A study of dexmedetomidine as an adjuvant to hyperbaric bupivacaine in subarachnoid block

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Background: No drug, used as adjuvant to spinal bupivacaine, has yet been identified that specifically inhibits nociception without its associated side-effects. Dexmedetomidine, a novel alpha-2 agonist which holds promise as an intra-thecal adjuvant.

Aims: This observational study was conducted to evaluate the onset and duration of sensory and motor block as well as perioperative analgesia and adverse effects of dexmedetomidine given intrathecally with 0.5% hyperbaric bupivacaine for spinal anesthesia.

Materials and Methods: A total of 60 patients belonging to age group 18-60 years, urban population, classified as American Society of Anesthesiologists status I and II scheduled for lower abdominal and lower limb procedures were prospectively studied. Patients were randomly allocated to receive intrathecally either 12.5 mg hyperbaric bupivacaine plus 5 μg (0.5 ml) dexmedetomidine (group D, n=30) or 12.5 mg hyperbaric bupivacaine plus 0.5 ml NS (group B, n=30). Sensory and motor blockade characteristics- The onset time to reach peak sensory and motor level, the regression time for sensory and motor block, time for rescue analgesia, hemodynamic changes and side-effects were recorded.

Results: The onset times to reach T10 dermatome, peak sensory level and onset time to reach modified Bromage 3 motor block were similar in both groups. It was observed that adding dexmedetomidine intrathecally significantly prolonged sensory and motor block time. time for first analgesic request was also significantly prolonged in group BD. Statistically there were no significant differences in hemodynamic alterations and other adverse effects between the groups. Conclusion: clinical advantage of dexmedetomidine is that it facilitates the spread of the block and offers prolonged post-operative analgesia. The groups were similar with respect to hemodynamic variables and there were no significant side-effects in either of the groups. However, prolonged duration of motor blockade with dexmedetomidine may be undesirable for short-term surgical procedures or ambulatory surgeries.

Keywords: Dexmedetomidine, Bupivacaine, Spinal Anesthesia, Intrathecal, Adjuvant
Introduction

Spinal anesthesia is the preferred mode of anesthesia for lower abdominal & lower limb elective and emergency surgeries because of its rapid onset, superior blockade, easy administration, less failure rates, safety and cost effectiveness. It also has intra and postoperative antinociceptive effect, lower incidence of hemodynamic fluctuation compared to general anesthesia, considerable effect in reducing intraoperative bleeding and postoperative thromboembolic complications [1].

Regional anaesthesia techniques provide important advantages compared with general anaesthesia and systemic analgesia, including excellent pain control, reduced side-effects, and shortened stay in the post-anaesthesia care unit. However, these early advantages can be short-lived and limited by the relatively brief duration of action of currently available local anaesthetics, potentially resulting in block resolution before the period of worst postoperative pain.

Also, may be associated with visceral pain, nausea and vomiting. Increasing the volume (dose) of LAs may prolong the duration of analgesia but may also increase the risk of accompanied LA systemic toxicity and systemic side effects. Although continuous catheter-based nerve blocks can extend postoperative analgesia, their placement requires additional time, cost, and skill [2,3,4].

It is particularly important to select small doses of bupivacaine to avoid prolonged detrusor block and inability to void. Use of intrathecal adjuvants has come up to overcome these disadvantages of SAB and also to prolong analgesia. Opioids are most commonly used as intrathecal adjuvants- morphine was used first. Fentanyl and sufentanyl are the most commonly used lipophilic drugs and are most studied.

However, opioid-induced side effects, such as pruritus, nausea, or vomiting, delayed respiratory depression could be an obstacle in common use, and has made the need to find an alternative analgesic devoid of the side effects and better clinical efficacy. [4,5].

Alpha 2 adrenergic receptor (α2AR) agonists like clonidine and dexmedetomidine have come into focus for their sedative, analgesic, anxiolytic, anesthetic sparing effect, peri-operative sympatholytic properties.

Clonidine (15–150 μg) has been frequently used in spinal anesthesia to improve the quality of local anesthetics. But, side effect such as hypotension, bradycardia, and sedation are increased as dose of clonidine is increased. Dexmedetomidine affinity to α2-adrenoceptor is 10 times as compared to clonidine, hence it has a wider safety margin.

