Original Research Article

Comparison of intraoperative and postoperative analgesic efficacy of Fentanyl versus Dexmedetomidine as an adjuvant to epidural Ropivacaine in patients undergoing major abdominal surgeries: an observational study

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Received: 01-11-2020 / Revised: 30-12-2020 / Accepted: 18-01-2021

Abstract

Background: Epidural analgesia is a common method for the management of postoperative pain after major abdominal surgeries. The aim of the study was to compare the intraoperative and postoperative analgesic effect of dexmedetomidine and fentanyl as an adjuvant to epidural ropivacaine in adult patients undergoing major abdominal surgeries. **Materials & Methods:** This study included 80 patients between 25- 60 years age group of ASA class I- II scheduled to undergo elective major abdominal surgeries and classified randomly into two groups (each=40). Group D (Dexmedetomidine group): received 50 µg dexmedetomidine with 10 ml of 0.125% ropivacaine intraoperative over 10 mins after induction of general anesthesia followed by 2 ml (100 µg) dexmedetomidine mixed with 48 ml of 0.125% ropivacaine in a 50 ml syringe and infused epidurally at a rate of 5ml/hr for the postoperative 48 hours. Group F (fentanyl group): received 50 µg fentanyl with 10 ml of 0.125% ropivacaine intraoperative over 10 mins after induction of general anesthesia followed by 2 ml (100 µg) Fentanyl mixed with 48 ml of 0.125% ropivacaine in a 50 ml syringe and infused epidurally at a rate of 5ml/hr for the postoperative 48 hours. Patients were evaluated for rescue analgesic requirements (intraoperative fentanyl and postoperative tramadol, and diclofenac), hemodynamic stability, postoperative pain, sedation and any adverse events. **Results:** The quality of analgesia was better with dexmedetomidine than fentanyl group ($p<0.05$), and the requirement for rescue analgesia (intraoperative fentanyl and postoperative tramadol and diclofenac) was significantly lower with dexmedetomidine than fentanyl group ($p<0.05$). The incidence of motor block, sedation, bradycardia, hypotension and dry mouth was significantly higher with dexmedetomidine than fentanyl group ($p<0.05$). The incidence of nausea and vomiting, pruritis, urinary retention, and respiratory depression was significantly higher with fentanyl compared to dexmedetomidine group ($p<0.05$). **Conclusion:** Dexmedetomidine is an ideal adjuvant to epidural ropivacaine for postoperative analgesia compared to fentanyl in patients undergoing major abdominal surgeries.

Key words: Dexmedetomidine, fentanyl, epidural ropivacaine, major abdominal surgeries, adjuvants, postoperative pain, thoracic epidural

Introduction

Major abdominal surgeries are usually associated with large surgical incisions and extensive gut handling and manipulation, which increases the need for intraoperative and postoperative analgesia. Uncontrolled intraoperative and postoperative pain and pathophysiological response to surgery make these patients prone to high stress, sympathetic activation and slow convalescence, and may cause significant complications of many organ systems.[1] Improving the pain management techniques and rehabilitation programs has a significant impact on postoperative outcome.[2]

Thoracic epidural analgesia provides good perioperative pain relief and facilitates deep-breathing exercises and early ambulation postoperaively, also decreases the sympathetic outflow, preventing ileus and the incidence of postoperative myocardial infarction by providing favourable redistribution of coronary blood flow, attenuating the stress response and hypercoagulability.[3, 4] Although adjuvants like epidural opioids with and without local anesthetics provides a good intraoperative and postoperative pain relief, but it is associated with many side effects[5- 8] like pruritus, urinary retention, postoperative nausea and vomiting and respiratory depression.[9,10]

Recently α2-agonists have shown promise as an adjuvant to local anaesthetics in epidural anaesthesia.[11–14]

