Original Article

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The Effect of Intrathecal Dexmedetomidine as an Adjuvant to Spinal Anesthesia: Double Blind Study

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Abstract

Dexmedetomidine is a highly selective á$_2$adrenoreceptor agonist recently introduced to anesthesia. It produces dose dependent sedation, anxiolysis and analgesia without respiratory depression. *Methods*: This prospective randomized double-blind study was carried out on 100 patients, aged 20 to 70 years with American society of Anesthesiology (ASA) class I and II of either gender, for lower limb surgery, who met the inclusion criteria of spinal anesthesia. The randomly selected patients received Bupivacaine 0.5% 15 mg (3ml) + 0.5 ml of normal saline in group BS (n=50) and Bupivacaine 0.5% 15 mg (3ml) +Dexmedetomidine 10 mcg in 0.5ml NS in group BD(n=50). The onset time to reach sensory and motor level, the regression time of sensory and motor block, requirement of first rescue analgesic, hemodynamic changes and side-effects if any were recorded. *Result:* The onset time to reach T10 dermatome and modified bromage 3 motor blocks were not significantly different between the groups. Time to achieve sensory regression to L1 in Group BD (284.4±62.84 min) were prolonged as compare to Group BS (149.3±24.91min) (p=0.00). The regression time of motor block to reach modified bromage 0 was (379.5±75.42 min) and (231.6 ±44.55 min) in group BD and BS respectively (p=0.004). The first rescue analgesic was required at 200.90 ± 40.33 min and 327.60 ± 60.05 min in group BS and group BD respectively, were comparable (p=0.104). *Conclusion*: Intrathecal Dexmedetomidine as an adjuvant to intrathecal Bupivacaine prolong sensory and motor block with minimal side effects. So it is an attractive alternative choice for long duration surgery.

Keywords: Bupivacaine; Dexmedetomidine; Lower Limb Surgery; Spinal Anesthesia.

Introduction

Spinal anesthesia is a simple technique with rapid onset of action and usually used for patients undergoing below umbilical surgery. Various adjutants like Buprenorphine, Ketamin, Tramadol, Midazolam, Ramifentanyl, Sufetanyl, Pethidine, Various adjuncts have been used to prolong the analgesic effect of bupivacaine. Intrathecal use of clonidine and fentanyl has been shown to significantly increase the duration of spinal anesthesia. [1-5].

Intrathecal α_2 receptor agonists have antinociceptive action for both somatic and visceral pain. Dexmedetomidine shows more specificity towards á$_2$ receptor (α_2/α_1 1600:1) compared with clonidine (α_2/α_1 200:1) [6]. Several studies have shown that á$_2$ receptor agonists when administered intrathecal will enhance the analgesia provided by sub therapeutic doses of local anesthetics like bupivacaine due to synergistic effects with minimal hemodynamic effects [6,7,8.].

Materials and Methods

After approval from Institutional Ethics Committee a prospective randomized double blind study was conducted on 100 adults of either sex belonging to American Society of Anesthesiology (ASA) class I and II. The selected patients scheduled for lower limb surgery under spinal anesthesia. Patients with contraindication to spinal Anesthesia, history of spine surgery, infection at the injection site, coagulopathy, and pre existing cardiac disease, neurological disorders, allergic to

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study drugs, psychiatric illness and pregnancy were excluded from the study.

All patients were examined and investigated a day prior to surgery, and were taught to scale their pain on VAS scale in post operative period [9]. They were advised fasting for 6 hours and Tab. Alprazolam 0.5 mg at night before surgery.

All patients were randomly divided in to two groups of 50 each. To provide double-blindness, three anesthesiologists were involved in the study. One anesthesiologist prepared the drug, another gave spinal anesthesia and data were recorded by an independent third anesthesiologist who was unaware of group allocation, patients were also unaware of the drug regimen received.

Group BS: received 3 ml of 0.5% Bupivacaine (15 mg)+0.5 ml NS.

Group BD: received 3 ml of 0.5% Bupivacaine (15mg) + Dexmedetomidine 10μg in 0.5 ml NS.

