Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 2, April - June 2017 (Part–2)
DOI: http: / / dx.doi.org / 10.21088 / ijaa.2349.8471.4217.16

A Comparative Study of Intrathecal Dexmedetomidine and Buprenorphine as Adjuvants to Hyperbaric Bupivacaine for Infraumbilical Surgeries

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Abstract

Background: Various adjuvants have been used with local anaesthetics in spinal anaesthesia to prolong the postoperative analgesia. Dexmedetomidine, alpha$_2$-agonist is now being used as a neuraxial adjuvant. The aim of the present study was to compare the block characteristics of dexmedetomidine 5mcg and buprenorphine 75mcg as adjuvants to 0.5% hyperbaric bupivacaine spinal anaesthesia in infra-umbilical surgeries. *Methods and Material:* Sixty four patients scheduled to undergo infra-umbilical surgeries were randomly allocated to receive either 12.5mg hyperbaric bupivacaine plus 5mcg dexmedetomidine (group D, n=34) or 12.5 mg hyperbaric bupivacaine plus 75mcg buprenorphine (group C, n=34) intrathecally. *Statistical Analysis Used*: Chi-square test and student t test was used where applicable to determine whether there was a statistical difference between the groups in the parameters measured. P less than 0.05 was considered as statistically significant. *Results*: Patients in group D had significantly longer regression of sensory and motor block time than patients in group B. The two segment regression time was 134±34.76 min in group D and 106.26±43 min in group B (P<0.05). The regression to Bromage 0 was 330±68 min in group D and 253±58 min in group B (P<0.05). *Conclusion*: Addition of dexmedetomidine to hyperbaric bupivacaine intrathecally prolongs the regression of sensory and motor blockade, but does not produce appreciable prolongation of postoperative analgesia or reduce the postoperative analgesic requirement when compared to buprenorphine.

Keywords: Bupivacaine; Dexmedetomidine; Spinal Anaesthesia; Buprenorphine.

Introduction

Prevention and treatment of pain is vital in the perioperative period as it enables early ambulation, reduces morbidity, shortens the length of hospital stay and improves the surgical outcome. The adequacy of postoperative pain control is an important factor in facilitating rehabilitation, hastening functional recovery, improve patient satisfaction and to enable early discharge [1].

Spinal anaesthesia is safe, economical and is most commonly employed technique for infra-umbilical surgeries [2,3]. One of the drawbacks of administering spinal anaesthesia with only local anaesthetic is its limited duration of action, thus needing early systemic analgesics in the postoperative period. In an effort to overcome this a number of adjuvants, both opioids (morphine, fentanyl, sufentanyl, buprenorphine) and non-opioids (midazolam, ketamine, neostigmine, clonidine, dexmedetomidine), have been used to prolong the duration of postoperative analgesia. Use of adjuvants enables the use of less local anaesthetic and increases the duration and quality of analgesia while minimising motor effects in the postoperative period. Intrathecal opioids potentiate the sensory blockage of local anaesthetics without affecting the sympathetic activity [4]. They provide prolonged postoperative analgesia but are associated with increased risk of nausea, vomiting, itching and respiratory depression [5]. Buprenorphine, a

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Received on 27.01.2017
Accepted on 07.02.2017

mu receptor partial agonist with low intrinsic activity has been safely used as an adjuvant for spinal anaesthesia. Its lipophilicity and high molecular weight prevents it from spreading rostrally and does not cause respiratory depression unlike the other hydrophilic opioids [6].

Dexmedetomidine, a highly selective alpha$_2$-agonist is under evaluation as a neuraxial adjuvant as it provides sedation, stable haemodynamics, good quality of intraoperative and prolonged postoperative analgesia with minimal side effets [7,8]. Dexmedetomidine possesses many properties of an ideal adjuvant and also does not cause respiratory depression thus making it a safe adjuvant [9]. Based on the findings in a few human studies, it is hypothesized that when 5mcg is administered intrathecally with hyperbaric bupivacaine it produces significantly prolonged postoperative analgesia with minimal side effects. [7, 8, 10]

The primary outcome of the present study was to compare the sensory and motor block characteristics between dexmedetomidine and buprenorphine as adjuvants to intrathecal bupivacaine in infra-umbilical surgeries. The secondary outcomes were to compare the the haemodynamic stability, time to rescue analgesia and postoperative analgesic consumption with the tow adjuvants.

