A Clinical Study Of Dexmedetomidine For Maintenance During General Anaesthesia For Laparoscopic Surgeries

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ABSTRACT

Laparoscopic surgeries under general anesthesia are associated with unique hemodynamic changes in the form of increased systemic vascular resistance, leading to hypertension, forcing the anesthesiologist to increase the depth of anesthesia (DOA), and at times even requires the use of vasodilators to decrease raise in blood pressure, hampering the spirit of the day care surgery.

Pneumoperitoneum during laparoscopic surgeries affects several homeostatic systems leading to alterations in acid-base balance, cardiovascular physiology and stress response. The extent of cardiovascular changes associated with pneumoperitoneum include tachycardia, increase in mean arterial pressure, decrease in cardiac output and increase in systemic vascular resistance which in turn compromise tissue perfusion. Various antihypertensive drugs have been used . Dexmedtomidine(DEX) has recently been added to the anesthesia armamentorium. Dex due to its distinct properties can be used as an anesthetic adjuvant in the form of intravenous infusion .We studied the use of Dex in laparoscopic surgeries and evaluated its effects on stress response during laryngoscopy and intubation, hemodynamics, anesthetic and analgesic requirement and recovery profile.

Background
Dexmedetomidine(DEX) is a highly selective α_2 agonist with properties of sedation, analgesia and anxiolysis, making it an ideal anesthetic adjuvant. Using an anesthetic adjuvant that decreases requirement of anesthetics and analgesics may predispose the patient to awareness. In the earlier studies it was noted that Dex as an adjuvant maintains adequate depth of anesthesia and provides excellent recovery profile.

Keywords:Anesthetic adjuvant, Dexmedtomidine, laparoscopic surgery, Early recovery profile

Introduction

Now a days most of the abdominal surgical problems are being addressed by laparoscopic surgeries because of its dexterity, magnification,less morbidity, less convalescence and early discharge if not as early as day care

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surgery. But there are few problems with laparoscopy like it needs experience and technical expertise from surgeon's side and patient's problems like secondary effects of pneumoperitoneum (Intraoperative hypertension, increased systemic vascular resistance, hypercapnia, tachycardia, compromise in cardiac output and respiratory dynamics). Anesthesiologists have been waiting for adrug which can address above problems effectively. Dex can answer many of them but with its on inherent alfa 2 agonist problems like bradycardia and hypotension etc.

Dex possesses the properties of sedation, analgesia ,anxiolysis and opioid sparing effect with minimal respiratory depression

The purpose of the present study was to evaluate the effects of intravenous administration of DEX during general anesthesia for laparoscopic surgeries in minimizing the doseof induction agents,attenuating the hemodynamic response to laryngoscopy and intubation, intraoperative hemodynamic stability and minimising maintenance dose anesthetics and analgesics intraoperatively , recovery profile and early discharge criteria.

Materials and Methods

After approval of the Institutional Ethics Committee, fifty patients posted for elective laparoscopic surgery under general anesthesia were enrolled for the study. Inclusion criteria were: patients belonging to American Society of Anesthesiologists (ASA) grade I and II; aged between 18 to 50 years; of either sex; scheduled for laparoscopic surgeries like laparoscopic cholecystectomy and laparoscopic appendicectomy. Exclusion criteria were: patients with ASA grade III/IV; and contraindication to the use of Dex e.g. liver, renal or cardiac disorder , patients'denial and patients with any degree of heart block, pre-existing hypertension, allergies to the drugs used, or acute cholecystitis as well as pregnant ladies and lactating mothers were excluded from the study. Patients concomitantly taking clonidine, methyl-dopa, beta blocking

drugs, benzodiazepines, MAO inhibitors, patients in whom surgery could not be completed laparoscopically and open surgery had to be performed were also excluded from the study.

Patients were admitted one day prior to the scheduled surgery and examined, interviewed and written consent taken. No hypnotic medication was given. After pre-anesthetic checkup, written, valid and informed consent was taken from patients posted for laparoscopic surgery under general anesthesia foruse of study drug.

Two IV lines were secured : one for IV fluids and drugs and another for administering of dexmedetomidine. Dexmedetomidine was prepared in infusion syringe at 1mcg/ml.

Baseline monitors like electrocardiogram (ECG), pulse oximetry, noninvasive blood pressure (NIBP), Temperature were attached. ETco2 monitor was connected .Baseline values of heart rate (HR), saturation (SpO$_2$), blood pressure (BP) and ETCo2 were noted. Patients were premedicated with glycopyrrolate 4 mcg/kg, midazolam 0.03 mg/kg, inj. Butorphanol (0.01mg/kg) and ondansetron 4 mg intravenously (IV) and loading dose of DEX 1 Mcg/kg over 10minutes . Patients were induced with inj.Propofol 1mg/kg i.v until loss of eyelash reflex. Intubation was achieved with appropriate sized cuffed endotracheal tube with inj.vecuronium bromide 0.1mg/kg iv administered 3 minutes before intubation. Thereafter infusion was started 0.5mcg/kg/hr till the end of the procedure.50 mg of diclofenac sodium (aqeous)was added to intravenous fluids.

