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Original Research Article

Effect of Dexmedetomidine as an Adjuvant to Bupivacaine on Duration of Analgesia, Motor and Sensory Blockade and the Intraoperative Hemodynamic Profile of Patients

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Conflict of interest: Nil

Abstract:

Background: The addition of dexmedetomidine also allows for a reduction in the total dose of the local anaesthetic used, which translates into better hemodynamic stability in the intraoperative period. Dexmedetomidine has also been shown to have significant analgesic affect in the post-operative period much after the regression of the motor blockade which allows for early and pain free ambulation. In the view of these facts, this study was planned to compare the effect of dexmedetomidine on duration of analgesia, motor and sensory blockade and the intraoperative hemodynamic profile when used as an adjuvant to bupivacaine.

Methods: This was a prospective study was done in Department of Anaesthesiology, Calcutta National Medical College during February, 2012 to March, 2013 among the patients (age: 18-65 years) undergoing elective infra-umbilical surgery. Total sample size i.e. 60 patients were randomly divided into 2 groups (Group B and Group D) of 30 patients each using a computer generated random number table. Motor blockade was assessed by using the modified Bromage scale bilaterally every 2 minutes. The regression for sensory and motor block was checked every 15 minutes in a post anaesthesia care room. Differences in demographic, anaesthetic and post-operative data were tested by independent Student's t-test (continuous data) or by Pearson Chi-square test and Fisher's exact test (categorical data). A p value less than 0.05 is taken as significant.

Results: In our study, there was no fall or excess rise of heart rate in any group at any specific time period and mean heart rate in both groups were comparable over time. As oxygen saturation of different groups were almost identical with each other, it can be concluded that there was no hemodynamic and respiratory problem in any group. Group-B patients took 172.5±12.92 minutes to regain Bromage score 0, and group-D patients took 260.5±20.27 minutes. So, motor blockade was prolonged in dexmedetomidine group. Group-B patients asked after 156.5±18.76 minutes, but group-D patients requested for analgesic much later i.e. after 249±22.83 minutes. So, the inference would be that dexmedetomidine increases the time of post-operative analgesia.

Conclusion: Our conclusion from the study is that dexmedetomidine as intrathecal adjuvant significantly prolongs the sensory and motor blockade of intrathecal hyperbaric bupivacaine without altering the onset of spinal anaesthesia.

Keywords: Dexmedetomidine, Normal Saline, Hyperbaric Bupivacaine, Spinal, Infraumbilical.

Introduction

Lower limb and lower abdominal surgeries can be done under general anaesthesia as well as central neuraxial block or local nerve block. However central neuraxial block especially subarachnoid block has gained popularity because of its ease of administration, high success rates, ability to provide good operative conditions, quick onset and better muscle relaxation [1]. Spinal anaesthesia with local anaesthetic alone has a short duration of action. The short duration of action creates lots of difficulties for surgeons, anaesthesiologist and the patient as duration of spinal anaesthesia sometimes falls short than the duration of surgery. It limits the type of surgeries that can be performed with spinal anaesthesia. Many a time it also warrants conversion to general anaesthesia midway between surgeries due to wearing off of the effect of spinal anaesthesia. Moreover, early analgesic intervention is required to manage postoperative pain control after spinal anaesthesia with local anaesthetics alone. Hence number of adjuvants, such as clonidine, dexmedetomidine, midazolam, opioids, neostigmine and magnesium sulphate has been studied to prolong the effect of spinal anaesthesia [2,3]. Adjuvants are added to increase the duration and density of block but they are not free from side effects. For example, opioids cause pruritus, respiratory depression, urinary retention [4] and neostigmine produces severe nausea & vomiting and pruritus [5]. So, the search goes on for a better intrathecal adjuvant. Dexmedetomidine, a highly selective, specific, and potent α2 adrenergic agonist (1620:1 α2 to α1) [6], has come into use in recent times. Dexmedetomidine has been repeatedly demonstrated to prolong sensory and motor block when used intrathecally with local anaesthetics [2,3,7]. Dexmedetomidine has also been known to affect blood pressure in a complex fashion after intrathecal administration, because of opposing actions at multiple sites. The addition of dexmedetomidine also allows for a reduction in the total dose of the local anaesthetic used, which translates into better hemodynamic stability in the intraoperative period [2,3]. Dexmedetomidine has also been shown to have significant analgesic affect in the post-operative period much after the regression of the motor blockade which allows for early and pain free ambulation [8,9]. In the view of these facts, this study was planned to compare the effect of dexmedetomidine on duration of analgesia, motor and sensory blockade and the intraoperative hemodynamic profile when used as an adjuvant to bupivacaine. This study also aims to ascertain the safety of these drugs for use in routine hospital practice.