Dexmedetomidine is a more potent and selective α2-adrenoceptor agonist than clonidine. It has additional advantages like minimal respiratory depression, better hemodynamic stability, cardio protection, neuroprotection and renoprotection [6].

Through this study it was aimed to find out whether dexmedetomidine acts as a good synergistic agent to low-dose bupivacaine spinal anesthesia and render effective spinal anesthesia and postoperative analgesia with stable hemodynamics, minimal side effect, as compared to the local anesthetic only group.

Materials and Methods

Study design/Type of study: Observational study, Time frame of the study is 15 months

Duration of study-GROUP I: Patients receiving 2.5 ml (12.5 mg) of 0.5% hyperbaric bupivacaine with 0.5 ml of NS. GROUP II: Patients receiving 2.5 ml of 0.5% hyperbaric bupivacaine with 5 mcg of dexmedetomidine in 0.5 ml NS. Number of cases belonging to each group - 30. This study was carried out in a tertiary health centre – batra hospital and medical research centre, New Delhi between Jan 2013- March 2014

Inclusion & Exclusion criteria: 60 patients of both sex aged between 18-60 years belonging to American society of anesthesiologists grade I and II, undergoing elective surgeries on lower abdomen and lower limb under subarachnoid block of an expected duration over 90min Patients belonging to ASA grade III, IV and V, Liver and renal dysfunction, cardiac dysrrythmias, on ARBS, calcium channel blockers, weight > 120 kg or height <150 cms., with contraindications for spinal anesthesia- past history of spine surgery, infection focus at back, coagulopathy, hypersensitivity to local anaesthetics, allergy to the study drugs, sedative drugs consumption, history of uncontrolled, labile hypertension, failure of spinal block and the need for general anesthesia, pregnant females were excluded from the study.
Data collection procedure: Cases were selected depending on the consultant anesthesiologist’s choice and randomly allocated to two groups, those receiving only Bupivacaine and those who received adjuvant Dexmedetomidine, 30 patients in each group and informed consent was obtained. The age, sex, weight and height of the patients were recorded.

Follow-up: Intra-operatively basal pulse rate, blood pressure and respiratory rate were obtained. The patients were connected to monitors such as ECG, SpO2, noninvasive blood pressure recording device. Vital parameters were monitored using electrocardiogram, non-invasive arterial pressure, and peripheral oxygen saturation.

Evaluation of the response to intervention- The time to reach T10 dermatome sensory block, peak sensory level and bromage 3 motor block were recorded before surgery. analgesic supplementation during operation noted. The regression time for sensory and motor block were recorded in PACU. All durations (initial period of onset of analgesia, the highest dermatomal level of surgical analgesia, the complete establishment of motor blockade, the time to two segment regression of analgesic level, regression of analgesic level to S1 dermatome and time to complete recovery) were calculated considering the time of spinal injection as 'time zero'. Level of sedation was evaluated by a five-point ramsay sedation scale. Sedation scores were recorded just before the initiation of surgery and thereafter, every 20 minutes during the surgery.

The vital signs were recorded every 2 minutes for 20 minutes and then every 5 minutes for the entire intra-operative period and also at the completion of the surgery. Hypotension (>20% decrease in mean arterial pressure from baseline) was treated with intravenous fluids and Ephedrine 6mg intravenous boluses. Bradycardia (pulse<60/min) was treated with intravenous atropine sulphate. Intra and peri-operative nausea and vomiting, pruritus, additive analgesia, sedation or any other side-effects were recorded. Post operatively, the patient was shifted to the Post anaesthetic care unit (PACU) and hemodynamic parameters as detailed above monitored by nurse in-charge.

Statistical Analysis Used: Statistical testing was conducted with the statistical package for the social science system version SPSS 17.0. Continuous variables were presented as mean±SD or median if the data was unevenly distributed. Categorical variables were expressed as frequencies and percentages. The comparison of normally distributed continuous variables between the groups was performed using Student’s t test. Nominal categorical data between the groups was compared using Chi-squared test or Fisher’s exact test as appropriate. Non-normal distribution continuous variables were compared using Mann Whitney U test. For all statistical tests, a p value less than 0.05 was taken to indicate a significant difference. After getting the required information, the collected data were coded, tabulated and analysed. The various statistical techniques i.e. the mean, standard deviation and test of significance (t-test and chi-square-test) were used for drawing valid conclusions.

