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Complications of Dexmedetomidine in Patients Undergoing Laparoscopic Surgery: A Descriptive Study

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Abstract

Background: Stress response is common in any of the operative or laparoscopic procedure. Anesthetic agents like Dexmedetomidine are roped into, to attenuate these hemodynamic responses and to smoothen the operative and postoperative period. This study evaluates the side effects or complications encountered in patients receiving Dexmedetomidine infusion. *Methods:* This was a descriptive study done in patients with age group 18-65 years age of either sex undergoing laparoscopic surgery and receiving the Dexmedetomidine infusion. *Result:* Total of 30 patients were included in the study. The mean + SD age of the patients were 31+13.2 years. Bradycardia and hypotension was present in 10% of patients receiving Dexmedetomidine infusion. *Conclusion:* Bradycardia and hypotension were most common side effects seen with Dexmedetomidine infusion though were self resolving. Thus it is effective in attenuating haemodynamic response to laryngoscopy, intubation, surgery and pneumoperitoneum without significant complications.

Keywords: Complications; Dexmedetomidine; Laparoscopic; Surgery.

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Introduction

Stress response usually gets exaggerated during any of the surgical procedure including the perioperative or the postoperative period. Anesthetic agents are roped in, to attenuate these stress responses and to maintain the physiological and hemodynamic stability. Dexmedetomidine has almost 8 times more affinity for α-2 adreno-receptors as compared to Clonidine [1].

Dexmedetomidine is a novel α2 agonist with sedative, sympatholytic and analgesic properties and hence, it can be a very useful adjuvant in anaesthesia as stress response buster, sedative and analgesic [2]. It also reduces the catecholamine levels and its release in response to surgical stress or any nociceptive stimuli [3,4,5]. Though the Opioids are also effective in attenuating the stress response; however, the dose required is very high for similar results [1]. The pneumo-peritoneum created during the laparoscopic surgeries poses an extra risk for haemodynamic instability [6,7]. Hence, the study was proposed to assess the side effects related with the use of dexmedetomidine infusion in patients undergoing laparoscopic surgery.

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Methods

This was a descriptive study conducted at a tertiary care teaching institute in western India. Institute ethical Committee approval was taken before the initiation of the study. Part of the study describing the hemodynamic changes with the use of Dexmedetomidine compared with controls has already been accepted and under process for publication. [8] All patients receiving Dexmedetomidine during laparoscopic surgery were included in the study after informed consent. A total of thirty patient of ASA Grade I & II, aged 18–65 years of either sex scheduled for elective laparoscopic surgeries i.e Lap. Choleycystectomy, Lap. Appendicectomy, Lap assisted VH, Diagnostic Laparoscopic procedure under general anaesthesia were included in the study. ASA Grade III & IV patients with decreased autonomic control such as the elderly, diabetic patients, patients with chronic hypertension or severe cardio - pulmonary disease, patients on drugs like β blockers or calcium channel blockers, pregnant or lactating women, patients with history of egg protein allergy and to drugs particularly α 2 agonists were excluded from the study.

Study subjects received injection Dexmedetomidine with loading dose 1 mcg/kg before induction over a period of 10 minutes followed by maintenance dose of 0.2 mcg/kg/hr throughout the pneumoperitoneum till extubation. The study drug was prepared in a similar 50 ml syringe by anaesthesiologist. Dexmedetomidine 200 mcg/ kg (2 ml) was added to 0.9% normal saline (48 ml) making a total volume of 50 ml (with concentration of 4 mcg/ml).

Patient on arrival to operation room were secured with two 18 G (iv) cannula, one for loading and infusion of study drug and other for induction and maintenance of general anaesthesia.

Routine vital monitor, ECG (Electrocardiography), Pulse Oximetry, Non Invasive Blood Pressure (NIBP) monitors were attached and baseline parameters like Heart Rate (HR), SpO_2. Blood Pressure were recorded at pre decided interval. Loading dose of Dexmedetomidine infusion at 1 mcg/kg was started and infused over a period of 10 minutes, thereafter maintenance infusion was given at a rate of 0.2 mcg/kg/hr.