In the operation theatre ECG, pulse oximetry and non invasive blood pressure were attached and baseline parameters of each patient were recorded. Intravenous access was secured and all patients were preloaded with an infusion of 500 ml ringer lactate. Subarachnoid block was administered at the level L_{2-3} or L_{3-4} using 25G spinal needles with patient in the sitting position under aseptic and antiseptic precaution.

Demographic data such as age, weight, height, type and duration of surgery were noted. The sensory block was assessed by pinprick method (26G hypodermic needle) in mid-clavicular line bilaterally, loss of sensation to pin prick was considered as sensory block. Motor block was assessed according to the modified Bromage scale [10].

0: Patient able to move hip, knee, ankle.

1: Unable to move hip, able to move knee and ankle.

2: Unable to move hip and knee, able to move ankle.

3: Unable to move hip, knee and ankle.

Time to reach T10 dermatome sensory block and Bromage 3 motor block were noted. All time durations were calculated considering the time of spinal injection as time zero. Sensory and motor block level were recorded every 2 min for 20 min. Heart rate (HR), mean arterial blood pressure (MAP) and oxygen saturation were monitored and recorded after the block every 5 minutes for half an hour then every 15 minutes until the end of surgery.

Intraoperative sedation was measured every 15 min using Ramsay sedation score [11].

After operation HR, MAP, oxygen saturation, sedation score and VAS score were recorded during the first hour at 15 min interval, and thereafter every hour up to 8 hour then at 12hour and 24 hour. The time from intrathecal injection to sensory regression to L_1 dermatome and motor block regression to modified Bromage 0 were recorded. All time durations were calculated in relation to the time of spinal injection. Duration of pain relief was defined as the time from spinal injection to the first request for rescue analgesics. Post operative pain was accessed by VAS Score and if VAS score >3, Inj. Tramadol 100 mg diluted in 100 ml NS was given IV as a rescue analgesic. Occurrence of nausea, vomiting, pruritus and respiratory depression were recorded throughout the study duration. Hypotension (defined as adecrease in systolic blood pressure > 30% of the baseline value or systolic blood pressure < 90 mm Hg) was treated with Inj. Ephedrine 6 mg. Bradycardia defined as a pulse rate of < 50 beat/ min was treated with Inj. Atropine 0.3- 0.5 mg. Respiratory depression (RR <8 or SpO2 < 95%) was treated with oxygen supplementation and respiratory support if required. All data were observed and collected by third observer.

Statistical Analysis

Statistical analysis was done by SPSS version. Data was expressed as means and standard deviation (SD), medians and ranges. The comparison was studied using Fisher's exact test as appropriate, with P value reported at the 95% confidence interval (CI). $P \leq 0.05$ was considered statistically significant

Results

Both the groups were comparable with respect to age, height, weight, sex, and ASA physical status. There was no significant difference in the type and duration of surgery (Table 1).

Sedation was analyzed by Ramsay sedation score. In Group BS 45 (90%) patients achieved sedation score 2 and 5(10%) patients achieved sedation score 1. In group BD 40(80%) patients achieved sedation score 3 and 10(20%) patients achieved sedation score 2 (Table 2).

The time to reach T-10 sensory level (Group BS/ BD=3.55±0.71/2.75±0.85 min) was statistically not significant ($p > 0.05$). The median and range of the peak sensory level reached were T8 (T6 –T10) in group BS and T6 (T4-T10) in group BD, not statistically

different among the groups.

All patients in Group BD achieved modified bromage 3 motor block (4.020 ± 1.70 min), while in group BS 48 (96%) patients achieved modified bromage 3 motor block (8.268 ± 2.75 min),) which was statistically not significant (p=0.062), (Table3).

Time to achieve sensory level regression to L1 in Group BD (284.4±62.84 min) were prolonged as compare to Group BS (149.3±24.91 min), which was statically significant (p=0.00).

Time to achieve motor block regression to modified bromage 0 in Group BD (379.5±75.42 min) were significantly prolong as compare to Group BS (231.6 ±44.55 min) (p=0.004).