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Dexmedetomidine, a highly selective α2-adrenoreceptor agonist, has effective analgesic, antihypertensive and sympatholytic and sedative properties[15, 16] and lacks opioid-related side effects.[17, 18] It improves the quality of perioperative anesthesia and analgesia. A study comparing the analgesic efficacy of dexmedetomidine with fentanyl as an adjunct to ropivacaine in lumbar epidural in patients undergoing lower limb orthopaedic procedures under regional anaesthesia demonstrated that dexmedetomidine may be a better alternative to fentanyl as it provided early onset of sensory anaesthesia and prolonged postoperative analgesia.[19]

The aim of the present study was to compare the perioperative analgesic efficacy of dexmedetomidine and fentanyl as an adjuvant to continuous infusion of epidural ropivacaine in adult patients undergoing major abdominal surgery. The primary outcome of this study was to compare intraoperative and postoperative rescue analgesic requirements while the secondary outcomes were postoperative pain score, haemodynamic stability and adverse effects.

Materials & Methods

After receiving approval from our institutional ethics committee and obtaining written informed consent from the patients, this prospective, observational, randomized, double-blind controlled trial was conducted in 80 patients between 25-60 years age group of ASA class I–II, undergoing elective major abdominal surgery.

The exclusion criteria included patients with coagulopathy, cardiac conduction defects, renal or hepatic dysfunction, patients on beta-blockers or antipsychotic drugs, who refused the postoperative continuous infusion of analgesia, morbid obesity, high risk for postoperative nausea and vomiting (history of smoking, motion sickness or excessive postoperative vomiting) and patients with

hypersensitivity to bupivacaine, dexmedetomidine or fentanyl or any contraindication to epidural catheter insertion (local infection, spine deformities etc.)

80 patients between 25-60 years age group of ASA class I–II, scheduled to undergo elective major abdominal surgery were classified randomly (by simple randomization) into two groups (n=40 each): Group D (Dexmedetomidine group, n= 40): received 50 µg dexmedetomidine with 10 ml of 0.125% ropivacaine intraoperative over 10 mins after induction of general anesthesia followed by 2 ml (100 µg) dexmedetomidine mixed with 48 ml of 0.125% ropivacaine in a 50 ml syringe. The rate of epidural infusion through the syringe pump was 5ml/hr for the postoperative 48 hours.

Group F (Fentanyl group, n= 40): received 50 µg fentanyl with 10 ml of 0.125% ropivacaine intraoperative over 10 mins after induction of general anesthesia followed by 2 ml (100 µg) Fentanyl mixed with 48 ml of 0.125% ropivacaine in a 50 ml syringe. The rate of epidural infusion through, the syringe pump was 5ml/hr for the postoperative 48 hours. The intervention was discontinued if there were untolerated side effects of the study medications in the two groups.

Anaesthetic Procedure

The patients underwent preoperative anaesthesia assessment on the previous evening and were premedicated with alprazolam 0.25 mg and ranitidine 150 mg orally the evening before and at 6:00 am on the morning of surgery. On arrival to operating theatre routine monitors were attached and baseline readings of heart rate, non-invasive blood pressure (NIBP) and oxygen saturation (SpO2) were taken. Peripheral line secured with 18 G intravenous catheter and maintainance fluid started as per 4-2-1 formula. Under standard aseptic precautions a thoracic epidural catheter was placed at the T8–T9 or T9–T10 intervertebral space, with the patient in the sitting or lateral position with an 18-G Tuohy epidural needle via a midline approach with a loss of resistance technique. Epidural catheter passed through needle and fixed at around 12- 13 cm mark. An epidural test dose given with 3 ml of 2% lignocaine with 1:200 000 adrenaline to rule out Intrathecal or intravascular access. Catheter secured and patient positioned back for induction of general anesthesia.

Premedication given with glycopyrolate 20µg/ kg i.v and anaesthesia induced with morphine 0.1 mg/kg followed by propofol 2–3 mg/kg until loss of verbal response. Muscle relaxation was achieved with atracurium 0.5 mg/kg to facilitate endotracheal intubation. After confirming tube position by bilateral chest auscultation and sustained endtidal capnography tube secured and lungs were ventilated with positive pressure ventilation to maintain end-tidal carbon dioxide (EtCO2) between 32 and 36 mmHg. Anaesthesia was maintained by isoflurane 1- 1.2% with 50: 50% nitrous oxide in oxygen mixture. Intraoperative muscle relaxation was maintained with top-ups of atracurium 0.1 mg/kg. The epidural drug was administered according to the group allocation immediately after intubation over a period of 10 minutes.