Results
The 2 groups were matched with respect to - Age; Height, Weight, Duration of surgery. The sensory block onset was significantly faster in dexmedetomidine (DB) group when compared to control (B) group, p=0.000. The mean time to reach T10 sensory dermatome was 6.717±1.0168 in group DB, 8.970±1.1648 in group B. The median and range of the peak sensory level reached were T7 (T5-T10) in group DB, T8 (T6-T10) in group B. Motor block onset was also significantly quicker in dexmedetomidine group (DB), P= 0.001 Mean time to reach modified bromage score 3 was 12.077±2.4506 in group DB, 14.617±3.1048 in group B. All patients achieved complete motor block, modified Bromage.

Hemodynamic: Systolic, diastolic arterial blood pressures, heart rates and oxygen saturations remained stable intraoperatively and in PACU, and there was no significant difference between the groups.
Intraoperative hypotension was observed equally in both the groups, which showed prompt response to iv fluids and vasopressors.

Bradycardia occurred in one patient in group DB which was easily treated with iv atropine. No patients experienced respiratory depression at any time interval.

The SpO2 was higher than 97% in all patients in both the groups, either in the intraoperative or in the PACU time and did not require additional oxygen. No patient had respiratory rate below 8/ min.

Both the group patients were arousable throughout the surgery. Complete recovery of sensory and motor function was observed in all studied patients, was uneventful. [Figure 1-7].

**Sensory Block Regression:** Regression of the sensory block was significantly prolonged in dexmedetomidine group, p=0.000. Mean time of two segment regression (in minutes) was 111.67 ±11.929 in DB group, 86.17±7.178 in B group. Mean time of regression to S1 dermatome (in minutes) was 315.20±25.795 in DB group, 202.40 ±19.586 in B group.
Postop Analgesia: The duration of analgesia was significantly prolonged with addition of dexmedetomidine, where a longer time was recorded to need first analgesia, p=0.000. TFAR, time to first rescue analgesic was 410.70 ± 14.962 minutes in group DB, 259.0 ± 14.1 minutes in group B. Total amount of analgesics required in first 12 hrs was significantly decreased in dexmedetomidine group, p=0.000.33 ±0.547 times in group DB vs 7.50 times in group B.

Per OP Sequele, Adverse Reactions: No statistically significant difference was determined between the groups with regard to the frequency of side effects. Hypotension occurred only in 2 patients in each group, which was easily manageable. No significant differences were observed between both groups regarding any of the encountered complications – shivering occurred more frequently in group B, but wasn't found to be significant, p=0.013. Bradycardia occurred in one patient in group DB which responded to atropine. Nausea occurred in one patient in group B. The modified Ramsay sedation score was between 0 and 2 intra- and post-operatively in both studied groups, score of 3 intraoperatively in two patients in DB group. Intra-operative nausea in 1 patient in group BD, 2 patients in group B. Adequate nerve block was established in both groups and none of the patient’s required additional analgesia.

Discussion

It is important to limit the block level to minimize the hemodynamic instability during spinal anesthesia. Although there are several factors influencing the spinal block level, it could be more influenced by total dosage of drug, not volume, concentration, or block position, therefore, the dose of intrathecal local anesthetic should be decreased to limit the block level.

Dexmedetomidine has made its application from a novel sedating agent in the intensive care unit to its use as an adjuvant in various regional anesthetic techniques because of its “cooperative sedation” without any respiratory depression. It has a favorable pharmacokinetic profile suitable to be used in the perioperative period to reduce the requirements of opioids and anesthetic drugs. There are few side-effects of dexmedetomidine, which should always be kept in mind before choosing the patients for its use. The various side-effects associated with dexmedetomidine include, but are not limited to hypotension, bradycardia, worsening of heart block, dry mouth, and nausea [4]. Dexmedetomidine is a more potent and selective α2-adrenoceptor agonist than clonidine, thus providing better analgesia and better therapeutic window. The present study aimed to evaluate the role of dexmedetomidine added to heavy bupivacaine 0.5% intrathecally for lower abdominal surgeries.

