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Effects of Intravenous Dexmedetomidine on Bupivacaine Spinal Anaesthesia: A Placebo Controlled Randomised Trial

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Abstract

Background and Aims: Spinal anaesthesia is the most commonly used technique for lower abdominal & lower limb surgeries as it is very economical and easy to administer. However, postoperative pain control is a major problem because spinal anaesthesia using only local anaesthetics is associated with relatively short duration of action and thus early analgesic intervention is needed in the postoperative period. Dexmedetomidine, a new α-2 agonist agent is hypothesized to prolong the effect of spinal anaesthesia when given intravenously and more studies are awaited to prove its efficacy. Hence, this randomized clinical trial was conducted to study the effects of intravenous dexmedetomidine on 0.5% hyperbaric bupivacaine spinal anaesthesia. *Methods:* Total number of 60 cases undergoing abdominal or lower limb surgeries were selected. Patients were divided into 2 groups of 30 each (Group D & Group P). Group D patients received dexmedetomidine as loading dose & maintenance infusion. Group P patients received normal saline as loading dose & maintenance infusion (placebo). Postoperatively, the pain score, onset and duration of sensory and motor blockade were assessed. *Results:* Both groups were comparable in terms of age, weight, sex, ASA grade, and height. Duration of sensory blockade was significantly prolonged in dexmedetomidine group [(354.3±7.55 minutes) compared to Placebo group (268.3±11.30 minutes] (P value = 0.0001). Duration of motor blockade was significantly prolonged in dexmedetomidine group (310.83 ±13.36 minutes) compared to placebo group (234.97±10.0 minutes) (P value = 0.0001). *Conclusion:* Dexmedetomidine prolongs sensory and motor blockade due to spinal anaesthesia.

Keywords: Spinal anaesthesia, lower abdominal surgeries, dexmedetomidine

Introduction

Spinal anaesthesia is the most commonly used technique for lower abdominal & lower limb surgeries as it is very economical and easy to administer. However, postoperative pain control is a major problem because spinal anaesthesia using only local anaesthetics is associated with relatively short duration of action and thus early analgesic intervention is needed in the postoperative period. Hence an effective pain relief after surgery is essential for optimal care of surgical patients. Any method of post-operative analgesia must meet three basic criteria. It must be effective, safe and feasible (Morgan M 1982). A number of adjuvants such as clonidine and midazolam and others have been studied to prolong the effect of spinal anaesthesia [1,2]. Clonidine prolongs duration of intrathecally administered local anaesthetics & has potent antinocieptive properties [3,4,5].

Dexmedetomidine, a new α-2 agonist agent is hypothesized to prolong the effect of spinal anaesthesia when given intravenously and more studies are awaited to prove its efficacy [6].

In clinical studies conducted dexmedetomidine given by intravenous route prolongs the duration of sensory and motor blockade produced by spinal anaesthesia, along with providing sedation and analgesic effect.

Hence, this randomized clinical trial was conducted to study the

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effects of intravenous dexmedetomidine on 0.5% hyperbaric bupivacaine spinal anaesthesia.

Materials and Methods

Study Design

This study is a prospective, open labeled, placebo controlled, single center study.

The study was conducted in collaboration with a tertiary care level institute.

A synopsis of the study protocol was submitted to the Institutional Review Board / Ethics Committee and approval was obtained.

Selection

Total number of 60 cases undergoing abdominal or lower limb surgeries were selected.

Patients were divided into 2 groups of 30 each (Group D & Group P)

Randomization of the patients was done using computerized randomization charts.

Pre anaesthetic check up was done.

Group D patients received dexmedetomidine as loading dose & maintenance infusion.

Group P patients received normal saline as loading dose & maintenance infusion (placebo)

Inclusion and Exclusion Criteria

Inclusion Criteria

1. Age 18 to 50 years.
2. ASA grade I & II.
3. Sex male or female
4. Patient undergoing abdominal or lower limb surgeries

Exclusion Criteria

1. Hypertension
2. Ischaemic Heart disease
3. Valvular Heart disease
4. Diabetes Mellitus
5. COPD
6. Old age > 50 Yrs
7. Pediatric age < 16 yrs
8. Morbid obesity
9. Coagulation abnormalities
10. Pregnancy
11. Peripheral vascular disease
12. Liver and kidney disease
13. Allergy to local anaesthetic

Patients included in the study underwent thorough preoperative assessment including detailed case history, clinical examination and all necessary investigations.