Post operative pain was accessed by VAS Score and if VAS score >3, Inj Tramadol 100 mg diluted in 100 ml NS was given intravenous as a rescue analgesic. Time of requirement of the first rescue analgesic in Group BS was 200.90 ± 40.33 min and in Group BD 327.60 ± 60.05 min were comparable, (p=0.104). The requirement of first rescue analgesic was prolonged in Group BD.

The mean values of MAP and HR were comparable between the two groups throughout the study. After 15 min of spinal anesthesia mean MAP was 74.9 mm Hg in Group BD and mean MAP 85.35 mm Hg in Group BS (non significant).

Both group showed a fall in HR after 15 min of spinal anesthesia. Mean HR in Group BS was 77.6 / min and in Group BD was 70.07/ min (non significant).

The most common intraoperative adverse effect were Hypotension /bradycardia, were observed 30% (n=15)/20 %(n=10) in Group BD and 16% (n=8) /6 %(n=3) in Group BS respectively. Inj Ephedrine 6 mg was used to treat hypotension in 8 patients from Group BD and 2 patients from Group BS. Inj Atropine 0.3-0.5 mg was used to treat bradycardia.

Incidence of vomiting was observed in 3 patients in Group in BS and 8 patients in Group BD at different intervals of time, which was treated with Inj Ondansetrone 4 mg.

Table 1: Demographic data

Patients data	BS group	BD group
Age (year)	41 ± 4	42 ± 6
Sex (M/F)	28/32	29/31
Weight (kg)	55 ± 4	58 ± 6
Height (cm)	156 ± 8	160 ± 7
Duration of Surgery	130 ± 35	138 ± 40

Table 2: Ramsay sedation score

Ramsay score	Group BS	Group BD
1	5(10%)	-
2	45(90%)	10(20%)
3	-	40(80%)

Table 3:

Variable (min)	BS group (n = 50)	BD group (n = 50)	F Test	p value
Time to reach T10 Sensory level	3.5510 ± 0.71	2.747 8± 0.85	1.748	.189
Time to reach BR-3	8.268 ± 2.75	4.020 ± 1.70	3.577	.062
Time to regression L1 sensory level	149.30 ± 24.91	284.40 ± 62.84	29.249	.000
Time to regression BR-0	231.60 ± 44.55	379.50 ± 75.42	8.768	.004
Time for rescue analgesic	200.90 ± 40.33	327.60 ± 60.05	2.693	.104