The regional versus general anaesthesia debate is an age-old debate that has brought about few clear answers. Most concur that multiple factors including the patient, the surgery, the method of regional and general anaesthesia, and the quality of perioperative care, all influence surgical outcome.

In this age of evidence-based medicine, the heterogenous data available need to be reconciled with the advances in perioperative care and the significant decline in complications associated with the surgical process as a whole. Gulur P et al did work on comparison of regional anaesthesia versus general anaesthesia, and its morbidity and mortality.

Their review considers general issues such as the type of available evidence, and its limitations, particularly with regard to the relatively broad question of neuraxial versus general anaesthesia. It then assesses current evidence on regional versus general anaesthesia for specific scenarios such as hip fracture surgery, carotid endarterectomy, Caesarean section, ambulatory orthopaedic surgery, and postoperative cognitive dysfunction in elderly patients after non-cardiac surgery [6].

Watson B et al in their work on spinal anaesthesia and day case surgery. They worked on Local anaesthetic adjuvants in neuraxial versus peripheral nerve block. They presented a review of the literature on the importance and the clinical characteristics relevant to adjuvants added to local anaesthetics in neuraxial and peripheral nerve blocks.

Recent findings In neuraxial anaesthesia, both opioids and alpha-2 receptor agonists have beneficial effects. Opioids and alpha-2 receptor agonists are important as neuraxial adjuvants to improve the quality of peroperative and postoperative analgesia in high-risk patients and in ambulatory procedures [7].
Clinically useful adjuvants in regional anaesthesia and current opinion in anaesthesiology was studied by Förster JG et al. In this review, emphasis is placed on adjuvant drugs that are already in clinical use.

The list of adjuvants studied during the review period includes adrenaline, clonidine, ketamine, neostigmine, nondepolarizing muscle relaxants, and nonsteroidal anti-inflammatory drugs. Some future aspects are considered in a couple of experimental studies on slow-release local anaesthetic formulations. Several recent studies have shown a synergism of clonidine with local anaesthetics in various types of blocks, as well as with spinal opioids.

Bradyarrhythmia and hypotension may be associated with the use of clonidine. Neostigmine may cause antinociception both in the spinal cord and in peripheral nerves. Biodegradable microcapsules containing bupivacaine and dexamethasone have been tested in humans and found to produce analgesia for several days (intercostal block). Local inflammatory reactions and paraesthesias, however, were observed in 30% of cases. Further development is needed concerning extra-long acting analgesic formulations [8].

Davis FM, Woolner DF et al did a prospective, multi-centre trial of mortality following general or spinal anaesthesia for hip fracture surgery in the elderly. From the point of view of mortality, subarachnoid anaesthesia did not appear to confer any advantages over general anaesthesia in non-prosthetic surgery for hip fracture in the elderly [9]. Sunil BV et al like the present study, studied dexmedetomidine as an adjuvant with hyperbaric bupivacaine for spinal anaesthesia. It was a double-blind controlled study.

Intrathecal adjuvants have gained popularity with the aim of prolonging the duration of block, quality of block and decreased resource utilization compared with general anaesthesia. The purpose of this study was to evaluate the optimum dose, onset and duration of sensory and motor block as well as adverse effects of adding Dexmedetomidine to hyperbaric bupivacaine for spinal anaesthesia.

The onset time to reach T10 sensory and Bromage 3 motor level, the regression time for S1 sensory and Bromage 0 motor block, Sedation scores, hemodynamic changes and side effects were recorded.

They concluded that there is a dose dependent prolongation of sensory and motor block regression time with the addition of Dexmedetomidine up to 10 μg as an adjuvant without any significant increase in the side effects. The results were very similar to the present study [10]. Bajwa SJ et al explored this drug Dexmedetomidine and concluded it be an adjuvant making large inroads into clinical practice. The introduction of newer more selective α−2 adrenergic agonist, dexmedetomidine has made a revolution in the field of anaesthesia owing to its varied application.

