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Efficacy of dexmedetomidine as intrathecal adjuvant in subarachnoid block and postoperative analgesia

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Abstract

Introduction: Various adjuvants have been used intrathecally to improve the quality and duration of the spinal anaesthesia along with better postoperative analgesia We studied the effect of dexmedetomidine as intrathecal adjuvant to local anaesthetic agent in subarachnoid block. The primary goal was to study the onset and duration of sensory and motor block. The secondary goal was to note the time for first rescue analgesic, total requirement of rescue analgesic, quality of block and any complications.

Materials and Method: Sixty patients age 18 to 60 years, ASA I-II , posted for lower limb orthopaedic surgeries were randomly allocated into two equal groups based on computer generated randomization: **Group B**: Inj.Bupivacaine 0.5% hyperbaric 3ml(15mg) + 0.15cc normal saline. **Group D**: Inj.Bupivacaine 0.5% hyperbaric 3ml(15mg) + Inj.Dexmedetomidine 15µg(0.15ml). All the patients were observed for onset of sensory and motor block, two segment regression time, total sensory and motor block duration, time to first rescue analgesic, total number of doses of rescue analgesia in 24 hours postoperatively and side effects if any.

Results: The demographic variables were comparable in the two groups. The onset of sensory block was faster in group B ($p=0.002$) with no significant difference in the onset of motor block in two groups. The duration of sensory and motor block in Group D was significantly prolonged ($p<0.0001$).The quality of block was better in Group D.

Conclusion: Dexmedetomidine as an adjuvant to local anaesthetic agents in subrachnoid block delays onset of sensory block with no effect on the onset of motor blockade. The duration of sensory and motor blockade is significantly longer. The time for first rescue analgesic is prolonged with decreased requirement of rescue analgesics postoperatively. Apart from improving the quality and duration of the subarachnoid block, additional properties of dexmedetomidine like sedation and as antishivering agent are additional benefits when used as intrathecal adjuvant.

Keywords: Subarachnoid block; Dexmedetomidine; Bupivacaine

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Introduction

Subarachnoid block is the commonest mode of anaesthesia for lower limb orthopaedic surgery. It is easy to perform, provide fast onset and effective motor and sensory block. However, the limitation with spinal anaesthesia is their limited duration of action which made epidural anaesthesia popular as they could be used to supplement spinal anaesthesia for long duration surgeries and also provided adequate postoperative analgesia. But epidural anaesthesia has its own complications, is costly and requires skills. Therefore different drugs were then added as intrathecal adjuvant to local anaesthetic agent which not only prolong the duration of spinal anaesthesia and provide postoperative analgesia but at the same time decrease the need for placing an epidural catheter.

Various adjuvants have been used intrathecally to improve the quality and duration of the spinal anaesthesia along with better postoperative analgesia. Opioids are most commonly used intrathecal adjuvant however their side effects like respiratory depression, nausea, vomiting, urinary retention and pruritus have resulted in limited use of opioids in subrachnoid block. Various other drugs such as clonidine, magnesium sulfate, neostigmine, ketamine and midazolam, have also been used but none is without associated adverse effects.(1)

Dexmedetomidine, a selective alpha-2 adrenoceptoragonism, is a new emerging drug which when used as an adjunct to local anaesthetic agents in subrachnoid block helps avoid the side effects involving alpha-1 receptors. Administration of an alpha-2 agonist via intrathecal or epidural route provides an analgesic effect in postoperative pain without severe sedation. This effect is due to the sparing of supraspinal CNS sites from excessive drug exposure, resulting in robust analgesia without heavy sedation. Hence our present study was designed to study the effects of dexmedetomidine when used as adjunct to local anaesthetic in subarachnoid block.

The aims and objectives were to study the onset of sensory and motor block, the total duration of sensory and motor block, total time for two segment regression, time for first rescue analgesia, total number of doses of rescue analgesic required in first twenty four hours postoperatively and to study side effects and manage complications as required.