Premedication was done for all subjects with inj. Glycopyrolate 4 mcg/kg, inj.midazolam 0.03 mg/kg and inj. ondansetron 4 mg, inj. Fentanyl 2 mcg/kg i.v. Patients were preoxygenated with 100% oxygen, induced 5 minutes after infusion of loading dose with inj.Thiopentone 5 mg/kg i.v, inj.succynylcholine 1.5 mg/kg. All the patients were intubated with appropriate size endotracheal tube and correct position of tube was confirmed by auscultation and $EtCO_2$ measurements. Anaesthesia was maintained with nitrous oxide and oxygen gas mixture (60:40) and Isoflurane on a closed circuit. Injection Vecuronium was administered for neuromuscular blockade. Carbon di oxide was insufflated in to the peritoneum (at a rate of 2 litre/min) to create pneumoperitoneum. Intraabdominal pressure was maintained upto 12-14 mmHg throughout the procedure. All the patients were observed for vital parameters like pulse rate, mean arterial pressure and SpO_2 levels at regular intervals at baseline, during laryngoscopy, intubation, 1,3,5 minutes after intubation, before pneumoperitoneum, 15 and 30 minutes after pneumoperitoneum and after extubation.

Dexmedetomidine infusion was continued till extubation of patient. Residual neuromuscular blockade was reversed by appropriate dose of Neostigmine and Glycopyrolate and tracheal extubation performed. Any adverse effects like hypotension, hypertension, bradycardia, respiratory depression were recorded. Patients were observed in recovery room for 2 hrs and thereby shifted to ward.

Throughout the study, patients were observed for any adverse events like bradycardia, tachycardia (pulse rate less than or more than 20% of pre-operative level respectively on two consecutive readings), hypotension and hypertension (MAP less than or more than 20% of pre-operative level respectively on two consecutive readings), sedation score more than RSS(Ramsay sedation score) 4, respiratory depression (SaO_2 < 90%) and dryness of mouth and were managed conservatively.

Hypotension was managed with fluid bolus of normal saline. If it didn't responded to fluid administration then injection Mephentermine 5mg i.v was administered. Any incidence of bradycardia was treated with inj. Atropine 0.6 mg i.v. Any hypertension (MAP >20% Preoperative value) was treated by increasing Isoflurane concentration to maintain SBP within 20% of preoperative value.

Statistical Analysis

All the data which was expressed as mean±SD or as n (%) was filled in the predesigned proforma and then entered in the computer using Excel sheet. The analysis of data was done using SPSS software version 17.0.

Results

Total of 30 patients were enrolled in the study. Demographic profile of the patients is described in Table 1. The mean age ± SD of patient was 31+13.2. Side effects of the Dexmedetomidine infusion are described in Table 2. The common side effects which were seen in the present study were bradycardia, hypotension. The other minor side effects were dry mouth, nausea, fever, chills, vomiting and agitation.

Table 1: Demographic variables of study population

Variables	Study population (n=30)
Age(Years) Mean±SD	31±13.2
Weight(Kg) Mean±SD	50.5±9.7
Sex (M:F)	8:22
ASA Grading (I/II)	5:25

Legend; SD- Standard Deviation, ASA- American Society of Anaesthesiologists.

Table 2: Side effects seen in the study population with use of Dexmedetomidine infusion

Variables	n(N = 30)	% ages
Bradycardia	3	10%
Tachycardia	2	6.7%
Hypotension	3	10%
Hypertension	1	3.3%
Nausea	3	10%
Dry mouth	3	10%
Fever	1	3.3%
Vomiting	1	3.3%
Agitation	1	3.3%
Chills	1	3.3%
Hyperglycemia	-	-
Hypothermia	-	-
Hyperthermia	-	-
Desaturation (Spo2<90%)	-	-
Post Procedure bleeding	-	-
Oliguria	-	-
Bronchospasm	-	-
Metabolic acidosis	-	-
RSS *score >4	2	6.7%

*RSS: Ramsay sedation score

Discussion

Anaesthetic manoeuvres like direct laryngoscopy, tracheal intubation and extubation involve severe sympathetic stimulation. Moreover, the pneumoperitoneum and carbon dioxide insufflations required in laparoscopic surgeries, lead to increase in plasma nor-epinephrine, epinephrine levels and plasma renin activity [7]. All these changes lead to tachycardia, hypertension and increased systemic and pulmonary vascular resistance, and reduced cardiac output.