Patients were maintained with O2:N20 mixture of 40:60 connected toclosed circuit. Only few patients were given inhalational agent isoflurane when light plane of anesthesia, guided by hemodynamic parameters, was suspected.

Muscle relaxation was maintained with inj. Vecuronium bromide (0.02 mg/kg).At the end of

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the procedure, dexmedetomidine was discontinued.

At the end of surgery before the closing the ports 15 mlof 0.25% of bupivacaine was instilled in gallbladder bed/appendicular bed and 3ml injected around each port site.

Patients were reversed with inj .neostigmine 0.05mg/kgi.v . and inj . glycopyrolate 10mcg/kg i.v. Patients were extubated after adequate return of muscle power and protective reflexes.

Intraoperative monitoring was documented during the pre-induction, at the induction of anesthesia, during laryngoscopy and intubation, and at pneumoperitoneum and then every 15 min till the end of surgery and continued during extubation and post operatively. At the end of surgery, diclofenac sodium 50mg was added to the IV fluid for postoperative analgesia. Any side effects like hypotension, bradycardia, respiratory depression, postoperative nausea and vomiting were noted. Patients were observed in the recovery room for 2 hours before shifting to ward.

24 hrs after the completion of surgery, Patient were assessed for discharge criteria and recorded.

Results:

A total of fifty patients were enrolled in our study. Table 1 depicts the demographic data. Mean HR on starting was 81.76 which fell to lowest mean of 57.8; $P = 0.00$ [Figure 1]. There was a transient yet significant fall in HR at beginning of the Dex infusion. HR was however sustained for the entire duration of infusion. Patients had sinus bradycardia (HR < 60) at the start; but none required any therapy for treatment of this bradycardia. This reduction although statistically significant was not clinically relevant as no intervention was required. Mean MAP to start with was 79.92, and fell to 65.2 with loading dose of Dex ($P = 0.00$),which was minimally
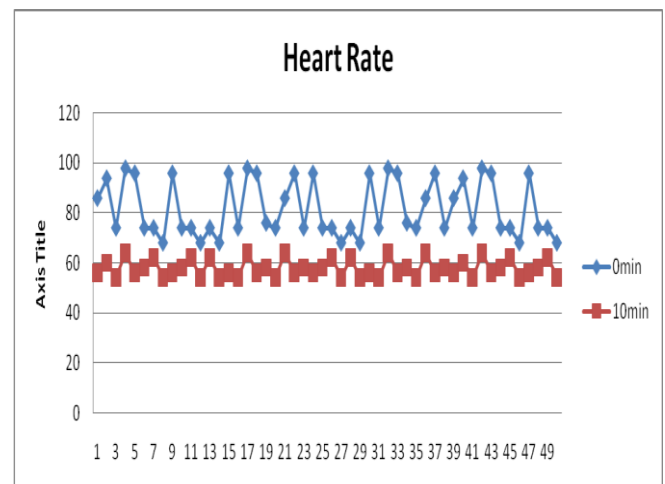
significant. After that minimal change was observed for entire duration of infusion. Similar observations were made at the time of creation of the pneumoperitoneum. [Figure 2]. There was good control over the vasopressor response during laryngoscopy, with minimal or no change in BP with pneumoperitoneum. None of the 50 patients needed either metoprolol or nitroglycerine to counter the hypertension effect of pneumoperitoneum as we conventionally practice in our institute for HTN surge.

		weight	Age
Male	24	62.7	27 +/- 5
Female	26	54.9	36 +/- 7

Table 1

Demographic data of the patients enrolled in the study

HEART RATE	MEAN	SD
O MINUTE	81.76	11.3
10 MINUTE	57.8	3.5

Figure 1

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Changes in heart rate of the patients as observed in the study

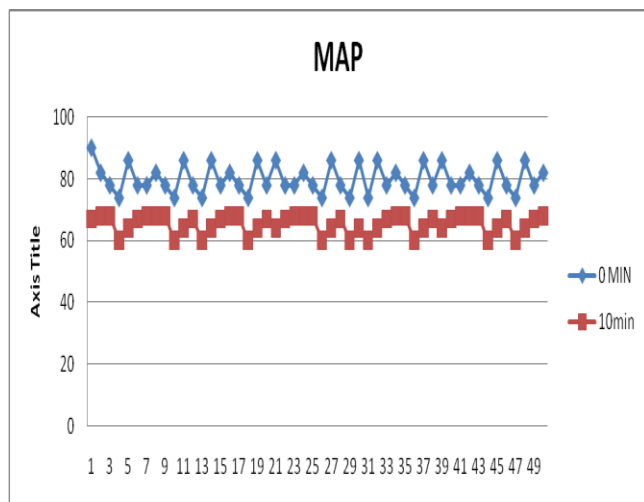| MAP	MEAN	SD
O MINUTE	79.92	4.52
10 MINUTE	65.2	3.04

Figure2

Changes in MAP of the patients as observed in the study

The mean dose of propofol required for induction was 37.5(5) mg.only 30%of the induction dose was required. The mean total requirement of Butorphanol in the entire intraoperative period was 500(8) mcg. We also studied that requirement of isoflurane to maintain stable BP only for 5 patients(10% of sample). It was observed that the end-tidal concentration of isoflurane required was between 0.5 to 0.75 all through the surgery; with peak requirement at the beginning immediately after intubation, and then again during creation of pneumoperitoneum. The end-tidal concentration of isoflurane as compared to the traditional requirement was observed to be almost 30% less with Dex in those 10% of the patients.