Material and Method

A prospective randomised double blinded controlled study of 60 patients was carried out in the department of anaesthesiology of a tertiary care hospital. Before starting the study, approval from the institutional ethics committee was taken. Patients of ASA I-II physical status between ages 18-60 years, to be operated for lower limb orthopaedic surgery were enrolled for the study.

Patients having sinus bradycardia, local site infection, deranged coagulation profile, hypotension, uncontrolled diabetes mellitus, uncontrolled hypertension, pregnancy, acute or chronic respiratory disease, cognitive or psychiatric disturbances, pre-existing neuropathy and beta-blocker therapy were not included in the study.

All patients underwent thorough pre-anaesthetic check up and were kept nil per oral for eight hours before the surgery. Routine laboratory investigations were done. The anaesthetic procedure to be carried out was explained and the patients were reassured to alleviate their anxiety. They were educated regarding Visual Analogue Scale(VAS) for pain. A prior written and informed consent was taken from all patients. Patients did not receive any premedication. The patients were randomly divided into one of the following group based on the computer generated randomization table.

Group B: Inj.Bupivacaine 0.5% hyperbaric 3ml(15mg) + Inj.Normal Saline 0.15ml

Group D: Inj.Bupivacaine 0.5% hyperbaric 3ml(15mg) + Inj.Dexmedetomidine 15µg(0.15ml)

ECG, SpO_2 and NIBP were attached. IV line was taken and IV Inj.Ringer Lactate or Inj. Normal Saline was started. Under all aseptic and antiseptic precautions subarachnoid block was conducted, with patient in sitting position at L_{3-4} intervertebral space, in midline approach using Quincke's 25G spinal needle. After confirmation of clear free flow of CSF, the drug was injected at the rate of 0.2ml/sec. Both the operator and investigator were blinded about the drug, which was prepared by an independent investigator. Immediately after subrachnoid block was given, the patient was asked to lay supine. The completion of injection was taken as time zero of induction of anaesthesia.

Assessment of sensory block was done with the help of pin prick technique using the short bevelled end of 24G hypodermic needle, performed every one minute from the time patient was made supine and continued till complete sensory block was achieved till T10 dermatomal level. Sensory block was assessed based on the following grading:

Grade 0: Sharp pin felt

Grade 1: Analgesia, dull sensation felt

Grade 2: Anaesthesia, no sensation felt

Onset of sensory block was defined as the time from the completion of subarachnoid block till attainment of grade 1 sensory block as assessed by pin prick technique.

The motor block was assessed by the same observer every one minute till the complete motor blockade was achieved after completion of subarachnoid block. Onset of motor blockade was defined by attainment of grade 1 motor block on Bromage scale. Motor block assessment was done according to Bromage scale on a 4 point scale as follows:

Grade 0: No paralysis

Grade 1: Not able to raise extended legs

Grade 2: Not able to flex knees

Grade 3: Not able to flex ankle

Timings recorded in minutes:

T0-Time at completion of drug injection

T1- Time at achievement of Grade 1 sensory block

T2- Time at achievement of Grade 2 sensory block

T3- Time when sensory block reverts back to Grade 0

Tos-Time of onset of sensory block (Tos=T1-T0)

Tds- duration of sensory block (Tds=T3-T1)

T4- Time of achievement of Grade 1 on Bromage scale

T5- Time of achievement of Grade3 on Bromge scale

T6- Time when motor block reverts back to Grade 0 on Bromage scale

Tom- Time of onset of motor block (Tom=T4-T0)

Tdm-Duration of motor block (Tdm=T6-T4)

T7- Time at which VAS≥3 and the patient received first rescue analgesia

Tav-Time when first rescue analgesia was required (Tav=T7-T0)

Patient was monitored for heart rate, non invasive blood pressure and arterial oxygen saturation every 2 minutes for the initial 20 minutes, then every 10 minutes until discharged from the recovery room and thereafter hourly up to 12 hours. After commencement of surgery, patient's anxiety and sedation level was assessed using Modified Ramsay Sedation Score as follows:

Grade1: Anxious, agitated or both

Grade2: Co-operative, oriented, tranquil and alert

Grade3: Responds to commands only.