Materials and Methods

After obtaining ethical committee clearance and written informed consent 68 ASA physical status 1 and 2 patients aged 18-60 years of either sex schedule to undergo infra-umbilical surgeries were enrolled in the study. Patients with contraindications to spinal anaesthesia and allergy to opioids and local anaesthetics were excluded from the study. Patients were randomly assigned into two groups of 34 each by a computer generated random number table. Patients in group D received 12.5mg (2.5mL) of 0.5% hyperbaric bupivacaine with 5 mcg of dexmedetomidine and those in group B received 12.5mg (2.5mL) of 0.5% hyperbaric bupivacaine with 75 mcg of buprenorphine. The study solution was prepared in an aseptic manner by an anaesthesiologist not involved in the study. For patients assigned to group D 2.5mL of 0.5% bupivacaine with 5 mcg of dexmedetomidine in 0.25mL to constitute a final volume of 2.75mL. Dexmedetomidine 50 mcg / mL was diluted to 2.5mL with normal saline and 0.25mL of this solution was drawn with a BD 1mL syringe. For patients assigned to group B 2.5ml of 0.5% bupivacaine with 75 mcg of buprenorphine in 0.25mL to constitute a final volume of 2.75mL. From an ampule of buprenorphine containing 300 mcg / mL 0.25mL of solution was drawn with a BD 1mL syringe. Anaesthesiologist blinded to the group allocation administered spinal anaesthesia and collected all the study data.

In the operation room after instituting minimal mandatory monitoring and securing an intravenous access lumbar puncture was performed with a 25G Quinke spinal needle in L3-4 or L4-5 interspace with patient in sitting position by midline approach. Intrathecal injection of the study solution was administered over 10-15sec after noting a free flow of clear CSF. Patients were then turned supine.

All patients received oxygen at 5L / min via a face mask. Hypotension, defined as a decrease in systolic blood pressure by more the 30% from baseline or a fall below 90mmHg, was treated with incremental iv doses of ephedrine 3mg and iv fluid as required. Bradycardia, defined as heart rate <50bpm, was treated with iv atropine 0.3-0.6mg. Sensory testing was done with loss cold sensation and dermatome level was tested every 2min until the highest level had stabilized by two consecutive tests. On achieving T10 sensory blockade level, surgery was allowed. Testing was then conducted every 10min until the point of two segment regression of the block was observed.

Haemodynamic parameters were noted every 5min for the first 30min and every 10min for next 90min. Spinal motor blockade was assessed with Bromage scale, while the highest sensory level achieved, time to highest sensory level and two segment regression were noted for assessing sensory characteristics. Pain was assessed with visual analogue scale postoperatively at 0,1,2,4,6,12 and 24 hours after arrival in the postoperative area. Tramadol 50mg was given intravenously as rescue analgesia when VAS was > 4. The time for first analgesic request and the analgesic consumption in the first 24hrs were also noted. In addition any adverse effects like nausea, vomiting, pruritus, respiratory depression, urinary retention or any other effects were noted. The level of sedation was assessed by Ramsay sedation scale.

In previous studies [3,6] the onset of motor block as assessed by Bromage scale was 11.6±1.8min with dexmedetomidine and 12.3±3min with buprenorphine. In the present study to get similar results the sample size required was 34 subjects in each group with a precision of 95% confidence, 80% power. Statistical analysis was done using SPSS statistics for Windows, version 18 (SPSS Inc., Chicago,

Ill., USA). Chi-square test and student t test was used where applicable to determine whether there was a statistical difference between the study groups in the parameters measured. P less than 0.05 was considered as statistically significant.

Results

The demographic characteristics were comparable between the two groups (Table 1). There was no significant difference in the duration and type of surgeries between the two groups. The sensory and motor characteristics are summarized in Table 2. There was no difference between the two groups in the highest level of block achieved or the time to reach the highest sensory level. The two segment regression was significantly slower with dexmedetomidine (134±34.76min) compared to buprenorphine (106.26±43min). There was no difference in the onset to Bromage 3 motor block, but the regression of motor block to Bromage 0 was significantly slower with the addition of dexmedetomidine (Table 2). The time to first analgesic request and postoperative tramadol consumption were similar between the two groups (Table 3). Haemodynamic parameters (heart rate & Mean arterial pressure) and sedation scores were comparable in both groups throughout the intraoperative and postoperative period (Fig 1, 2, & 3). The pain scores as assessed by VAS during the postoperative period was comparable between the two groups. The adverse effects noted were also similar in the two groups. Six patients in group D and 4 patients in group B required ephedrine for treatment of hypotension. Two patients in group D and one patient in group B had bradycardia requiring atropine.

