ORIGINAL RESEARCH PAPER

Volume-7 | Issue-3 | March-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

COMPARISON OF EPIDURAL DEXMEDETOMIDINE AND TRAMADOL AS ADJUVANTS TO BUPIVACAINE IN THE LOWER LIMB SURGERY : A RANDOMIZED CLINICAL STUDY

Anaesthesiology

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ABSTRACT

Background and Aims: Various opioids, α-2agonists, magnesium sulphate, neostigmine are used as adjuvants with local anesthestic in epidural space. The present study aims at comparing the efficacy of epidurally administered dexmedetomidine& tramadol when combined with bupivacaine.

Methods: A total of 60 patients of both gender aged 18-60 years, ASA physical status I and II who underwent lower limb orthopaedic surgery were enrolled into the present study. Patients were randomly divided into two groups: Bupivacaine + Dexmedetomidine(BD) and Bupivacaine + Tramadol (BT), comprising 30 patients each. Inj. Bupivacaine12 ml of 0.5% was administered epidurally in both the groups with addition of1 µg/kg of dexmedetomidine in BD group and 1 mg/kg of tramadol in BT group diluted to 3cc with total volume of study drug of 15ml. Besides cardio-respiratory parameters and sedation scores, various block characteristics were also observed which included time to onset of analgesia at T10, maximum sensory analgesic level, time to complete motor blockade, time to two segmental dermatomal regressions, and time to first rescue analgesic. At the end of study, data was compiled & analysed using ANOVA with post-hoc significance, Chi-square test and Fisher's exact test. Value of $P<0.05$ is considered significant.

Results: Demographic data was comparable in both groups. Onset of sensory analgesia at T10 (7.22±1.86 vs 10.02±2.26) and establishment of complete motor blockade (19.02±3.34 vs 23.45±5.65) was significantly earlier in the BD group. Postoperative analgesia was prolonged significantly in the BD group (355.88±14.52). Sedation scores were much better in the BD group and highly significant on statistical comparison ($P<0.001$).

Conclusions: Dexmedetomidine seems to be a better alternative to tramadol as an epidural adjuvant as it provides early onset, and establishment of sensory anaesthesia, prolonged post-operative analgesia and much better sedation levels.

KEYWORDS

Tramadol, Dexmedetomidine, Bupivacaine, Epidural anaesthesia, Lower limb surgery.

INTRODUCTION

The most common and anticipated problem during & following surgery is pain. Regional anesthesia with poly-pharmacological approach is a safe technique & common practice with the advantage of intra-operative anesthesia & prolonged post-operative analgesia. Epidural anesthesia is the most commonly used technique for providing not only peri-operative surgical anesthesia but post-operative analgesia in lower abdominal and lower limb surgeries.[1]Early postoperative mobilization and rehabilitation with minimally associated pain and discomfort is the most desirable feature in modern orthopaedic surgery.[2-4] Many time for achieving desired peri-operative anesthetic effect, invariably large volumes of local anesthetic are used, thereby increasing the possibilities of local anesthetic toxicity and deleterious hemodynamic consequences. The most commonly preferred amide local anesthetic 0.5% bupivacaine has longer duration of action.[5,6]Various adjuvants are used in regional anesthesia to enhance and prolong local anesthesia. Narcotic analgesics are commonly used as adjuncts to local anesthetics (LA) in epidural anesthesia. Opioids like tramadol have been used traditionally as an adjunct for epidural administration in combination with a lower dose of local anesthetic to achieve the desired anesthetic effect.[7] The addition of opioid does provide a dose sparing effect of local anesthetic and superior analgesia but there is always a possibility of an increased incidence of pruritis, urinary retention, nausea, vomiting and respiratory depression.[8,9] Dexmedetomidine is a new addition to the class of alpha-2agonist which has got numerous beneficial effects when used through epidural route.[10] It acts on both pre and postsynaptic sympathetic nerve terminal and central nervous system thereby decreasing the sympathetic outflow and nor-epinephrine release causing sedative, anti-anxiety, analgesic, sympatholytic and hemodynamic effects.[11-13]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.[14-15]

METHODS

The study was initiated after approval by Institutional Ethical Committee. It was prospective, randomized, double-blind study. Informed consent was obtained from all the patients who were a part of this study. All the patients with significant systemic illness, with history of spine surgery or presence of infectious focus on the back, refusal for epidural anaesthesia, allergy to local anaesthestics were excluded from the study and only ASA I and II patients were included in the study. None of the patients had any contraindications to epidural anaesthesia [5]. The study was conducted in 60 patients, aged 18-55 years, height between 150-170cms & who were scheduled for lower limb surgeries from February 2017 to December 2017 at McGann Hospital Shimoga. Using a computer generated random number table, patients were enrolled into 2 groups.