Grade4: Brisk response to light glabellar tap.

Grade5: Sluggish response to light glabellar tap.

Grade6: No response.

Duration of surgery was calculated from the time of skin incision to the end of skin closure. The block was considered fail when no signs of sensory or motor block were present up to 20 minutes after completion of subarachnoid block and were excluded from the study. The incidence of side effects such as nausea, vomiting, shivering, itching, pruritus, respiratory depression, sedation and hypotension were recorded. Nausea/vomiting was treated with injection ondansetron 4 mg IV. Pruritus was treated with injection promethazine 25 mg IM which was repeated after 1 hour if needed. Oxygen by Hudson mask was provided if SpO_2 decreased to <94%.

Postoperative pain was assessed using Visual Analogue Scale(VAS) between 0-10 (0 = no pain, 1-3 = mild pain, 4-7 = moderate pain, 8-10 = severe pain), every 1 hour for first 2 hours, every 2 hours for next 8 hours and then every 4 hours till 24 hours. Time of first rescue analgesia was calculated from the time the subarachnoid block was given till the patient first complained of pain(VAS≥3 at rest, VAS≥5 on movement). Inj.Diclofenac sodium 1mg/kg IV was given as rescue analgesia with at least 8 hours interval between two doses of rescue analgesia. Total number of doses of rescue analgesics required by each patient in the 24 hours were observed and compared. At the end of

surgery, quality of anaesthesia was assessed by the patient according to the following numeric scale:
Grade 3: (excellent) no complaint
Grade 2: (good) minor complaint which did not require supplemental analgesics
Grade1: (average) complaint that required supplemental analgesia

All patients were catheterised with Foley's catheter before the start of surgery. The patients were observed intraoperatively as well as postoperatively for the side effects of any drug or any other complications pertaining to the block performed and if found , were managed accordingly. Study ended at 24 hours after the induction of anaesthesia.

Statistical Analysis: Data obtained were tabulated and analyzed using Statistical Package for Social Science(SPSS 17.0 evaluation version).To calculate the sample size, a power of study was taken as 90% and 30 patients per group were required for the study. Data was expressed as means and standard deviation (SD), medians and ranges, or numbers and percentages. For categorical covariates (sex, ASA class, nausea/vomiting, use of rescue analgesia, hypotension, and bradycardia) Chi-square test or Fisher's exact test was used as appropriate, with *P* value reported at the 95% confidence interval (CI).

Results

We studied total 60 patients between the ages of 18 to 60 years, 30 patients per group. There was no failed subarachnoid block.

The demographic data like age, height, weight, and duration of surgery were comparable between Group B and Group D(Table 1).

Table 1: Demographic characteristics

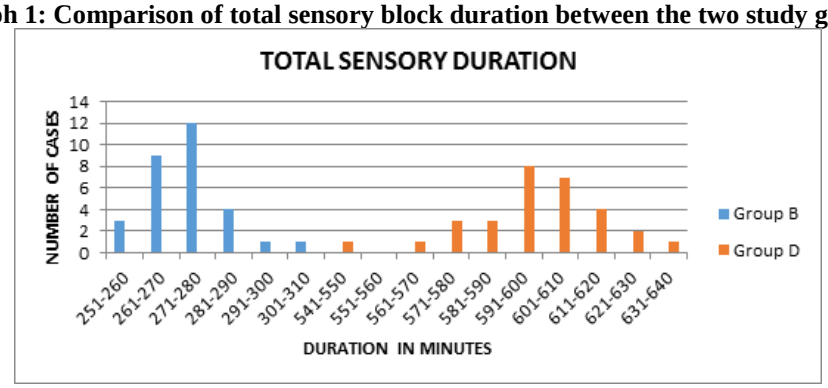
Parameter	Group B	Group D
Age(yrs)	41.30±13.87	37.13±13.39
Height(cm)	150±8.43	152±6.84
Weight(kg)	61.63±8.43	61.70±9.12
Duration of surgery (hrs)	2.08±0.23	2.13±0.26