Modern day anaesthesia practices, therefore, plan to prevent sympathetic discharge and provide haemodynamic stability perioperatively. [2] Various agents in the form of opioid analgesics, benzodiazepines, beta blockers, calcium channel blockers and vasodilators have been used to achieve this goal with variable success. Recently, a great enthusiasm has been shown toward the use of α2 agonists in anaesthesia practice because of their anxiolytic, sedative, sympatholytic and analgesic sparing properties [9].

Dexmedetomidine is a highly selective novel α 2 adrenergic agonist. It acts through three types of α 2 receptors- namely α 2 A, α 2 B and α 2 C situated in brain and spinal cord. The resultant action is sedation, anxiolysis, analgesia and sympatholysis, the latter leading to decrease in the blood pressure and heart rate [2]. Activation of α 2 A receptors in brain stem vasomotor centre results in suppression of norepinephrine release, hypotension and bradycardia. Stimulation of α 2 A adreno receptors and α 2 C adreno receptors in locus ceruleus causes sedation. In the spinal cord, activation of both α 2 A and α 2 C receptors directly reduce pain transmission by reducing substance P release [2].

Therefore, the Dexmedetomidine has proven analgesic, sedative, anxiolytic and sympatholytic activity [10-13]. The added advantage of dexmedetomidine is that it provides conscious sedation and analgesia without causing much respiratory depression leading to a cooperative patient [14]. Dexmedetomidine infusion in the perioperative period decreases serum catecholamine levels by 90%, [13] blunt the haemodynamic response to laryngoscopy, tracheal intubation, pneumoperitoneum and extubation, [15] provides sedation without respiratory depression [16] and decreases post-operative analgesic requirements also [17].

The Dexmedetomidine has been used in IV infusion form with or without bolus dose. Infusion rates range from from 0.1 to 10 mcg/kg/h [10,18,19] However, with higher dose infusion, higher incidence of adverse cardiac effects have been observed [13]. A biphasic response on blood pressure occurs with a bolus dose [7]. Initially, there occurs hypertension followed by fall in blood pressure. This response is seen often more in young and healthy patients [14]. Stimulation of α 2 B adreno-receptors in vascular smooth muscles is responsible for this biphasic response. Low dose infusion of 0.25–0.5 mcg/ kg/h results in a monophasic response of 10–15%

fall in mean arterial blood pressure and pulse rate. [13] Furthermore, in low dose, dexmedetomidine exhibits linear kinetics, meaning that a constant amount of drug is eliminated per hour rather than a constant fraction of drug.

Dexmedetomidine was found to have sympatholytic effect while preserving the baro-reflex mechanisms [20]. It is associated with hypotension and bradycardia [21] which was seen in the present study too. Both of these problems usually resolve without intervention [22] as was seen in the present study too. Significant bradycardia was noted in 3 (10%) patients receiving Dexmedetomidine. Bradycardia appeared mostly in the first 30 minutes of Dexmedetomidine infusion especially during loading dose administration as was seen in study by Bhagat N et al. [1] Current study also observed hypotension in 10% of the patients. Other minor side effects were nausea, vomiting, fever, chills, vomiting and sedation seen in the present study.

Conclusion

Dexmedetomidine infusion is effective in attenuating haemodynamic response to laryngoscopy, intubation, surgery and pneumoperitoneum. without significant complications. Though bradycardia and hypotension are common adverse event but most of the time they are self resolving.

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