Group BD-Bupivacaine+Dexmedetomidine
Group BT-Bupivacaine+Tramadol

comprising of 30 patients each. All patients were pre-medicated with oral alprazolam 0.25 mg a night before and oral ranitidine 150mg half an hour before the surgery. Patients were thoroughly counseled during the pre-operative evaluation and were properly explained about the nature of study before taking the written consent. In the operation theatre, a good venous access was secured with 18G cannula and all the patients were pre-hydrated with 15ml/kg of lactated Ringer's solution. All the baseline parameters were observed and recorded which consisted of electrocardiography (ECG), heart rate (HR), non-invasive blood pressure (NIBP), and pulse oximetry (SpO2). Lumbar epidural anesthesia was induced using 18GTuohy needle- Portex Continuous Epidural (Smith Med. Inc.) with patients in the sitting position in L3-L4interspace and location of epidural space was confirmed by loss of resistance technique. A test dose of 3 ml of 2% lignocaine with adrenaline was administered into epidural space and thereafter epidural catheter was secured 4-5 cm into the epidural space and patients were placed supine. 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: 12 ml of 0.5% bupivacaine associated to1 µg/kg of dexmedetomidine in group BD (n=30) and1 mg/kg of tramadol in group BT (n=30) diluted to 3cc. The total volume of the study drug is 15ml. The following parameters were observed immediately after the

administration of epidural block.

1. Time to onset of analgesia at T10
2. Maximum sensory level achieved
3. Time to achieve the maximum sensory level
4. Time to complete motor blockade
5. Time to two segmental dermatomal regression
6. Regression to S1
7. First feeling of pain/rescue analgesia.

Pain was assessed hourly using visual analog scale (0 – no pain; 10 – worst pain). Duration of effective analgesia (time from epidural drug injection to the first dose of rescue analgesic) was recorded. 0.5% bupivacaine was given as the rescue analgesic if the pain score was 4 or more.

Sedation was also assessed at intervals of 20 minutes intraoperatively 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
3=inability to flex ankle and foot)

before surgery and at regular intervals of 1 hour post-operatively. Power analysis was carried out before the initiation of study. Any untoward incident and side effects during the study period were carefully observed for and recorded and managed symptomatically. All the data are expressed as mean and standard deviation (SD) unless specified. At the end of study data was compiled systematically and was subjected to statistical analysis using statistical package for the social sciences (SPSS) version 15.0 for windows and employing analysis of variance (ANOVA) with posthoc significance, Chi-square test and Fisher's exact test for sedation and analgesia. Value of $P<0.05$ was considered significant.

RESULTS

The demographic characteristics in both the groups exhibited marked similarities and did not show any statistical significant difference ($P>0.05$) [Table 1].

Tab-1 DEMOGRAPHIC DATA

Demographic Characteristics	BD (n=30)	BT (n=30)	P
Age (years)	36.58±4.02	35.45±5.23	0.3562
Weight (kg)	67.43±8.36	66.35±4.36	0.5329
Body mass index	22.45±2.56	25.66±3.88	0.1691
ASA (I/II)	18/12	16/14	<0.0001
Male/Female (M/F)	21/9	17/13	<0.0001
Mean duration of surgery (min)	118.56±18.46	110.68±22.86	0.1473

Tab-2 INITIAL BLOCK CHARACTERISTICS

Initial block characteristics	**Group BD(n=30)**	**Group BT (n=30)**	P
Onset time of sensory block at T10 (in minutes)	7.22±1.86	10.02±2.26	<0.0001
Maximum sensory block level	T4-6	T5-7	<0.0001
Time to maximum sensory block level (in minutes)	12.48±3.56	17.14.±2.28	<0.0001
Time in minutes for complete motor block	19.02±3.34	23.45.±5.65	<0.0001

In recent times there is a lot of demand for Dexmedetomidine as a sedative agent and similar findings were observed in our study as 30% and 46.66% of patients exhibited grade II and grade III sedation as compared to 10% and 3.33% of patients in the BT group, respectively [Table 3].