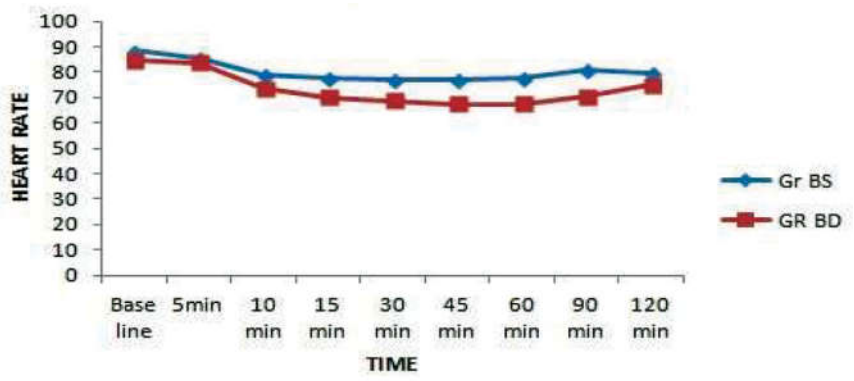

Fig. 1: Comparison of heart rate

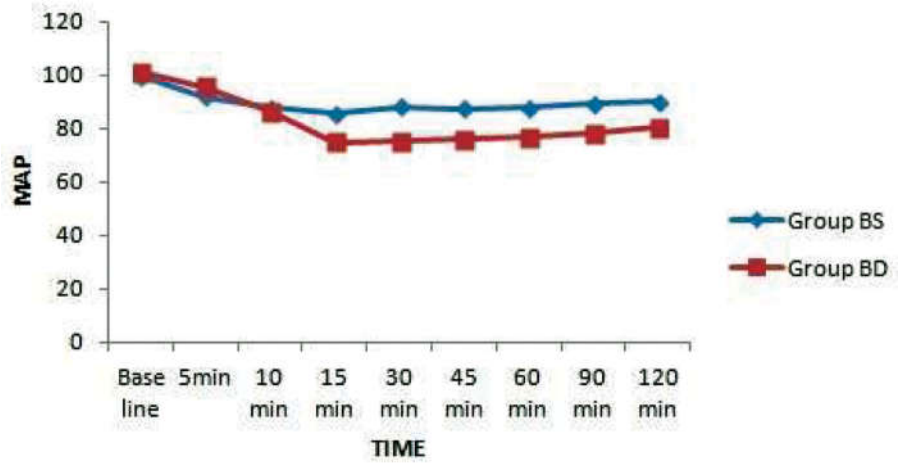

Fig. 2: Comparison of MAP

Discussion

In this study 100 patients were randomly divided in to two groups of 50 each. Group BS: received 3 ml of 0.5% Bupivacaine (15 mg) + 0.5 ml NS. Group BD: received 3 ml of 0.5% Bupivacaine (15mg) + Dexmedetomidine 10µg in 0.5 ml NS. Our study shows significant prolongation of the duration of spinal anesthesia by intrathecal administration of dexmedetomidine as an adjunct to hyperbaric bupivacaine for patients undergoing lower limb surgery.

Dexmedetomidine is a α_2 adrenoreceptor agonist which has about ten times higher affinity for α_2 adrenoreceptor than clonidine [12-14]. The intrathecal use of other α_2- agonist clonidine for postoperative analgesia alone [15]or co-administered with local anesthetics [3, 4, 5]or opioids [16] has been studied previously. It is thought that intrathecal Dexmedetomidine produces its analgesic effect by inhibiting the release of C fibers transmitters and by hyperpolarization of post-synaptic dorsal

Horn neurons [17] the prolongation of motor effect might be caused by direct impairment of excitatory amino acid release from spinal interneuron [18]. The complementary action of local anesthetics and α_2 adrenoreceptor agonists accounts for their profound analgesic properties. The prolongation of the motor block of spinal anesthetics may be the result of binding of α_2 adrenoreceptor agonists to the motor neurons in the dorsal horn[19,20].

In current study patients who received Dexmedetomidine shows significantly delayed requirement of rescue analgesic than those who received spinal bupivacaine alone. Hala et al concluded that intrathecal Dexmedetomidine in doses of 10µg and 15µg significantly prolong the anesthetic and analgesic effects of spinal hyperbaric bupivacaine in a dose- dependent manner which is similar to our study [21].

Vidhi et al studied that intrathecal Dexmedetomidine is associated with prolonged motor and sensory block, hemodynamic stability, and reduced demand of rescue analgesics in 24 hours as compared to clonidine, fentanyl or lone bupivacaine [2].

Kanazi et al [19] reported that intrathecal dexmedetomidine 3 µg were equipotent to intrathecal clonidine 30 µg when used with bupivacaine for spinal anesthesia.

In our study intrathecal 10mcg of Dexme zdetomidine (group BD) achieved T10 sensory level at 2.75±0.85 min, which is very short compare to Hala (7.7±3.6 min) [21]. Intrathecal Dexmedetomidine as an adjuvant is beneficial for lengthy complex surgery as an alternative to epidural or prolonged general anesthesia.

Hem Anand et al studied the Dexmedetomidine and fentanyl along with low dose bupivacaine for lower abdominal surgery and concluded that Dexmedetomidine facilitate the spread of the block and offers prolonged post operative analgesia [1].

Most of the clinical experience gained in the use of intrathecal α_2 adrenoreceptor agonists has been described with clonidine [22, 23] and there has been a need for more clinical studies related to intrathecaldexmedetomidine to prove its efficacy, safety, and the suitable dose for supplementation to spinal local anesthetics. In our study, the intrathecal dose of dexmedetomidine selected was based on previous human studies wherein no neurotoxic effects

have been observed [20, 24].

In our study total duration to achieve motor block bromage 3 was 8.27±2.75 min in BS group and 4.02±1.7 min in BD Group (p =0.062).