Anaesthesia Procedure

All patients received diazepam 0.2 mg / kg orally, the night before surgery. The patients were preloaded with Lactated Ringer's solution 15 mL / kg. They were monitored with automated noninvasive blood pressure, pulse oxymetry, and electrocardiogram. 25G Pencil point spinal needles were introduced through L3–L4 interspaces in sitting position using aseptic precautions. Patients were randomly divided into the following groups: Group D—to receive 3 mL volume of 0.5% hyperbaric bupivacaine + Loading dose of 1µg / kg of dexmedetomidine intravenously over 10 minutes followed by 0.5µg / kg / hr. till the end of surgery Group P—to receive 3 mL volume of 0.5% hyperbaric bupivacaine + an equivalent quantity of normal saline as dexmedetomidine intravenously by infusion pump. Intrathecal injection was given over approximately 10–15 seconds. Immediately after completion of the injection patients were made to lie supine.

Oxygen (2 L / min) was administered via a mask if the pulse oximeter reading decreased below 90%. Hypotension, defined as a decrease of systolic blood pressure by more than 30% from baseline or a fall below 90 mmHg, was treated with incremental IV doses of mephentermine 6 mg and IV fluid as required. Bradycardia, defined as heart rate < 50 beats per minute, was treated with IV atropine 0.3–0.6 mg. The incidence of adverse effects, such as respiratory depression, sedation, bradycardia and hypotension were recorded. Sensory testing was assessed by loss of pinprick sensation to 23G hypodermic needle and dermatomes levels were tested every 2 min until the highest level had stabilized by consecutive tests. On achieving T7 sensory blockade level, surgery was allowed. Testing was then conducted every 15 min until the point of two segment regression of the block was observed. Further testing was performed at 30-min intervals until the recovery of S2 dermatome. The surgeon, patient, and the observing anesthesiologist

were blinded to the patient group. Data regarding the time to reach the highest level of sensory blockade from the time of injection, time to S1 level sensory regression, and incidence of side effects were recorded. Sedation was assessed by a modified Ramsay sedation scale.

Modified Ramsay Sedation Scale

1. Anxious, agitated, restless.
2. Cooperative, oriented, tranquil.
3. Responds to commands only.
4. Brisk response to light glabellar tap or loud noise.
5. Sluggish response to light glabellar tap or loud noise.
6. No response.

Postoperatively, the pain score was recorded by using visual analog pain scale (VAS) between 0 and 10 (0 = no pain, 10 = most severe pain), initially every 1 h for 2 h, then every 2 h for the next 8 h and then after every 4 h till 24 h. Diclofenac was given intramuscularly as rescue analgesia when VAS was >4. A follow-up was carried out 1 week postoperatively by the blinded anesthesiologist, who asked about postoperative headache as well as postoperative pain and dysesthesia in the buttock, thighs, or lower limbs.

Statistical Analysis

The data was managed in Microsoft excel spreadsheet. Demographics are described with average, standard deviation, minimum and maximum observation. Demographics and General information like count, average and percentage for various parameters with all permutations and combinations were calculated in Microsoft excels."Two Sample T Test" is used to investigate and model impact of various parameters like Sensory onset, Motor onset, Duration of Motor Blockade, Duration of Sensory Blockade, Duration of surgery and Duration of Analgesia. A P value <0.05 was considered statistically significant. All graphs are drawn and all statistical analysis was done using Minitab 16.

Results

Both groups were comparable in terms of age, weight, sex, ASA grade, and height.

Both groups were comparable in terms of duration of surgery, onset of sensory and motor blockade and duration of analgesia.

Duration of sensory blockade i.e. time for regression to S1 dermatome was significantly prolonged in dexmedetomidine group [(354.3±7.55 minutes) compared to Placebo group (268.3 ± 11.30 minutes] (P value = 0.0001) (Table 1).

Duration of motor blockade given by the regression time required to reach the modified Bromage scale 0 was significantly prolonged in dexmedetomidine group (310.83 ± 13.36 minutes) compared to placebo group (234.97±10.0 minutes) (P value = 0.0001) (Table 2).

Significantly higher number of patients in dexmedetomidine group [7/30] had bradycardia (heart rate < 60) as compared to placebo group [0/30](P value = 0.003) in the present study. A significantly higher incidence of hypotension (lowest SBP > 20% below baseline values) was noted in patients of dexmedetomidine group [9/30] as compared to placebo group [2/30](P value = 0.014) in the present study.