Materials and Methods

Study design and subjects

This was a unicentric prospective randomized, single blinded, observational study done in Department of Anaesthesiology, Calcutta National Medical College in association with Urology, orthopaedic and gynaecology & obstetrics during February, 2012 to March, 2013. The patients (age: 18-65 years) undergoing elective infra-umbilical surgery in supine position having American Society of Anaesthesiology physical status I and II.

The patients with allergy to study drugs, contra-indication to spinal anaesthesia, obstetric patients, uncontrolled and labile hypertension, addiction to any substances like opium, alcohol, patients taking sedative drugs, suffering from uncontrolled diabetes, any kind of neurological illness, psychological illness, having spinal deformity, Hepatic or renal disorders or Haematological disorder were excluded from the study. Clearance from the institutional ethics committee is obtained first. Informed consent from patients were also obtained.

Sample size

Sample size was calculated from a similar study done by Kanazi et al., [3] in 2006, taking that as our reference study. Kanazi et al., in 2006 found the mean duration of 2 segment regression in dexmedetomidine group was 122 minutes (standard deviation 37 minutes). Using this data, the minimum number of patients required in each group is 25 [taking significant p value <0.05 (i.e. α error 5%), power of study 80% (i.e. β error 0.2) and software used is "computer programmes for epidemiologists (PEPI) by J. H. Abramson and Paul M. Gahlinger version 4.0x"].For convenience 30 patients have been taken in each group. So, total sample size is 30+30 = 60. Total sample size i.e. 60 patients were randomly divided into 2 groups of 30 patients each using a computer generated random number table. Groups were designated according to the study drug received, as follows: Group B- received 2.6 ml of hyperbaric bupivacaine(13 mg) and 0.4 ml of normal saline, and Group D- received 2.6 ml of hyperbaric bupivacaine(13 mg) and 5 μg of dexmedetomidine (0.05 ml) and 0.35 ml of normal saline.

Procedure

The patients were again checked on the day before surgery and counselled again about the anaesthesia procedure. They were also advised to take a tablet ranitidine 150 mg before supper, light meal and tablet alprazolam 0.25 mg at bed time on the night before surgery and would remain nil by mouth after that. They were asked to take tab ranitidine 150 mg on the morning of surgery with sips of water and also to continue their usual medication, if any. On arrival to the operating theatre, the identity of the patient was confirmed and consent was checked. Then monitors are attached and baseline parameters were noted. ECG, SpO2 and non-invasive blood pressure (NIBP) were monitored before, during and after the surgery.

The subarachnoid block was performed with the study drugs with the patient in standard sitting position with a 25G Quinke's needle at L3-L4 intervertebral space using midline approach maintaining strict aseptic condition. After spinal injection patients were positioned in supine position and oxygen was provided through a nasal cannula at 2 litres per min. After 2 minutes, every 2 minutes sensory nerve block was assessed bilaterally by using insensitivity to cold (when cotton swab soaked with alcohol was applied) in the midclavicular line. Motor blockade was assessed by using the modified Bromage scale [10] bilaterally every 2 minutes. The regression for sensory and motor block was checked every 15 minutes in a post anaesthesia care room. Patients were discharged from the post anaesthesia care room after sensory block regresses to S1 dermatome level and motor block to Bromage 0. No analgesic drug was given in the immediate post-operative period until the patient requested for analgesia and time for first analgesia will be recorded.

Any incidence of adverse effects in the intraoperative or immediate postoperative period were noted and again patients were followed up at 24 hours in the ward for incidence of nausea, vomiting or any other adverse reaction.