The onset of sensory block was earlier in Group B than Group D and they were statistically significant (p=0.002). The time for two segment regression and the total duration of sensory block was greater in Group D than Group B and was statistically as well as clinically significant.(Table 2 & Graph 1)

Table 2: Comparison of sensory characteristics between the Group B and Group D

Parameter(In minutes)	Group D	Group B	P value
Mean time to reach T10(SD)	5.70(0.74)	5.13(0.57)	0.002
Segment regression(T10-T12)(SD)	207.83(8.97)	111.16(6.90)	<0.0001
Mean total sensory duration(SD)	602.16(18.96)	277.33(11.12)	<0.0001

Graph 1: Comparison of total sensory block duration between the two study groups

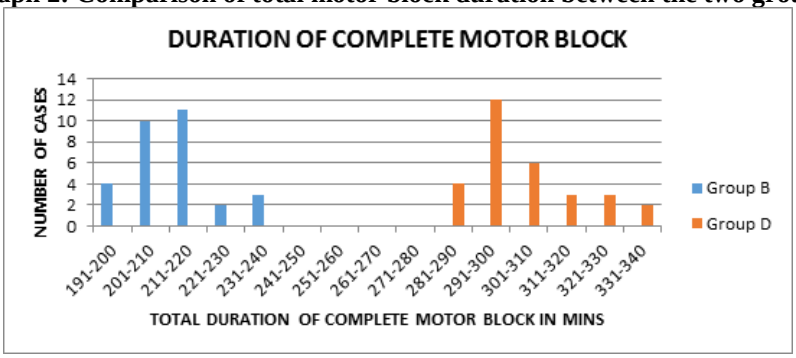


There was no significant difference in the onset of motor block between the two groups. However the total duration of motor block was greater in group D than group B and was statistically significant (p<0.0001). (Table 3 & Graph 2)

Table 3: Comparison of motor block characteristics between Group B and Group D

Parameter(in minutes)	Group B	Group D	P value
Mean time taken to reach Bromage scale B1(SD)	3.40(0.56)	3.60(0.56)	0.174
Mean total duration of complete motor block(SD)	216.0(10.85)	307.50(14.42)	<0.0001

Graph 2: Comparison of total motor block duration between the two groups



The mean time to first rescue analgesia (VAS≥3) in group D was 15.90±1.70 hours and in group B was 6.20±0.76 hours, which was highly significant (p<0.0001) both clinically as well as statistically. The total number of analgesic doses in first 24 hours was greater in group B than group D and they were statistically significant (p<0.0001). (Table 4)

Table 4: Comparison of analgesic characteristics between the two study groups

Parameter	Group B	Group D	P value
Mean time to first rescue analgesia(SD)	6.20(0.76)	15.90(1.70)	<0.0001
Mean total number of analgesic doses in first 24 hours	2.82(0.18)	0.94(0.21)	<0.0001
Mean highest VAS score observed in first 24 hours	6.40(0.56)	4.03(0.31)	<0.0001

The quality of anaesthesia was better in group D compared to group B which was statistically(p<0.0001) as evident from Table 5.

Table 5: Comparison of quality of anaesthesia judged by patients in both the study groups

Quality	Group B	Group B(%)	Group D	Group D(%)
Excellent	3	10	4	13.3
Good	7	23.3	16	53.3
Fair	20	66.7	10	33.3

In both group patients were hemodynamically stable, with equal incidence (3.3%) of intraoperative hypotension which responded to Inj.Glycopyrolate 0.2mg IV. There was no incidence of pruritus, nausea, vomiting and respiratory depression observed in either group. In the absence of supplemental intravenous sedation, 16 patients out of 30 in group D were sedated; scoring ≥3 on Ramsay Sedation Scale, while none of the patients in group B was sedated. In group D only 6.7% of the patients experienced intraoperative shivering and in group B 26.7% of the patients experienced intraoperative shivering which was statistically and clinically significant(p=0.038).