The aim of the current review was to highlight the various clinical and pharmacological aspects of dexmedetomidine in daily routine practice of anaesthesiology and intensive care besides its potential role in other clinical specialties. This review of dexmedetomidine was carried out after searching the medical literature in Pubmed, Science direct, Scopus, Google scholar and various text books and journal articles using keywords anesthesia, dexmedetomidine, neuro-surgery, pediatric surgery, regional dexmedetomidine, anesthesia, regional, neurosurgery, and pediatric surgery [11]. Various adjuvants have been used with local anesthetics in spinal anesthesia to avoid intraoperative visceral and somatic pain and to provide prolonged postoperative analgesia.

Gupta R et al did a comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to bupivacaine. Dexmedetomidine, the new highly selective α2-agonist drug, is now being used as a neuraxial adjuvant. The aim of this study was to evaluate the onset and duration of sensory and motor block, hemodynamic effect, postoperative analgesia, and adverse effects of dexmedetomidine or fentanyl given intrathecally with hyperbaric 0.5% bupivacaine. It was observed that Intrathecal dexmedetomidine is associated with prolonged motor and sensory block, hemodynamic stability, and reduced demand for rescue analgesics in 24 h as compared to fentanyl [12].

Similar study was done by Kanazi GE et al who compared effect of low dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. The purpose of this study was to compare the onset and duration of sensory and motor block, as well as the hemodynamic changes and level of sedation, following intrathecal bupivacaine supplemented with either dexmedetomidine or clonidine.
The onset times to reach peak sensory and motor levels, and the sensory and motor regression times, were recorded. Hemodynamic changes and the level of sedation were also recorded. Dexmedetomidine (3 µg), when added to intrathecal bupivacaine, produces a similar prolongation in the duration of the motor and sensory block with preserved hemodynamic stability and lack of sedation [13].

Mahendru V et al compared three drugs. They did a comparison of intrathecal dexmedetomidine, clonidine, and fentanyl as adjuvants to hyperbaric bupivacaine for lower limb surgery. Various adjuvants are being used with local anesthetics for prolongation of intraoperative and postoperative analgesia. Dexmedetomidine, the highly selective 2 adrenergic agonist is a new neuraxial adjuvant gaining popularity.

The onset times to reach T8 dermatome and modified Bromage 3 motor block were not significantly different between the groups. Dexmedetomidine group showed significantly less and delayed requirement of rescue analgesic. Intrathecal dexmedetomidine is associated with prolonged motor and sensory block, hemodynamic stability, and reduced demand of rescue analgesics in 24 h as compared to clonidine, fentanyl, or lone bupivacaine [14,15].

Shaikh SI et al also studied dexmedetomidine as an adjuvant to hyperbaric spinal bupivacaine for infra-umbilical procedures. It was a dose related study. Various adjuncts have been used with local anesthetics in spinal anesthesia to provide good quality of intra-operative and better post-operative analgesia. Dexmedetomidine is a new α-2 adrenergic agonist, now being used as a neuraxial adjuvant. The aim of the present study was to investigate the effect of intrathecal administration of dexmedetomidine 5 µg and 10 µg, as an adjuvant to bupivacaine 0.5%, on the onset and duration of sensory and motor block, the hemodynamic effects, the duration of analgesia and the occurrence of side effects [16].

Sun Y et al did comparative evaluation of intrathecal bupivacaine alone, bupivacaine-fentanyl, and bupivacaine-dexmedetomidine in caesarean section. In this study, they aimed to compare the effects of bupivacaine alone, bupivacaine plus fentanyl, and bupivacaine plus dexmedetomidine for postoperative analgesia in women undergoing cesarean section under spinal anesthesia. Regression time to T10 was significantly longer in BvD group, sensory block was also prolonged in BvD group without any difference in duration of motor block. Onset of post-operative pain was delayed in BvD group. Sedation scores (VAS) were improved in case of BvD with least values of 0–3 followed by BvF. There was no significant difference in Apgar scores and neonatal arterial gas pressures across 3 groups. The use of dexmedetomidine as an adjuvant to bupivacaine in cesarean surgeries provides better intra-operative and post-operative analgesia without having significant impact on Apgar scores or incidence of side effects [17].