Data collection: A pretested proforma was used to collect the patients details such

demographic (Age, Sex, Body weight and Height, clinical parameters [Heart rate, Blood pressure - systolic, diastolic and mean arterial pressure, O2 saturation (SpO2), Time to achieve sensory block of T10, Time to achieve peak level of sensory block, Peak sensory block level, Time to achieve Bromage score3 motor block, Time to regress 2 segments from peak level, Time taken to regress to S1 segment, Time of 1st analgesic request and Time to regain Bromage score 0] and adverse effects (Bradycardia, Hypotension, Arrhythmia, Sedation, Respiratory depression, Nausea and vomiting, and Post Dural puncture headache).

Data Analysis

Discrete categorical data are presented as Number and percentage; continuous data are given as mean ± Standard deviation. Differences in demographic, anaesthetic and post-operative data were tested by independent Student's t-test (continuous data) or by Pearson Chi-square test and Fisher's exact test (categorical data). A p value less than 0.05 is taken as significant.

Results

A total of 60 patients (50% were male and 50% were female) were enrolled into study. In group-B 40% were male and 60% were female. In group-D 60% were male and 40% were female. In group-B 50% were Hindu and 50% were Muslim. In group-D 46.67% were Hindu and 53.33% were Muslim. When compared with student t test age, weight, height and BMI were comparable between all groups with all insignificant p values (Table 1).

Table 1: Baseline characteristics of the patients

Variables	GROUP-B	GROUP-D	p value
Age (years)	39±10.93	41.37±12.98	0.734
Weight (kgs.)	57.01±4.49	55.52±3.43	0.358
Height (cms.)	161.35±4.42	161.32±3.89	0.999
BMI (kg/m2)	21.95±2.15	21.37±1.73	0.557
Gender			
Female	18	12	0.121
Male	12	18	
Religion			
Hindu	15	14	0.796
Muslim	15	16	

In our study, maximum surgery performed were lower limb orthopaedic surgery (35%), then TURP (21.66%), then vaginal hysterectomy (23.33%) and total abdominal hysterectomy (20%). Type of surgery in different groups were almost identical. Number of ASA physical status I and ASA physical status II patients were comparable in both groups (Table 2).

Table 2: Surgical characteristics of the patients

Variables	GROUP-B	GROUP-D	p value
Type of surgery			
Total Abdominal Hysterectomy	7	5	0.840
TURP	7	6	
Lower Limb Orthopaedic Surgery	9	12	
Vaginal Hysterectomy	7	7	
ASA physical status			
ASA physical status I	22	23	0.765
ASA physical status II	8	7	

In our study, there was no fall or excess rise of heart rate in any group at any specific time period and mean heart rate in both groups were comparable over time. As oxygen saturation

of different groups were almost identical with each other, it can be concluded that there was no hemodynamic and respiratory problem in any group. There was no fall or rise of mean arterial pressure in any group intraoperatively or postoperatively and the mean arterial pressure of both groups were comparable ($p>0.05$) so, it can be said that dexmedetomidine preserve hemodynamic stability when used as intrathecal adjuvant to hyperbaric bupivacaine (Figure 1).