Udita et al studied intrathecaldexmedetomidine group achieved motor block Bromage 3 was 6.61±2.18 min[25], which shows 10 mcg intrathecal Dexmedetomidine has fast onset of motor block as compare to 5 mcg of intrathecal Dexmedetomidine.

The most significant side effects were reported with the use of intrathecal α_2 adrenoreceptor agonists were bradycardia and hypotension [26].

We observed hypotension and bradycardia in 30% (n=15), 20%(n=10)in Group BD and 16% (n=8) ,6%(n=3) in Group BS respectively. Inj Ephedrine was used to treat hypotension in 8 patients from Group BD and 2 patients from Group BS. Inj Atropine was used to treat bradycardia. Incidence of vomiting was observed in 3 patients in Group in BS and 8 patients in Group BD at different intervals of time, which was treated with Inj Ondansetrone.

We noted significantly delayed requirement of rescue analgesic with 10 µg Dexmedetomidine when compared to Bupivacaine with NS (p=0.104)[24,27].

Intrathecal Dexmedetomidine as an adjuvant to intrathecal Bupivacaine prolong sensory and motor block with minimal side effects. So it is an attractive alternative choice for long duration surgery.

References

1. Hem AnandNayagam, N Ratan Singh, and H Shanti Singh. A prospective randomised double blind study of intrathecal fentanyl and dexmedetomidine added to low dose bupivacaine for spinal anesthesia for lower abdominal surgeries.Indian J Anaesth. 2014 Jul-Aug; 58(4): 430–435.
2. Mahendru V, Tewari A, Katyal S, Grewal A, Singh MR, Katyal R. A comparison of intrathecal dexmedetomidine, clonidine, and fentanyl as adjuvants to hyperbaric bupivacaine for lower limb surgery: A double blind controlled study. J AnaesthesiolClinPharmacol. 2013; 29: 496-502.
3. Fogarty DJ, Carabine UA, MilliganKR. Comparison of the analgesiceffects of intrathecal clonidine andintrathecal morphine after spinalanaesthesia in patients undergoingtotal hip replacement. Br J Anaesth.1993; 71(5): 661-4.
4. Strebel S, Gurzeler JA, Schneider MC, Aeschbach A, Kindler CH. Small-dose intrathecal clonidine andisobaric bupivacaine for orthopedicsurgery: a dose-response study.AnesthAnalg. 2004; 99(4): 1231-8.
5. Van Tuijl I, Giezeman MJ, Braithwaite SA, Hennis PJ, Kalkman CJ, van Klei WA. Intrathecal low dose hyperbaric bupivacaine-clonidinecombination in outpatient knee arthroscopy: a randomized controlled trial. ActaAnaesthesiol Scand. 2008; 52(3): 343-9.
6. Reves JG, Glass PS, Lubarsky DA, McEvoy MD, Martinez-Ruiz R. Intravenous anesthetics. In: Miller RD, editor. Miller's Anesthesia. 7th ed. Philadelphia: Elsevier, Churchill Livingstone. 2010; pp. 751–7.
7. Dahlgren G, Hultstrand C, Jakobsson J, Norman M, Eriksson EW, Martin H. Intrathecalsufentanil, fentanyl, or placebo added to bupivacaine for cesarean section. AnesthAnalg. 1997; 85: 1288–93. [PubMed: 9390596].
8. Bajwa SJ, Arora V, Kaur J, Singh A, Parmar SS. Comparative evaluation of dexmedetomidine and fentanyl for epidural analgesia in lower limb orthopedic surgeries. Saudi J Anaesth. 2011; 5: 365–70. [PMCID: PMC3227304] [PubMed: 22144922].
9. Katz J, Melzack R. Measurement of pain. SurgClin North Am. 1999; 79: 231-52.
10. AnkornC , Casey WF: Spinal Anesthesia - A practical guide 2000; 12: 21-34.
11. Ramsay MA, Savege TM, Simpson BR, Goodwin R. Controlled sedationwith alphaxalone-alphadolone. Br MedJ. 1974; 22(2): 656-9.
12. Gertler R, Brown HC, Mitchell DH, Silvius EN. Dexmedetomidine: A novel sedative analgesic agent. Proc (BaylUniv Med Cent) 2001; 14: 13 21.
13. Murthy TV, Singh R. Alpha 2 adrenoceptor agonist - dexmedetomidine role in anaesthesia and intensive care: A clinical review. J AnaesthClinPharmacol 2009; 25: 267 72.
14. Coursin D B, Coursin D B, Maccioli G A. Dexmedetomidine. Current Opinionin Critical Care 2001, 7:221–226.
15. Chiari A, Lorber C, Eisenach JC, Wildling E, Krenn C, Zavrsky A, Kainz C, Germann P, Klimscha W. Analgesicand hemodynamic effects of intrathecalclonidine as the sole analgesic agentduring first stage of labor: a doseresponsestudy. Anesthesiology. 1999; 91(2): 388-96.
16. Julião MC, Lauretti GR. Low-dose intrathecal clonidine combined with sufentanil as analgesic drugs inabdominal gynecological surgery. J ClinAnesth. 2000; 12(5): 357-62.
17. Correa-Sales C, Rabin BC, Maze M. A hypnotic response to dexmedetomidine, an alpha 2 agonist, is mediated in the locus coeruleus in rats. Anesthesiology. 1992 Jun; 76(6): 948-52.
18. Palmeri A, Wiesendanger M. Concomitant depression of locus coeruleus neurons and of flexor reflexes by an alpha 2-adrenergic agonist in rats: a possible mechanism for an alpha 2- mediated muscle

