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COMPARISION OF FENTANYL AND DEXMEDETOMIDINE AS ADJUVANT TO BUPIVACAINE FOR EPIDURAL ANALGESIA IN LOWER LIMB ORTHOPEDIC SURGERY

Anesthesiology

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ABSTRACT

Background: Adjuvants are often used with local anesthetics for its synergistic effect by prolonging the duration of sensory-motor block and limiting the cumulative dose requirement of local anesthetics. Opioids have been in use for a long time and alpha agonist are being increasingly used for same.
Aim: The aim of this study was to compare the hemodynamic, sedative and analgesic effects of epidurally administered fentanyl with bupivacaine and dexmedetomidine with bupivacaine.
Methods: In this study a total of 100 patients with ASA grade 1 and 2 of either sex age between 20 and 60 years scheduled for lower limb orthopaedic surgery under epidural block were randomly divided into 2 groups(n=50) group BF and group BD. after epidural block with 15ml of 0.5% plain bupivacaine, group BF received 1 microgram/kg of fentanyl and group BD received 1 microgram/kg of dexmedetomidine. Besides cardiorespiratory parameters, sedation scores, onset and duration of sensory block, motor block, and time to request for the first rescue analgesia were recorded. The statistical analysis was performed using SPSS version 15, student t test, chi square test. Value of $p<0.05$ is considered significant.
Results: The demographic profile of patients was comparable in both the groups. Onset of sensory analgesia at T10 (7.84 ± 1.02 min vs10.22 ± 2.94 min) and time to maximum sensory block level (13.32 ± 1.34min vs 18.8 ± 1.58min) was earlier in group BD as compare to group BF. Sedation scores were much better in the BD group and Postoperative analgesia was prolonged significantly in the BD group (328.28±28.14min). In Group BD the majority of patients required less rescue doses than group BF.
Conclusions: Dexmedetomidine seems to be a better alternative to fentanyl as an epidural adjuvant as it provides comparable stable hemodynamics, early onset of sensory anesthesia, prolonged post-op analgesia, lower consumption of post-op LA for epidural analgesia, and much better sedation levels.

KEYWORDS

Bupivacaine, dexmedetomidine, epidural, fentanyl.

INTRODUCTION

Epidural anesthesia is the most commonly used technique for providing not only peri-operative surgical anesthesia but post-op analgesia in lower abdominal and limb surgeries [1]. Early postoperative mobilization and rehabilitation with minimally associated pain and discomfort is the most desirable feature in modern orthopaedic surgery. Many a time for achieving desired peri-operative anaesthetic effect, invariably large volumes of local anaesthetics are used, thereby increasing the possibilities of local anaesthetic toxicity and deleterious haemodynamic consequences. Evidence suggests that less than half of patients who undergo surgery report adequate postoperative pain relief [2]. Inadequately controlled pain negatively affects quality of life, function, and functional recovery, the risk of postsurgical complications, and the risk of persistent postsurgical pain. Opioids like fentanyl have been used traditionally as an adjunct for epidural administration in combination with a lower dose of local anaesthetic to achieve the desired anaesthetic effect [3]. The addition of opioid does provide a dose sparing effect of local anaesthetic and superior analgesia but there is always a possibility of an increased incidence of pruritis, urinary retention, nausea, vomiting and respiratory depression [4]. Also the incidence of motor block after epidural analgesia with amide local anesthetics (LA) and opioids is approximately 4-12% which itself defeats the novel purpose of early rehabilitation.

Dexmedetomidine is a new addition to the class of alpha-2 agonist which has got numerous beneficial effects when used through epidural route. It acts on both pre and post synaptic sympathetic nerve terminal and central nervous system thereby decreasing the sympathetic outflow and nor-epinephrine release causing sedative, anti-anxiety, analgesic, sympatholytic and haemodynamic effects.

