conclusion

Dexmedetomidine,even in lesser loading dose of 0.6mcg/kg,effectively attenuates hemodynamic stress response during laparoscopic surgery as compared to loading dose of 1 mcg/kg. So, Dexmedetomidine is an efficient preanaesthetic medication and intraoperative adjunct in laparoscopic gynecological surgeries. Dexmedetomidine, by the virtue of its sympatholytic, analgesic and sedative properties, could be beneficial for a wide range of clinical conditions like ICU sedation, paediatric Procedural sedation, awake fiberoptic intubation, neuro, cardiac and bariatric surgery and the list continues to grow. It appears to have promising future applications with wide Safety margin.

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