Extubation response was studied which appeared to be smooth in all patients with minimal change in hemodynamics. Patients showed immediate eye opening and were responsive to verbal commands indicating no residual effects of Dex. There was no difference in vecuronium requirement with the use of Dex. Patients were pain free in postoperative period. All patients were hemodynamically stable and comfortable in the recovery room. None of patients had postoperative nausea and vomiting (PONV), hypotension, bradycardia or episodes of respiratory depression and were shifted to the ward after two hours.

Discussion

Laparoscopic surgery offers intraoperative stress during pneumoperitoneum by increasing the systemic vascular resistance and blood pressure at the same time producing nociception.[2] Dex, an imidazole compound, displays specific and selective α_2 adrenergic receptor agonism.[4] In the past, xylazine and detomidine have been employed to induce analgesia and sedation in animals.[5] The unique properties of Dex render it suitable for analgesia during the perioperative period.[6] The major sedative and antinociceptive effects of Dex are attributable to its stimulation of α_2 A subtype located in locus coeruleus.[7] It is the specificity of dex for α_2 receptor that makes it a more effective sedative and analgesic agent than clonidine. Dex is eight times more specific for α_2 receptors than clonidine (α_2: α_1 ratio for dex is 1620:1 and that for clonidine is 220:1).

Dex potentiates anesthetic effects of all intraoperative anesthetics, regardless of the method of administration. The profound reduction in anesthetic requirement was shown to be mediated through central α_2 adrenergic receptors. Possible anesthetic effects also have been suggested in humans. IV and intramuscular administration has shown to reduce requirement of thiopentone by 17% in a group that receiving low dose Dex, and up to 30% in a group receiving high dose Dex.[8] We observed that Dex significantly reduces induction dose of propofol.

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When compare to the traditional induction dose of propofol (2 mg/kg), we observed a 62.5% reduction (0.75 mg/ kg) with the use of Dex. Dex also decreases and many times it avoids the requirement of inhalational agents. Routine end tidal concentration required for maintenance of anesthesia is 0.4%.[3] First report of reduced requirement of isoflurane with Dex in humans was published in 1991,[9] which showed a 25% reduction of maintenance and concentration of isoflurane in patients who received Dex. A 35-50% reduction of isoflurane requirement in patients treated with either low or high doses of isoflurane without premedication has been reported.[10] Similar observations regarding isoflurane requirement were made in our study.

Dex has been shown to attenuate the sympathoadrenal stimulation during intubation effectively.[11] We observed that Dex effectively attenuates the vasopressor response of laryngoscopy, and intubation and the sympathoadrenal response occurring with pneumoperitoneum. Analgesic properties have been demonstrated in studies that used Dex as a sole analgesic for minor surgeries.[12] Opioid requirements in the intra and post-operative period are reduced by Dex. The α_2 mechanism of action is involved in modulation of nociception at the level of spinal noradrenergic systems.[13] There is a clear evidence that α_2 receptors located in dorsal horn neurons of spinal cord might release endogenous opiate compounds.[14]. Dex has been shown to provide good hemodynamic stability. Dex maintained HR and BP during perioperative period including during laryngoscopy and pneumoperitoneum.

At clinically effective doses, Dex has been shown to cause much less respiratory depression than any other sedatives.[15] The danger of respiratory depression with sedative agents often necessitates their discontinuation well before extubation period; however, Dex infusion can be continued safely through extubation.[16] In our study, none of the 50 patients had episodes of respiratory depression in the post-operative period. Dex use permits lower doses of anesthetics to be used and decreases the opioid requirement, thus resulting in a more rapid recovery from anesthesia. Patients are able to return to the baseline level of consciousness when stimulated. This feature was shown by Hall *et al*. using bispectral index (BIS) monitoring system and other psychometric tests.[1] Studying Dex could invariably result in under-dosing the patient with anesthetics and analgesics, possibly resulting in inadequate DOA.

The only limitation of our study is the lack of a control group. Our intention was to observe the effects of Dex as an anesthetic adjuvant while maintaining the adequate anesthetic depth. We observed that Dex is a good anesthetic adjuvant that decreases the requirement of anesthetics and opioids, attenuates sympathoadrenal response, maintains the stable hemodynamics and adequate Depth of Anesthesia, and provides an excellent recovery profile.

Footnotes

Source of Support: Nil

Conflict of Interest: None declared.

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