Dexmedetomidine does cause a manageable hypotension and bradycardia but the striking feature of this drug is the lack of opioid-related side effects like respiratory depression, pruritis, nausea, and vomiting.[5]

Keeping the benefits of epidural adjunct to bupivacaine in consideration, our study is designed to compare the fentanyl versus dexmedetomidine in combination with bupivacaine for postoperative analgesia in orthopedic surgery.

METHODS

After obtaining the research ethics committee approval and the informed and written consent, 100 patients of both genders, aged 20–60 years, American Society of Anaesthesiologist (ASA) I and II who underwent lower limb orthopedic surgery, were enrolled into the present study. Patients with diabetes mellitus, cardiac disease, hypertension, chronic obstructive respiratory disease, coagulation abnormalities, spinal deformities, and patients allergic to amide type of local anesthetics were excluded from the study. Patients were divided randomly into two groups: Group Bupivacaine+Dexmedetomidine (BD) and Group Bupivacaine+Fentanyl (BF), comprising of 50 patients each. The patients visited before surgery for preanesthetic check, and standard institutional preoperative advices were given. The patients were asked nil per oral for solid food for 8 h and clear liquids for 2 h before surgery. On the day of surgery, the patients were wheeled in operation theater, and noninvasive monitors such as pulse oximeter, noninvasive blood pressure (NIBP), and ECG were attached, and baseline parameters were recorded. Intravenous (IV) access was secured and fluid was started.

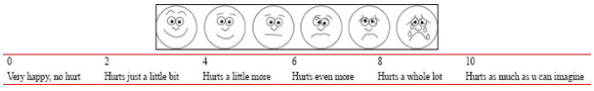
The patients were made to sit and under strict aseptic precautions, 18G Tuohy's needle was inserted into L_2–L_3 interspinous epidural space. Epidural space was confirmed by loss of resistance method and epidural catheter was threaded 3–4 cm inside the epidural space and fixed, after institution of test dose (3 ml injection lidocaine 0.2% with adrenaline). The study solutions were prepared by an anesthesia technician who was given written instructions and was unaware of the study design. The following solutions were randomly administered: 15 ml of 0.5% bupivacaine associated to 1 μg/kg of dexmedetomidine in group RD (n=50) and 1 μg/kg of fentanyl in group RF (n=50) .

Hemodynamic parameters were recorded at baseline (T0), immediately after the study drug is given (T_1), every 5 min thereafter till 15 min, and then every 15 min thereafter till end of surgery and postoperatively till demand of first rescue analgesic. Patients with block failure and having surgeries lasting longer than 2 h were excluded from the study. After completion of surgery, the patients were shifted to the postoperative ward; hemodynamic parameters and duration of analgesia were recorded in postoperative period at every 30 min interval. Pain was assessed using 10-point visual analog scale (VAS) in which a score of "0" indicated "no pain" and a score of "10" indicated "worst pain imaginable." Duration of analgesia was recorded as the first complaint of pain (VAS >4) in the postoperative period and rescue analgesic was administered. Rescue analgesic as 10 ml 0.25% bupivacaine was administered at the onset of pain (VAS >4) in postoperative period and at each incidence of complaint of pain (VAS

>4) in next 24 h. The number of rescue analgesic epidural doses was recorded during the first 24 h. Sedation was also assessed at intervals of 20 minutes intra-operatively and at intervals of 1 hour during post-op period using subjective sedation scale (Grade 0=awake, conscious, no sedation, to slightly restless; Grade 1=calm and compose; Grade 2=awake on verbal command; Grade 3=awake on gentle tactile stimulation; Grade 4=awake on vigorous shaking; Grade 5= unarousable). Motor blockade was assessed using modified Bromage scale (0=no block, 1=inability to raise extended leg, 2=inability to flex knee and 3=inability to flex ankle and foot) before surgery and at regular intervals of 1 hour post-operatively.

VAS, vomiting, shivering, sedation, hypotension, pruritus, and urinary retention were documented and managed.