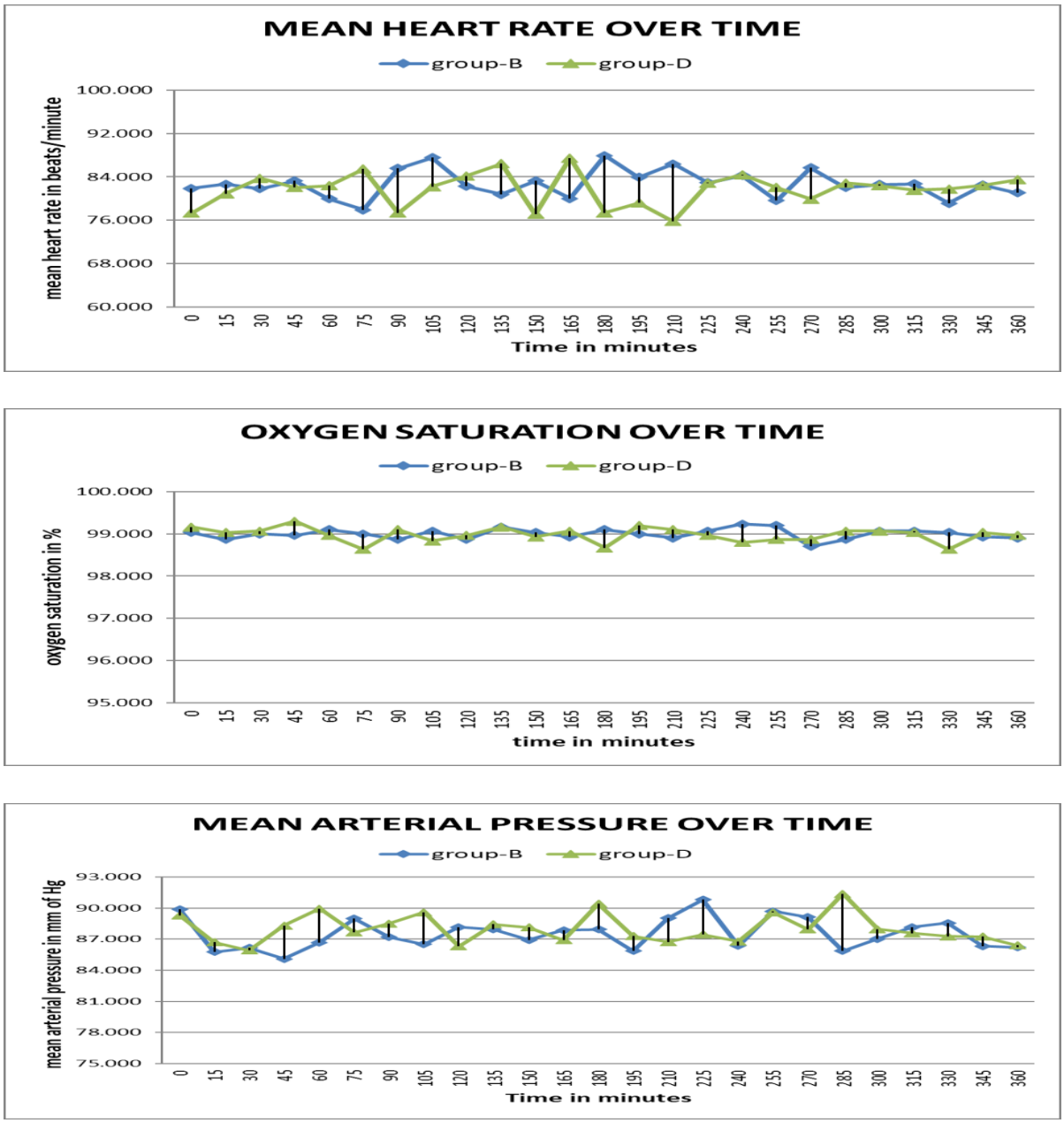

Figure 1: Comparison of hemodynamic and respiratory parameters among patients

In our study the mean time to achieve T10 level sensory block in group-B was 5.73±1.46 minutes, in group-D was 6±1.49 minutes. In group-B patients time for 2 segment regression was 92.5± 13.11 minutesand in group-D patients higher (157±11.64 minutes). So, it can be said that dexmedetomidine is superior in prolonging 2 segment regression time.In group-B patients S1 regression time was 195±14.74 minutes and in group-D patients highest (303±25.66 minutes). So,

it can be said that dexmedetomidine is better alternative in prolonging the time for regression to S1 level. Group-B patients took 172.5±12.92 minutes to regain Bromage score 0, and group-D patients took 260.5±20.27 minutes. So, motor blockade was prolonged in dexmedetomidine group. Group-B patients asked after 156.5±18.76 minutes, but group-D patients requested for analgesic much later i.e. after 249±22.83 minutes. So, the inference would be that dexmedetomidine increases the time of post-operative analgesia (Table3).