Tab-3 SEDATION SCORES

Sedation scores during surgery	Group BD No. of patients (%)	Group BT No. of patients (%)	P
1	5(16.66)	26(86)	<0.0001
2	9(30)	3(10)	<0.0001
3	14(46.66)	1(3.33)	<0.0001
4	2 (6)	0	-
5	0	0	-

Tab-4 POST-OP BLOCK CHARACTERISTICS

Post-op block characteristics (in minutes)	Group RD (n=50)	Group RF (n=50)	P
Mean time to two segmental regression	138.56±8.78	108.84±5.42	<0.0001
Mean time for regression to bromage 1	263.48±21.38	170.28±22.66	<0.0001
Mean time to sensory regression at S1	322.90±24.40	204.64±26.38	<0.0001
Time to first rescue top-up	355.88±14.52	285.58±20.72	<0.0001

Tab 5- SIDE EFFECTS

Side effects	Group BD (n=30)	Group BT (n=30)	P
Nausea	4(14)	13(26)	<0.0001
Vomiting	2(8)	6(12)	<0.0001
Shivering	0(0)	2(4)	-
Headache	1(4)	1(2)	<0.0001
Dizziness	1(4)	3(6)	<0.0001
Dry mouth	4(14)	1(2)	<0.0001
Respiratory depression	0	0	-
Urinary retention	3(10)	4(8)	<0.0001

DISCUSSION

Lower limb surgeries are usually performed under regional anaesthesia. Most commonly used regional anesthesia techniques for lower limb surgeries include neuraaxial blocks such as spinal & epidural anaesthesia which provide intra-op anaesthesia & post-op analgesia. Opioids & α-2 agonists as epidural adjuvant to LA improve the quality of the block and provide a dose-sparing effect. Epidural analgesia offers superior pain relief and early mobilization especially when local anesthetic dose is combined with an adjuvant as compared to LA used alone.[2] The synergism between epidural local anesthetics and opioids is well established but evidence regarding combination of LA with dexmedetomidine through epidural route is scarce in literature.[16-17] The demographic profile in the present study was comparable in both groups. The time to reach peak sensory level was significantly (P=) shorter in group BD (12.48±3.56min) as compared to group BT (17.14±2.28min) as equally was the strikingly significant difference between the two groups regarding onset of sensory analgesia at T10 dermatomal level. Throughout the surgery, patients were comfortable in both the groups but sedation scores were better in the BD group as 30% and 46% of patients had grade II and III sedation scores during the peri-operative period as compared to 10% and 3.33% of patients in the BT group. The sedative properties of dexmedetomidine are far more superior to tramadol. The analgesia was assessed using visual analogue scale (VAS) and patients in both the groups showed 0 scores during the entire surgical period. 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. Post-operatively, the number of analgesic top-up doses of bupivacaine in group BD was significantly lower than the requirement for bupivacaine in group BT. Hemodynamic stability was one of the most remarkable features observed with addition of dexmedetomidine and tramadol to epidural bupivacaine. Decrease in heart rate was exhibited by dexmedetomidine approximately 30-35 minutes after the epidural injection of the drugs. Thereafter, the heart rate remained stable 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-2agonist can again be explained on the basis of their central action whereby they decrease sympathetic outflow and nor-epinephrine release.[11-13] 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. The side effect profile of both the groups exhibited a strikingly significant picture. Nausea and vomiting occurred in 26% and 14% of the patients in group BT as compared to 14% and 4% in group BD. This higher incidence of nausea and vomiting was observed despite a low dose of tramadol used epidurally.

Similarly, the absence of respiratory depression in the present study can be explained on the basis that tramadol is less likely to induce respiratory depression as compared to morphine and we also used tramadol in a lower dosage. As far as α-2 agonists are concerned, the respiratory depression is not a known feature of this group of drugs. The background of the present study mainly revolved around the potential side effects of epidural opioids and the available literature for intravenous dexmedetomidine has established a significant dose sparing action of the latter on opioid requirement after general anesthesia.[18,19] Avoidance of respiratory depression in the patients who were administered dexmedetomidine was one of the most remarkable observations and the evidence is similar to the earlier studies where researchers have found complete absence of clinically detectable respiratory depression in the previous multiple human studies.[14,20,21]

CONCLUSIONS

Dexmedetomidine has been found to be a better alternative to tramadol as an adjuvant to bupivacaine as it provides early onset and establishment of sensory block, prolonged post-op analgesia, comparable hemodynamic stability and much better sedation levels.

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