- Hypotension (defined by decrease in MAP below 20% of baseline or systolic blood pressure (SBP) (<90 mmHg)) was treated by injection mephentermine 6 mg boluses
- Bradycardia (heart rate [HR] <50 bpm) was treated by atropine 0.6 mg IV
- Respiratory depression (relative risk <8 breaths per min or SpO_2 <95%) was treated by oxygen supplementation and respiratory support if required
- Nausea and vomiting were treated with injection ondansetron 0.1 mg/kg IV.



Statistical tools employed

The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 15.0 Statistical Analysis Software. The values were represented in number (%) and mean ± standard deviation. To test the significance of two means, the student "t"-test was used, Mann–Whitney U-test was performed for nonparametric data, Chi-square test was used for categorical outcome and Fisher's exact test for sedation and analgesia. Value of P<0.05 was considered significant and P<0.001 as highly significant. The confidence level of the study was 95%.

RESULTS

A total of 100 patients who underwent lower limb surgery were enrolled for the study and were randomly divided into two groups. The demographic characteristics in both the groups exhibited marked similarities and did not show any statistical significant difference (*P*>0.05) [Table 1]

Table 1: Demographic profile of the patients of both the groups

Demographic characterstics	BF	BD	P value
Age(years)	33.74 ± 9.13	35.10 ± 9.17	0.45
Weight(kg)	65.36 ± 9.54	67.48 ± 7.42	0.21
Body mass index	23.86 ± 4.24	22.48 ± 4.19	0.10
Male/female	42/8	38/12	0.81

The onset of analgesia at T10 dermatomal level was significantly earlier in the BD group (7.84±1.02) as compared to the BF group (10.22±2.94). (P=<0.0001) The other early block characteristics also exhibited similar results as dexmedetomidine not only provided a higher dermatomal spread but also helped in achieving the maximum sensory anaesthetic level in a shorter period (13.32±1.34) as compared to Fentanyl (18.8±1.58). (P=<0.0001) Motor block was assessed using modified Bromage scale and complete motor block was achieved significantly earlier in the (17.10±1.43) patients who were administered dexmedetomidine as compared to BF group (23.65±1.55). (P=< 0.0001). [Table 2]

Table 2: The comparison of initial block characteristics in both the groups

Initial block characteristics	Group BF	Group BD	P value
Onset time of sensory block at T10 (in minutes)	10.22 ± 2.94	7.84 ± 1.02	< .0001
Maximum sensory block level	T5-T7	T4-T6	------
Time to maximum sensory block level (in minutes)	18.8 ± 1.58	13.32 ± 1.34	< .0001
Time in minutes for complete motor block	23.65 ± 1.55	17.10 ± 1.43	< .0001

Dexmedetomidine has gained a lot of popularity as a sedative agent and similar findings were observed in our study as 38% and 42% of patients exhibited grade II and grade III sedation as compared to 16% and 2% of patients in the BF group, respectively. These sedation scores were highly significant on statistical comparison (*P*<0.001). Only 16% of the patients in the BD group had sedation scores of 1 as compared to 82% wide and awake patients in BF group which was a highly significant statistical entity (*P*<0.001). [Table 3]

Table 3: The comparison of intra-operative sedation scores in patients of both the groups

Sedation scores during surgery	Group BF No. of patients (%)	Group BD No. of patients (%)	P value
1	41 (82)	8 (16)	<0.001
2	8 (16)	19 (38)	<0.001
3	1 (2)	21 (42)	<0.001
4	0	2	---
5	0	0	---

The finding of Table 4 reveals statistically significant values on comparison of post-operative block characteristics among the two groups. Though both the adjuvants provided a smooth and prolonged post-operative analgesia but the effects of dexmedetomidine were more significant on statistical comparison as compared to fentanyl. The evidence was very much visible in the prolonged time to two segmental dermatomal regression (140.32±10.21 in BD vs 110.84±9.48 in BF) (*P*=0.001) as well as earlier return of motor power to Bromage I in the BF group (178.5±23.29) as compared to BD group patients (259.62±21.38) (*P*=0.001). As a result, the time for rescue analgesia was comparatively shorter (242.16±23.86) in the patients who were administered fentanyl as compared to BD group who experienced prolonged pain free period (366.62±24.42) (*P*=0.001). [Table 4]