Intraoperative analgesia maintained with morphine 0.1 mg/kg i.v given at the time of induction, acetaminophen 1 gm to all patients and epidural analgesia with 50 µg fentanyl or 50 µg dexmedetomidine with 10 ml of 0.125% ropivacaine as per group allocation. Intraoperative rescue analgesia given with fentanyl bolus and total fentanyl consumption monitored and compared in both groups.

Patient's heart rate, electrocardiography (ECG), SpO2, and EtCO2 were monitored continuously and blood pressure was taken at five minute intervals. The data were recorded every 5 minutes for the first 30 minutes and then every 15 minutes till completion of surgery.

Hypotension (MAP 20% below baseline) was treated with fluid bolus, and if required i.v. ephedrine 5 mg boluses. For bradycardia (heart rate of < 40 bpm) atropine 0.6 mg was administered intravenously. Antiemetic prophylaxis was given with ondansetron 0.15 mg/kg at the time of closure of the surgical wound. At the end of surgery residual neuromuscular blockade was reversed with neostigmine 60 µg/kg and glycopyrrolate 10 µg/kg and the endotracheal tube was removed after thorough endotracheal and oropharyngeal suctioning and when the patient starts breathing spontaneously and adequately. About 30 minutes before extubation epidural infusion of fentanyl or dexmedetomidine with 0.125% ropivacaine started @ 5ml/ hr as per group allocation. After surgery the patients were transferred to the Post Anesthesia Care Unit (PACU) and were monitored for 48 hours by an anaesthesia resident blinded to the patient's group allocation.

Postoperative hemodynamics, pain score and sedation level were assessed at 0 min, 30 min, 1hour, 6 hour, 12 hour, 18 hour, 24 hour, 36 hour and 48 hour.

The assessment of pain was done using modified visual analogue scale (VAS, 0–10, wherein 0 stands for 'no pain' and 10 stands for 'worst imaginable pain'). Postoperative rescue analgesia was managed with tramadol 100 mg and diclofenac 75mg in patient with VAS score > 4. The total amount of rescue drug required during 48 hours was noted.

Level of sedation was assessed using a modified observer's assessment of alertness/sedation (OAA/S) scale with a score of 1 = asleep/unrousable to 6 = awake/alert. [20]

All complications such as bradycardia, hypotension, hypoxia (SpO2<92) and respiratory depression (respiratory rate < 8) were noted and promptly corrected. Other postoperative adverse events like nausea, vomiting, pruritus and urinary retention were also recorded and treated accordingly. Postoperative nausea and vomiting (PONV) was treated by ondansetron 0.15 mg/kg i.v and pruritus was treated with iv diphenhydramine 0.2 mg/kg.

Statistical Analysis

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Statistical software SPSS (version 20.0) and Microsoft Excel were used to carry out the statistical analysis of data. Continuous variables were expressed as Mean ± SD and categorical variables were summarized as frequencies and percentages. Graphically the data was presented by bar and line diagrams. Student's independent t –test was employed for comparing continuous variables Chi-square test or Fisher's exact test, which ever appropriate, was applied for comparing categorical variables. A p value of <0.05 was considered statistically significant.

Results

There was no statistical difference regarding the demographic data, ASA class, and duration of surgery (p>0.05) (Table 1).