Table 1: Table showing comparison of mean duration of sensory blockade (minutes) in dexmedetomidine group and placebo group

Group	Number of patients	Duration of sensory blockade(minutes) Mean	SD	P-value
Dexmedetomidine	30	354.3	7.55	0.0001
Placebo	30	268.3	11.30	P<0.05;significant

Table 2: Table showing comparison of mean duration of motor blockade (minutes) in dexmedetomidine group and placebo group

Group	Number of patients	Duration of motor blockade(minutes) Mean	SD	P-value
Dexmedetomidine	30	310.83	13.36	0.0001
Placebo	30	234.97	10.00	P<0.05;significant

Discussion

The subarachnoid block has an important role in the practice of anaesthesia since the time it is known. It provides effective analgesia and adequate muscle relaxation and thus imparts optimal operating conditions with minimal physiological and biochemical alterations in the patients.

Spinal anaesthesia is the most commonly used technique for lower limb surgeries as it is very economical and easy to administer. But pain control is a major problem because spinal anaesthesia using only local anaesthetics is associated with relatively short duration of action and thus early analgesic intervention is needed in the post operative period.

Pain in the post-operative period is associated with various systemic side effects including respiratory, cardiovascular and other systems, which increases the morbidity and mortality.

One of the important roles of the anaesthesiologist is to provide analgesia during surgery as well as in the post-operative period. The effective management of post-operative pain is to ensure that the patient gets pain relief at the appropriate time without any complications.

Pain relief has always been bought at a price. Parenteral narcotic analgesia goes hand in hand with respiratory depression. Continuous epidural analgesia using local anaesthetics gives segmental pain relief but it also produces cardiovascular depression due to sympathetic blockade and is associated with high incidence of urinary retention.

Different drugs like epinephrine, phenylephrine, adenosine, magnesium sulphate, sodium bicarbonate, neostigmine and α_2 agonists like clonidine, dexmedetomidine have been used as adjuvants to local anaesthetics to prolong the duration of spinal anaesthesia. Among them clonidine an alpha$_2$ agonist is widely used by oral, intravenous and intrathecal routes as an adjuvant to prolong spinal anaesthesia. Recent studies have shown the efficacy of both intrathecal and intravenous dexmedetomidine in prolonging spinal anaesthesia. α_2-adrenoreceptor agonists act at pre- and postsynaptic adrenoceptors and their pharmacology is complex. The human α_2-adrenoreceptors can be classified into α_2A, α_2B and α_2C adrenoreceptors subtypes. These receptor subtypes are distributed ubiquitously and each may be responsible for a specific action of α_2-agonists. The predominant α_2-adrenoreceptor agonist subtype mediating sedative and antinociceptive actions is the α_2A-adrenoceptor. Whereas stimulation of α_2B-adrenoceptor mediates the vasoconstrictive cardiovascular effect, which causes the initial hypertension observed after the administration of α_2-adrenoreceptor agonists. The α_2C-adrenoreceptors subtype has in a wide range of anaesthetic been shown to modulate dopaminergic neurotransmission, hypothermia and a variety of behavioral responses. The hypnotic effect of dexmedetomidine is mediated by the hyperpolarization of noradrenergic neurons located in the locus ceruleus [7]. Dexmedetomidine acts through a G-protein coupled receptor that produces an inhibition of adenylcyclase and this results in decreased formation of cyclic AMP (cAMP), that is an important regulator of many cellular functions acting in various intracellular subsystem like the Placebo of phosphorylation state of regulatory proteins. Other effects of α_2-adrenoreceptor agonists include activation of potassium ion channels causing efflux of potassium and an inhibition of calcium entry into calcium channels in neuronal cell [8]. These effects lead to change in membrane ion conductance and produce hyperpolarization of the membrane which suppresses neuronal activity. The main effect is an inhibition of noradrenaline release causing a reduction of excitation, especially in locus ceruleus [9]. The locus ceruleus is small neuronal nucleus located bilaterally in the upper brainstem and is the major site of noradrenergic innervations in the brain. The locus ceruleus has also been implicated as a key modulator for a variety of important brain functions, including arousal, sleep, anxiety, antinociception [10] and drug withdrawal associated with CNS depressants, like opioids. Dexmedetomidine inhibits the release of Substance P from the dorsal horn of spinal cord, leading to primary analgesic effects [11].