Discussion

Spinal anaesthesia is the preferred anaesthesia technique for lower limb surgery. Bupivacaine is the most commonly used local anaesthetic agent in spinal anaesthesia. The use of adjuvants with local anaesthetics provides prolonged and superior quality of anaesthesia and postoperative analgesia with lower requirement of postoperative analgesia.

Dexmedetomidine has been used as an adjunct to local anaesthetic agents in neuraxial anaesthesia and also in peripheral nerve block. Several hypothesised mechanisms of action include vasoconstriction around the injection site,[(2)] direct suppression of impulse propagation through neurons as a result of a complex interaction with axonal ion channels or receptors,[(3)] local release of encephalin like substances,[(4)] a decrease in localised inflammatory mediators and an increase in anti-inflammatory cytokines through an α2 adrenoceptor mediated mechanism. Dexmedetomidine showed protective or growth promoting properties in tissues, including nerve cells from cortex. Dexmedetomidine helps prevention of local anaesthetic induced neurotoxicity when used together with local anaesthetic agents.

Animal studies have been conducted with intrathecal dexmedetomidine in dose range 2.5-100 µg, however, risk of neurotoxicity cannot be denied at dosage more than 3 µg.[(12-14)] Human studies have shown that 3-15 µg of dexmedetomidine co-administered with local anaesthetics has a dose-dependent effect on

anaesthesia, analgesia and haemodynamic stability.[9,15-18]

Abdallah et al[6] did a quantitative review on all randomised control trials comparing the effects of dexmedetomidine, added as an adjunct to local anaesthetic solution used for neuraxial and peripheral nerve blocks and concluded that addition of dexmedetomidine to local anaesthetic solution resulted in prolonged duration of analgesia.

G.E. Kanazi et al[7] studied the effect dexmedetomidine and clonidine on the characteristics of local anaesthetic used for subarachnoid block It was observed dexmedetomidine (3mcg) and clonidine (30mg) had equipotent effect.

Subhi M. Al-Ghanem et al[8] in their study compared dexmedetomidine and fentanyl as adjunct in subarachnoid block for gynaecological procedures. They observed that dexmedetomidine prolonged the duration of sensory and motor blockade significantly.

Our prospective, randomised double blind controlled study was conducted between two groups. After obtaining informed consent, patients were randomly divided into two groups based on the computer generated randomization table.

Group D: Inj.Bupivacaine 0.5% hyperbaric 3ml (15mg) + Inj Dexmedetomidine 15µg(0.15ml).

Group B: Inj.Bupivacaine 0.5% hyperbaric + Inj. NS 0.15ml.

The aims and objectives were to study the onset and duration of sensory and motor block, two segment regression time, quality of anaesthesia as assessed by the patient, time for demand of first rescue analgesic, total requirement of doses of rescue analgesia in 24 hours postoperatively and to analyse adverse effects and complications. In our study, demographic variables did not show any significant difference, Group B and Group D were comparable with respect to age, weight, height, sex distribution and duration of surgery.

The mean onset time of sensory block in Group B was 5.13±0.57 mins while in group D was 5.70±0.74 mins (p=0.002). Two segment regression time in group B was 111.16±6.90 and in group D was 207.83±8.97 mins (p<0.0001). Mean duration of sensory block in Group B was 277.33±11.12 mins and that in group D was 602.16±18.96mins (p <0.0001).

The mean time of onset of motor blockade in Group B was 6.40±0.56 mins while in Group D was 6.60±0.56 mins (p=0.174). The mean total duration of motor block in Group B was 216.0±10.85 mins while that in group D was 307.50±14.42 mins (p <0.0001).