Table 1 Demographic data, ASA class, and duration of surgery

Variables	**Group D** (n = 40) (mean ± SD)	**Group F** (n = 40) (mean ± SD)	p- value
Age (years)	35.45 ± 10.00	38.75 ± 12.09	0.440
Weight (kg)	54.85 ± 8.56	55.45 ± 8.32	0.481
Height (cm)	157.75 ± 6.22	156.10 ± 8.51	0.525
Gender (Male: Female)	29: 11	27: 13	0.468
ASA class (I: II)	14: 26	11: 29	0.545
Duration of surgery (min)	188.25 ± 9.182	186.9 ± 8.117	0.178

The number of patients with a VAS score > 4 were significantly higher in fentanyl than dexmedetomidine group, (p<0.05). No significant difference in intraoperative rescue analgesic (fentanyl) requirement seen between two groups, (p>0.05). However, the number of patients

requiring postoperative rescue analgesia (tramadol and diclofenac), was significantly lower in dexmedetomidine than fentanyl group ($p<0.05$). The incidence of sedation was higher in the dexmedetomidine group than the fentanyl group ($p<0.05$). (Table 2)
Table 3 Intraoperative clinical data.

Table 2 Postoperative VAS score, rescue analgesia requirement, sedation score

Variables	Group D (n = 40)	Group F (n = 40)	p- value
VAS score > 4	8	23	0.001
Rescue analgesia			
Intraoperative fentanyl	1	2	>0.05
Postoperative tramadol and diclofenac	6	23	<0.05
Sedation score > 3	28	5	<0.05

The heart rate and mean arterial blood pressure decreased in both groups, but the decrease was more in patients of dexmedetomidine group than fentanyl group and the comparison was significant between the two groups ($p<0.05$). (Figure 1 and 2)
The incidence of side effect such as bradycardia, hypotension, and dry mouth was higher in the dexmedetomidine group compared to fentanyl group ($p<0.05$). But the side effect such as nausea and vomiting, pruritis, urinary retention, and respiratory depression were significantly higher in the fentanyl group compared to dexmedetomidine group ($p<0.05$). (Table 3).

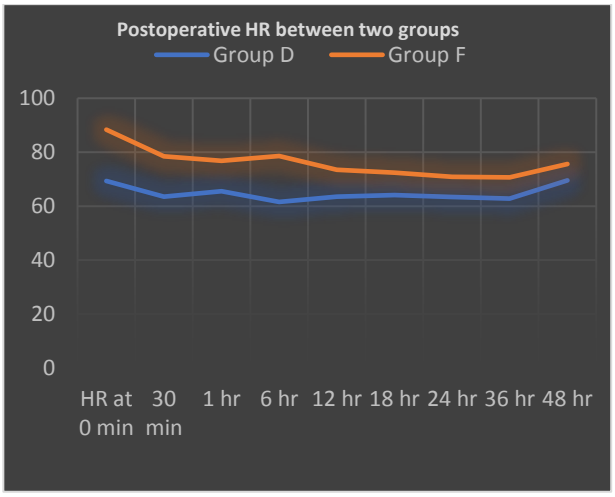

Figure 1 Postoperative HR between two groups

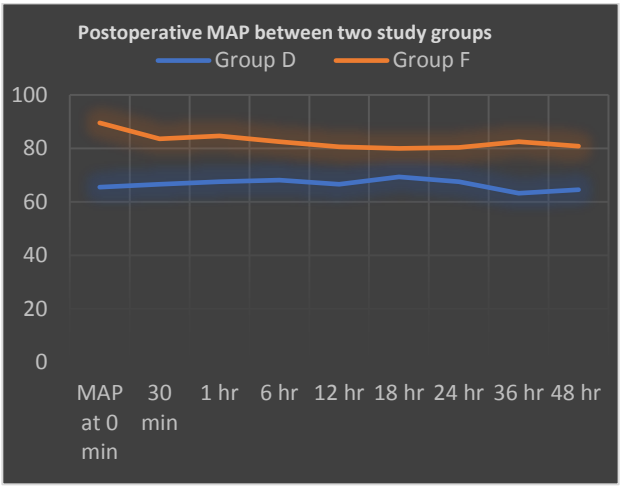

Figure 2 Postoperative MAP between two groups

Table 3 Complications of the epidural dexmedetomidine and fentanyl

Complications	Group D (n= 40)	Group F (n=40)	P-value
Dry mouth	31	11	0.001
Nausea and vomiting	8	22	0.001
Pruritis	0	23	0.001
Respiratory depression	0	12	0.001
Urine retention	0	14	0.001