relaxation. Neuroscience. 1990; 34(1): 177-87.

19. Kanazi GE, Aouad MT, Jabbour Khoury SI, Al Jazzar MD, Alameddine MM, Al Yaman, et al. Effect of low dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. ActaAnaesthesiolScand. 2006; 50: 222 -7.
20. Al Ghanem SM, Massad IM, Al Mustafa MM, Al Zaben KR, Qudaisat IY, Qatawneh AM, et al. Effect of adding dexmedetomidine versus fentanyl to intrathecal bupivacaine on spinal block characteristics in gynecological procedures: A double blind controlled study. Am J ApplSci. 2009; 6: 882-7.
21. Hala EA, Shafie MA, Youssef H. Dose related prolongation of hyperbaric bupivacaine spinal anesthesia by dexmedetomidine. Ain Shams J Anesthesiol. 2011; 4: 83 95.
22. Filos KS, Goudas LC, Patroni O, Polyzou V. Hemodynamic and analgesic profile after intrathecal clonidine in humans. A dose-response study. Anesthesiology. 1994 Sep; 81(3): 591-601.
23. De Kock M, Gautier P, Fanard L, Hody JL, Lavand'homme P. Intrathecalropivacaine and clonidine for ambulatory arthroscopy: A dose response study. Anesthesiology. 2001; 94: 574 8.
24. Al-Mustafa MM, Abu-Halaweh SA, Aloweidi AS, Murshidi MM, Ammari BA, Awwad ZM, Al- Edwan GM, Ramsay MA. Effect of dexmedetomidine added to spinal bupivacaine for urological procedures. Saudi Med J. 2009; 30(3): 365-70.
25. UditaNaithani, Mahendra Singh Meena, et al. Dose-dependent effect of intrathecaldexmedetomidine on isobaric ropivacaine in spinal anesthesia for abdominal hysterectomy: Effect on block characteristics and hemodynamics. J Anaesthesiol ClinPharmacol. 2015 Jan-Mar; 31(1): 72–79. doi: 10.4103/0970-9185.150549 PMCID: PMC4353158
26. Harada Y, Nishioka K, Kitahata LM, Kishikawa K, Collins JG. Visceral antinociceptive effects of spinal clonidine combined with morphine, [D-Pen2, D-Pen5] enkephalin, or U50, 488H.Anesthesiology. 1995; 83: 344–52. [PubMed: 7631957].
27. Gupta R, Verma R, Bogra J, Kohli M, Raman R, Kushwaha JK.A Comparative study of intrathecaldexmedetomidine and fentanyl as adjuvants to Bupivacaine. J Anaesthesiol Clin Pharmacol. 2011; 27: 339 43.