The mean time of request for first rescue analgesic(VAS≥3) in Group B was 6.20±0.76 hours while that in group D was 15.90± 1.70(p <0.0001). the mean total number of doses of rescue analgesia in 24 hours postoperatively in group B was 4.06±0.58 and in group D was 1.40±0.49(p<0.0001). The quality of anaesthesia was judged by patients was good in 53.3% in group D compared to only 23.3%in group B.

The Al-Ghanem et al[8] have reported the use of dexmedetomidine to be associated with a decrease in heart rate and blood pressure. In our study incidence of hypotension was comparable in the two groups which responded to Inj.Mephentermine 6 mg IV. Both groups had comparable incidence of bradycardia which responded to Inj.Glycopyrolate 0.2 mg IV. No sedation was observed in group B patients whereas in group D 53.3% of patients had sedation which when assessed on Ramsay Sedation Scale was 3 or more than 3. In group D only 6.7% of the patients experienced intraoperative shivering while in group B 26.7% patients had intraoperative shivering.

There are many studies where dexmedetomidine has been used as an adjunct in subarachnoid block but with dosage lower than that used in our study. There are only two studies which used the dose of dexmededomidine as used in our study.

1. In the study conducted by **Hale E. A. Eid et al**[9] in 2011 where they studied effect of different doses of dexmedetomidine on local anaesthetic when given as intrathecal adjuvant. 48 patients posted for ACL reconstruction were randomly divided into 3 groups receiving 3ml 0.5% hyperbaric bupivacaine and 0.5ml containing either 10µg(group D1), 15µg (group D2) dexmedetomidine or 05ml of normal saline (group B). All three groups were haemodynamically stable. Dexmedetomidine prolonged time to two segment regression, sensory regression to S1, regression of motor block to modified Bromage 0 and time to first rescue analgesic, effects were greater in group D2 than in group D1 with higher sedation scores and lower postoperative analgesic requirements than in group D1 or B.
2. In another study conducted by **Soumya Samal et al**[10] in 2014, efficacy of intrathecal buprenorphine (150µg) was compared with dexmedetomidine (15µg). Postoperative analgesia was significantly prolonged in buprenorphine group (mean±SD, 17.63±2.28 hrs) than dexmedetomidine group (mean±SD, 15.82±2.15 hrs) (p=0.002). There was no significant difference between both the groups in pulse rate, mean arterial pressure and oxygen saturation. The study concluded that intrathecal buprenorphine provides prolonged duration of postoperative analgesia when compared to dexmedetomidine but with more side effects.

Thus the findings of increased two segment regression time, prolonged duration of sensory block, prolonged duration of motor block, decreased requirement of rescue analgesia on adding dexmedetomidine to the local anaesthetics in subarachnoid block in our study were consistent with above two studies. No significant side effects were observed.

In the current study, we found faster onset with prolonged sensory and motor blockade with intrathecal dexmedetomidine. Alpha-2 receptors are seen in dorsal

horn laminae I, II, V with specific mRNA in ventral horn more than dorsal horn.[19] This could be the reason for potent anaesthetic action of dexmedetomidine.

Conclusion

To conclude, dexmedetomidine seems to be a promising alternative to opioids and other intrathecal adjuvants to local anaesthetics in subarachnoid block for long duration surgeries. We observed that intrathecal dexmedetomidine delayed onset of sensory block, however there is no significant affect on the onset of motor block. Dexmedetomidine prolonged the duration of motor and sensory block, maintained hemodynamic stability, and also decreased the requirement of rescue analgesic to a significant amount in the postoperative period. However, prolonged duration of motor blockade as seen with dexmedetomidine may be undesirable especially for short duration surgical procedures and ambulatory surgeries.

Limitations of the study

As this study included only 60 patients, multicentric study with larger sample size, using different dosages of dexmedetomidine, different volumes with different types and concentrations of local anaesthetic agents are required. Also studies on patients with ASA III and above physical status need to be done.

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