Discussion

In the present study, we found that addition of dexmedetomidine to epidural ropivacaine provided effective intraoperative as well as postoperative analgesia comparable to fentanyl. There was no significant difference in intraoperative fentanyl requirement between the two groups. The postoperative pain scores were comparable among groups at all-time intervals during the 48-hour postoperative period with lesser requirement for rescue analgesia in the dexmedetomidine group. Our results are similar to the previous study by Selim et al.,[21] which also reported comparable VAS scores in patients receiving dexmedetomidine and fentanyl (1 μg/kg each) for labour analgesia with greater patient satisfaction in the dexmedetomidine group.

Eskandar et al.,[22] assessed the postoperative effect of dexmedetomidine as an adjuvant to bupivacaine for 48 hours after total knee arthroplasty. They found that the visual analogue scale and the total dose of nalbuphine decreased significantly in the dexmedetomidine group compared to the control group.

Bajwa et al.,[19], evaluated the addition of dexmedetomidine or fentanyl to epidural ropivacaine in patients undergoing lower limb orthopedic surgeries and they found that the postoperative analgesia was prolonged significantly in the dexmedetomidine group and consequently the low dose consumption of local anesthetic was used in dexmedetomidine group, and the same result was shown by other studies.[23-26]

The analgesic effect of dexmedetomidine is mediated by its action at the brain, brainstem, spinal cord and peripheral tissues.[27] Dexmedetomidine causes hyperpolarisation of nerve tissues by altering transmembrane action potential and ion conductance at the brainstem locus ceruleus. In the spinal cord, the analgesic effect is related to the activation of the descending medullospinal noradrenergic pathway or to the reduction of spinal sympathetic outflow at presynaptic ganglionic sites. Epidural opioids have their major site of action on pre- and postsynaptic receptors in the substantia gelatinosa of the dorsal horn, producing selective block of nociceptive pathways.

The present study showed that the heart rate and the mean arterial blood pressure decreased with dexmedetomidine compared with fentanyl. These findings correlate with the result of other studies and the decrease in heart rate and mean arterial blood pressure can be explained by the central action of dexmedetomidine in decreasing the sympathetic outflow and catecholamines release.[28, 29]

Eskandar et al.,[22] found that the heart rate decreased significantly with dexmedetomidine, but the mean arterial blood pressure decreased significantly in the control group compared to dexmedetomidine.

Kaur et al.,[23] found that no significant changes in the heart rate and blood pressure by adding dexmedetomidine as an adjuvant to ropivacaine compared to the control group and the same result was shown by other studies.[24,30-32]

The incidence of side effects such as bradycardia, hypotension, and dry mouth was higher in the dexmedetomidine group compared to fentanyl group.

Bajwa et al.,[19] found that no difference in the incidence of bradycardia or hypotension between epidural fentanyl and dexmedetomidine to ropivacaine, but the dry mouth was associated with dexmedetomidine more than fentanyl.

Thimmappa et al.,[33] showed that the addition of dexmedetomidine to epidural ropivacaine was associated with significant bradycardia compared to clonidine and control group.

The incidence of sedation was higher in dexmedetomidine compared to fentanyl group, Eskandar et al.,[22] showed the same result in spite of the required nalbuphine was higher in the control group.

The side effects such as nausea and vomiting, pruritis, urinary retention, and respiratory depression were significantly lower in the dexmedetomidine group compared to fentanyl group and a similar result was shown by Gupta et al.[24]

Conclusion

From our study we concluded that dexmedetomidine is an ideal adjuvant to epidural ropivacaine for perioperative analgesia compared to fentanyl in patients undergoing major abdominal surgeries. Dexmedetomidine provides a better perioperative analgesia and reduces the postoperative rescue analgesic requirements and complications associated with opioids such as nausea and vomiting, pruritis, urinary retention, and respiratory depression compared to fentanyl. But the epidural dexmedetomidine is associated with a higher incidence of bradycardia, hypotension, and dry mouth compared to epidural fentanyl.

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Conflict of Interest: Nil Source of support: Nil