In the present study the effects of intravenous dexmedetomidine on 0.5% bupivacaine spinal anaesthesia was compared to effects of placebo on 0.5% bupivacaine spinal anaesthesia in patients posted for lower abdominal and lower limb for orthopaedic procedures. The onset and duration of sensory and motor block, postoperative analgesia, hemodynamic changes and any side effects were studied. It was observed that intravenous dexmedetomidine prolongs the duration of sensory and motor blockade due to spinal anaesthesia.

Conclusion

Inferences drawn from this study are as follows:

- There was no difference in the onset of sensory and motor blockade in both the groups. The duration of sensory and motor blockade was significantly prolonged when intravenous dexmedetomidine was administered with spinal anaesthesia as compared to placebo.
- The duration of analgesia was significantly prolonged when intravenous dexmedetomidine was administered with spinal anaesthesia as compared to placebo.
- Incidence of bradycardia was found in 7 patients out of 30 in dexmedetomidine group and none in placebo group. Bradycardia was managed by Atropine 0.6mg intravenously.
- Incidence of hypotension was found in 9 out of 30 patients in dexmedetomidine group and 2 out of 30 patients in placebo group. It was managed by mephenteramine 6mg intravenously.
- Incidence of sedation was found in all patients of dexmedetomidine group and none in placebo group.

To Conclude

1. Intravenous dexmedetomidine has no significant effect on the onset of sensory and motor blockade of bupivacaine spinal anaesthesia. However, intravenous dexmedetomidine significantly prolongs sensory and motor blockade of bupivacaine spinal anaesthesia.
2. There is significant bradycardia which is transient and can be managed with atropine. There is significant hypotension which can be managed with mephenteramine.
3. Intravenous dexmedetomidine prolongs duration of postoperative analgesia significantly.
4. Dexmedetomidine additionally provides excellent sedation during surgery and sedation scores reach normal within 15 minutes of stopping the drug.

References

1. Vadalouca A. Adjuvant drugs. Chapter in textbook of regional anaesthesia; Churchill Livingstone; 2002.p.215-229.
2. Rhee K, Kang K, Kim J, Jeon Y. Intravenous clonidine prolongs bupivacaine spinal anaesthesia. Acta Anaesthesiol Scand. 2003; 47:1001–5.
3. Fogarthy DJ, Carbine UA, Milligan KR. Comparison of analgesic effects of intrathecal Clonidine & intrathecal morphine after spinal anaesthesia in patients undergoing total hip replacements. British Journal of anaesthesia1993; 71:661-4.
4. Yaksh TL,Reddy SV.Studies in primate on the analgesic effects associated with intrathecal action of opiates, alpha adrenergic agonist & baclofen. Anaesthesiology 1981; 54:451-67.
5. Liu S,Chiu AA,Neal JM,et al.Oral Clonidine prolongs lignocaine anaesthesia in human volunteers. Anaesthesiology 1995; 82:1353-9.
6. J-Y. Hong, W. O. Kim, Y. Yoon, Y. Choi, S-H. Kim and H.K. Kil Effects of intravenous dexmedetomidine on low-dose bupivacaine spinal anaesthesia in elderly patients Acta Anaesthesiologica Scandinavica 2012; 56(3):382-387
7. Chiu TH, Chen MJ, Yang YR, Yang JJ, Tang FI. Action of dexmedetomidine on rat locus coeruleusneurones: intracellular recording in vitro. Eur J Pharmacol 1995; 285:261-8.
8. Khan ZP, Ferguson CN, Jones RM. alpha-2 and imidazoline receptor agonists. Their pharmacology and therapeutic role. Anaesthesia 1999; 54:146-65.
9. Jorm CM, Stamford JA. Actions of the hypnotic anaesthetic, dexmedetomidine, on noradrenaline release and cell firing in rat locus coeruleus slices. Br J Anaesth. 1993; 71:447–9.
10. Guo TZ, Jiang JY, Buttermann AE, Maze M. Dexmedetomidine injection into the locus ceruleus produces antinociception. Anaesthesiology. 1996; 84:873–81.
11. Arcangeli A, D'Alo C, Gaspari R. Dexmedetomidine use in general anaesthesia. Current Drug Targets 2009; 10:687-695.