Table 1: Demographic characteristics

Variable	Group D (n=34)	Group B (n=34)
Age (years)*†	40.8±13.19	43.6±13.01
Sex (Male/Female) †	26/8	25/9
Weight (Kg)* †	67.12±11.24	64±8.73
Height (cm)* †	166.21±7.54	164.56±7.55
BMI (kg/m^2)* †	24.19±2.92	23.67±3.05
ASA Class (1/2) †	23/11	19/15
Duration of Surgery (min)* †	63.82±31.34	66.47±35.32

*Data presented as Mean±SD; † P>0.05 statistically not significant

Table 2: Motor and sensory characteristics of spinal anaesthesia

Variable	Group D (n=34)	Group B (n=34)
Onset to Bromage 3 (min)*†	5.82±2.07	5.53±2.94
Regression to Bromage 0(min)*‡	330±68	253±58
Highest sensory level†	T5(T4-T9)	T6(T4-T10)
Time to achieve highest sensory level (min)*†	9.71±2.8	8.35±4.08
Two segment regression (min)*‡	134±34.76	106.26±43

*Data presented as Mean±SD; †P>0.05 statistically not significant; ‡P<0.05 statistically significant

Table 3: Postoperative analgesia

Variable	Group D (n=34)	Group B (n=34)
Time to first analgesic request (min)*†	425.17±93.93	415.22±139.12
Total analgesic consumption in first 24hr (mg) †	82±16.6	88±15.2

*Data presented as Mean±SD; †P>0.05 statistically not significant

Discussion

The present study has shown that use of dexmedetomidine 5 mcg or buprenorphine 75 mcg as adjuvant for bupivacaine spinal anaesthesia produces similar duration and quality of postoperative analgesia.

In order to obtain extended duration of postoperative analgesia following spinal anaesthesia the addition of adjuvants to intrathecal local anaesthetics came into practice. An ideal combination should provide adequate intraoperative anaesthesia, extended postoperative analgesia without prolonging the motor blockade or producing adverse haemodynamic or respiratory consequences. Since the first clinical use of intrathecal morphine in 1979, numerous studies have confirmed the efficacy of

spinal opioids for postoperative analgesia [11,12]. However, intrathecal opioids have disadvantages like nausea, vomiting and respiratory depression [13,14]. Several drugs have been studied as alternatives to intrathecal opioids, and recently alpha-2 agonists such clonidine and dexmedetomidine have been used. Of the two alpha-2 agonists, dexmedetomidine is an attractive choice since it is more selective alpha-2 agonist than clonidine [7,15]. In the present study we chose dexmdetomidine in the dose of 5 mcg, as it has been found to provide good quality prolonged analgesia in a previous study [3,8,10].

The exact mechanism as to how intrathecal alpha-2 agonists prolong the motor and sensory block of local anaesthetics is not well understood. They bind to presynaptic C-fibers and postsynaptic dorsal horn neurons. The analgesia is due to depression of C-fiber neurotransmitter release and hyperpolarisation of postsynaptic dorsal horn neurons [16]. The prolongation of motor block may be due to binding to motor neurons in the dorsal horn [17]. Intrathecal alpha-2 agonists have been found to be antinociceptive for both somatic and visceral pain [8].

Al-Ghanem et al in their study compared the effects of 5 mcg dexmedetomidine and 25 mcg fentanyl as adjuvants to intrathecal bupivacaine in gynecological surgeries and concluded that dexmedetomidine produces more prolonged motor and sensory block compared to fentanyl [8]. Mahendru V et al [18] in a placebo controlled study compared 5 mcg dexmedetomidine, 25 mcg fentanyl and 30 mcg clonidine as adjuvants to hyperbaric bupivacaine in lower limb surgeries. Intrathecaldexmedetomidine was associated with prolonged motor and sensory block compared to other adjuvants. Gupta R et al [3] in their study found the time to highest sensory level, time to two segment regression, and the highest sensory level to be 12.3±1.8min, 120±22.2min and T5 (T4-T8) respectively with dexmedetominde 5 mcg as adjuvant to hyperbaric bupivacaine. The results for the present study is similar to their study wherein we found time to highest sensory level, two segment regression, and highest sensory level as 9.71±2.8min, 134±34.76min and T5(T4-T9) respectively with dexmedetomidine. However, these sensory block characteristics were similar to buprenorphine as adjuvant. The motor block characteristics in the present study were also similar to the previous study [3].

Hypotension and bradycardia are thought be the most important problems with intrathecal alpha$_2$-agonists[16]. However, in the present study six patients had hypotension and two patients had bradycardia requiring intervention, which is similar to other studies [3,8,18]. In the present study the time to rescue analgesic requirement and the analgesic consumption with dexmemdetomidine and buprenorphine as adjuvants was similar. The time to rescue analgesic requirement is longer with both agents, however, we could not quantify it statistically as we had no placebo group.

Conclusion

Addition of dexmedetomidine to hyperbaric bupivacaine intrathecally prolongs the regression of sensory and motor blockade, but does not produce appreciable prolongation of postoperative analgesia or reduce the postoperative analgesic requirement when compared to buprenorphine. Demedetomidine as an intrathecal adjuvant results in haemodynamic stability that is comparable to burenorphine without producing excessive sedation or respiratory depression.

Acknowledgement

None

Conflict of Interest: None to declare

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