Al-Mustafa MM et al studied effect of dexmedetomidine added to spinal bupivacaine for urological procedures. The mean time of sensory block to reach the T10 dermatome was 4.7±2.0 minutes in D10 group, 6.3±2.7 minutes in D5, and 9.5±3.0 minutes in group N. The mean time to reach Bromage 3 scale was 10.4±3.4 minutes in group D10, 13.0±3.4 minutes in D5, and 18.0±3.3 minutes in group N. The regression time to reach S1 dermatome was 338.9±44.8 minutes in group D10, 277.1±23.2 minutes in D5, and 165.5±32.9 minutes in group N.

The regression to Bromage 0 was 302.9±36.7 minutes in D10, 246.4±25.7 minutes in D5, and 140.1±32.3 minutes in group N. Onset and regression of sensory and motor block were highly significant (N versus D5, N versus D10, and D5 versus D10, p<0.001). Dexmedetomidine has a dose dependent effect on the onset and regression of sensory and motor block when used as an adjuvant to bupivacaine in spinal anesthesia.[18]

Dexmedetomidine has made its application from a novel sedating agent in the intensive care unit to its use as an adjuvant in various regional anesthetic techniques because of its "cooperative sedation" without any respiratory depression. It has a favorable pharmacokinetic profile suitable to be used in the perioperative period to reduce the requirements of opioids and anesthetic drugs.

It maintains patient arousability and respiratory function or neurologic complications, produces prolonged sensory block, and it is evident that this type of block may be more suitable for major surgeries on the abdomen and lower extremities. Drawback of DXM supplemented spinal block characteristics in this study is the increase in the duration of motor block which may not suit short-term surgical procedures or ambulatory surgery [19,20].
Limitation

It provides good quality of intraoperative analgesia, hemodynamically stable conditions, minimal side effects, and excellent quality of postoperative analgesia.

Recommendations

01. Hemodynamically stable
02. No side effects
03. Prolonged sensory and motor block
04. Prolonged analgesia
05. No sedation

Conclusion

Intrathecal DXM supplementation of spinal block in the dose of 5 mcg seems to be a good clinical method especially in those that need quite long time with minimal side effects and excellent quality of spinal analgesia. As this produces earlier onset and prolonged duration of sensory and motor block without associated significant hemodynamic alterations. Five micrograms of DXM as adjuvant to spinal bupivacaine in surgical procedures of long duration has minimal side-effects, and Dexmedetomidine 5 μg given intrathecally improves the quality and the duration of postoperative analgesia.

What this study adds to existing knowledge?

Dexmedetomidine has made its application from a novel sedating agent in the intensive care unit to its use as an adjuvant in various regional anesthetic techniques because of its “cooperative sedation” without any respiratory depression. It has a favorable pharmacokinetic profile suitable to be used in the perioperative period to reduce the requirements of opioids and anesthetic drugs. There are few side-effects of dexmedetomidine, which should always be kept in mind before choosing the patients for its use. The various side-effects associated with dexmedetomidine include, but are not limited to hypotension, bradycardia, worsening of heart block, dry mouth, and nausea.

Author’s contribution

Dr. Richa Chauhan: Concept and Data collection

Dr. Sabih Ahmed: Data Analysis and Discussion

Dr. S K Bhattacharya: Guidance and Discussion

Reference


02. McCartney CJ, Brull R, Chan VW, et al. Early but no long-term benefit of regional compared with general anesthesia for ambulatory hand surgery. Anesthesiol. 2004;101(2)461-467. [Crossref]


05. Kuzma PJ, Kline MD, Calkins MD, Staats PS. Progress in the development of ultra-long-acting local anesthetics. Reg Anesth. 1997;22(6)543-51. [Crossref]


07. Watson B, Allen J. Spinal anaesthesia. Day Case Surgery. 2011;79. [Crossref]

08. Axelsson K, Gupta A. Local anaesthetic adjuvants- neuraxial versus peripheral nerve block. Curr Opin Anesthesiol. 2009;22(5)649-54. doi: 10.1097/ACO.0b013e32832ee847 [Crossref]

09. Förster JG, Rosenberg PH. Clinically useful adjuvants in regional anaesthesia. Curr Opin Anesthesiol. 2003;16(5)477-486. [Crossref]


16. Shaikh SI, Dattatri R. Dexmedetomidine as an adjuvant to hyperbaric spinal bupivacaine for infra-umbilical procedures- A dose related study. Anaes, Pain Intens Care. 2019;18(2)180-185. [Crossref]