Table 4: The comparison of post-op block characteristics in both the groups

Post op block characteristics (in minutes)	Group BF	Group BD	P value
Mean time to two segmental regression	110.84 ±9.48	140.32±10.21	.001
Mean time for regression to bromage 1	178.5±23.29	259.6±21.38	.001
Mean time to sensory regression at S1	204.64±26.38	328.28±28.14	.001
Time to 1st rescue top up	242.16±23.86	366.62±24.42	.001

DISCUSSION

In recent years, use of adjuvants during epidural anesthesia has gained popularity with the aim of prolonging the duration of block, better success rate, patient satisfaction, decreased resource utilization compared with general anesthesia, and faster recovery.

The common problem during infraumblical and lower abdominal surgeries under regional anesthesia is visceral pain, nausea, and vomiting. The addition of fentanyl to hyperbaric bupivacaine improves the quality of intraoperative and early postoperative block. The addition of opioid provides a dose-sparing effect of local anesthetic and superior analgesia, but there is always a possibility of an increased incidence of pruritus, urinary retention, nausea, vomiting, and respiratory depression [4].

Dexmedetomidine is a new addition to the class of α_2 agonist which has got numerous beneficial effects when used through epidural route. It acts on both pre- and post-synaptic sympathetic nerve terminal and central nervous system, thereby decreasing the sympathetic outflow and norepinephrine release causing sedative, antianxiety, analgesic, sympatholytic, and hemodynamic effects. Dexmedetomidine causes a manageable hypotension and bradycardia, but the striking feature of this drug is the lack of opioid-related side effects such as respiratory depression, pruritus, nausea, and vomiting [6]. Both dexmedetomidine (α_2 agonist) and fentanyl (opioid) are being used as adjunct with bupivacaine to increase duration of regional anesthesia.

Multimodal analgesia is a pharmacologic method of pain management which combines various groups of medications for pain relief such as local anesthetics, opioids, NSAIDs, and α^2 agonists. It has been seen that dexmedetomidine has been used successfully as part of a

multimodal analgesic plan and can be an alternative choice for opioid-tolerant patients [7].

With this background, the present study was carried out with an aim to evaluate the efficacy of epidural dexmedetomidine with bupivacaine versus epidural fentanyl with bupivacaine for pain relief.

For this purpose, a randomized controlled trial was carried out in which a total of 100 patients with ASA physical status classes I and II scheduled to undergo elective lower limb orthopedic surgery aged 20–60 years were enrolled in the study and were randomly allocated to one of the two study groups – Group BD (n = 50) received 15 ml of 0.5% bupivacaine with 1 μg/kg injection dexmedetomidine epidurally and Group BF (n = 50) received 15 ml of 0.5% bupivacaine with 1 μg/kg of injection fentanyl epidurally.

The demographic profile in the present study was comparable to similar other studies and did not show any significant difference on statistical comparison.

At baseline, the hemodynamic parameters were within normal limits and matched statistically between the two groups. Thus, the two study groups showed a statistical matching for all the demographic, clinical, and hemodynamic parameters and did not show the presence of any confounding factor.

Hemodynamic stability was one of the most remarkable features observed with addition of dexmedetomidine and fentanyl to epidural bupivacaine. Decrease in heart rate is a known clinical effect of opioids but in the present study similar negative chronotropic effect was exhibited by dexmedetomidine approximately 30–35 minutes after the epidural injection of the drugs. Thereafter, the heart rate remained stable in the range of 56–70/min in both the groups. Similarly, mean arterial pressure (MAP) decreased from the baseline in both the groups with a maximum decline of MAP at 30-50 minutes after the epidural injection but it never went below 65 mmHg . Postoperatively, HR and MAP remained stable in both the groups. The decrease in HR caused by α-2 agonist can again be explained on the basis of their central action whereby they decrease sympathetic outflow and nor-epinephrine release.[5] The requirement of vasopressors for maintenance of stable hemodynamic parameters did not reveal any significant difference between both the groups on statistical comparison. The stable hemodynamics can possibly be explained on the basis of lower volume of local anesthetics used and a suitable selection of the dose of adjuvant.

Compared to the present study, Prakash *et al.*[8] also found significant difference in HR among placebo, fentanyl, and dexmedetomidine group with dexmedetomidine group having minimum mean values as compared to other two groups. The difference between two studies could be owing to difference in drug interactions owing to different combinations of drugs being used. In the present study, 0.5% bupivacaine was used as the primary drug with 1 μg/kg dexmedetomidine or 1 μg/kg fentanyl, respectively, whereas Prakash *et al.* used 0.25% bupivacaine as the principal drug with same dose of dexmedetomidine or fentanyl as the adjuvants.

The findings in the present study in general are in accordance with the findings in literature. Gupta *et al*.[9] in their study found dexmedetomidine to offer a better hemodynamic stability as compared to fentanyl in their study which is similar to the findings made in present study. Hanoura *et al.*[10] in their study also indicated statistically no significant difference between fentanyl and dexmedetomidine groups with respect to hemodynamic stability.

In the present study, onset of sensory block was considered to be at T_{10} and the time to reach peak sensory level was significantly (P=0.0001) shorter in group BD (13.32 ± 1.34) as compared to group BF (18.8 ± 1.58) as equally was the strikingly significant difference between the two groups regarding onset of sensory analgesia at T10 dermatomal level group BD (7.84 ± 1.02) and group BF(10.22 ± 2.94). Throughout the surgery, patients were calm and compose in both the groups but sedation scores were better in a highly significant manner in the BD group as 38% and 42% of patients had grade II and III sedation scores during the peri operative period as compared to 16% and 2% of patients in the BF group. The sedative properties of dexmedetomidine are far superior to fentanyl as no patient required any other sedative during the peri-operative period. None of the patients in either of the group required any additional epidural top-up dose during the surgical period. The analgesia was assessed using visual analogue scale (VAS) and patients in both the groups showed 0 scores during the entire surgical period. In our study, remarkable synergistic properties of LA and dexmedetomidine have come to the fore. Not only we were able to decrease the dose of local anesthetic in both the groups but also the duration of post-operative analgesia was significantly prolonged in patients in whom dexmedetomidine was administered as adjuvant with LA. Bromage scale 3 was achieved in all the patients before the initiation of surgical procedure. The return of complete motor recovery was significantly earlier in the BD group as compared to BF group. Post-operatively, the number of analgesic top-up doses of bupivacaine in group BD was significantly lower than the requirement for bupivacaine in group BF. In the present study with respect to motor block too, time of onset and time taken to achieve complete motor block were shorter in dexmedetomidine group as compared to that in fentanyl group, and this difference was significant statistically too. Gill *et al.* [11] also recorded lower 24 h analgesic need in dexmedetomidine as compared to fentanyl group. Similar observations were also made by Gupta *et al.* [9]. Thus, as far as analgesic effect is concerned, the findings in the present study are in accordance with the empirical observations.

The findings in the present study showed that dexmedetomidine is a safe, complication-free, and hemodynamically stable drug that can be used as adjuvant in epidural anesthesia with similar safety profile as for fentanyl but with a relatively better analgesic profile. The findings showed that with the drug-dose schedule used in the present study, the side effects were well under control, and hemodynamic stability was maintained for both the adjuvants.

CONCLUSION

Dexmedetomidine seems to be a better alternative to fentanyl as an epidural adjuvant as it provides comparable stable hemodynamics, early onset and establishment of sensory anesthesia, prolonged post-op analgesia, lower consumption of post-op LA for epidural analgesia, and much better sedation levels.

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