Table 3: Comparison of sensory and motor block anaesthetic features among patients

Variables	GROUP-B	GROUP-D	p value
T10 sensory block time (minutes)	5.73±1.46	6±1.49	0.751
Peak level of sensory block			
T4	6	5	0.718
T5	15	13	
T6	9	12	
Peak sensory block time (minutes)	12.93±2.19	13.53±1.72	0.442
BROMAGE 3 motor block time (minutes)	7.73±2.39	7.13±1.63	0.487
2 segment regression from peak level (minutes)	92.5±13.11	157±11.64	<0.0001
Time to regress to S1 segment (minutes)	195±14.74	303±25.66	<0.0001
Time to regress to BROMAGE 0 motor block (minutes)	172.5±12.92	260.5±20.27	<0.0001
Time to 1st analgesic request (minutes)	156.5±18.76	249±22.83	<0.0001

The incidences of different side effects were low in the perioperative period up to a period of 24 hours and they were comparable between both the groups (p>0.05) (Table 4).

Table 4: Side effects of the anaesthesia among patients

Side effects	GROUP-B	GROUP-D	p value
Bradycardia	1	2	0.553
Hypotension	2	3	0.64
Nausea & Vomiting	3	2	0.64
Post Dural Puncture Headache	1	1	1

Discussion

Dexmedetomidine, the new highly selective α2-agonist drug, is now being used as a neuraxial adjuvant for spinal anaesthesia with bupivacaine. In our study the mean time to achieve T10 level sensory block in group-B was 5.73±1.46 minutes, in group-D was 6±1.49 minutes. In group-B patients time for 2 segment regression was 92.5± 13.11 minutes and in group-D patients higher (157±11.64 minutes). So, it can be said that dexmedetomidine is superior in prolonging 2 segment regression time.

In group-B patients S1 regression time was 195±14.74 minutes and in group-D patients highest (303±25.66 minutes). So, it can be said that dexmedetomidine is better alternative in prolonging the time for regression to S1 level.

Kanazi et al., [3] found that dexmedetomidine (3 μg), when added to intrathecal bupivacaine (12 mg), produces a significant prolongation in the duration of the motor and sensory block with preserved hemodynamic stability and lack of sedation. Al-Mustafa et al., [11] found that addition of dexmedetomidine with bupivacaine for spinal anaesthesia decreases onset of block and prolongs duration of block without any significant side effects. In another by Al-Mustafa et al., [12] concluded that in women undergoing vaginal reconstructive surgery

under spinal analgesia, dexmedetomidine produces prolonged motor and sensory block. Overall incidence of side effects was also less in dexmedetomidine receiving group.

In a study done by Gupta et al., [13]patients in dexmedetomidine group had a significantly longer sensory and motor block time. The mean time of sensory regression to S1 and regression time of motor block to reach modified Bromage 0 was significantly longer in dexmedetomidine group than bupivacaine. Shuklaet al., [14] reported that the onset time to reach peak sensory and motor level was shorter in dexmedetomidine group and had significant longer sensory and motor block times than patients in the control group. Singh et al., [15] in 2012 concluded dexmedetomidine prolonged duration of sensory and motor block of bupivacaine, dexmedetomidine is better in terms of longer duration of action. They did not find any increase in side effects.

Group-B patients took 172.5±12.92 minutes to regain Bromage score 0, and group-D patients took 260.5±20.27 minutes. So, motor blockade was prolonged in dexmedetomidine group. Group-B patients asked after 156.5±18.76 minutes, but group-D patients requested for analgesic much later i.e. after 249±22.83 minutes. So, the inference would be that dexmedetomidine increases the time of post-operative analgesia. Bogra et al., [16]concluded dexmedetomidine also has similar potential to prolong spinal anaesthesia of bupivacaine. Fewer studies are available which compare a combination of intrathecal dexmedetomidine and local anaesthetics. Fukushima et al., [17] administered 2 μg/kg epidural dexmedetomidine for postoperative analgesia in humans but did not report neurologic deficits. Gupta et al., [13] compared the duration of motor and sensory blockade and haemodynamic stability on adding dexmedetomidine with hyperbaric bupivacaine in patients who underwent lower abdominal surgeries and reported similar findings. Our study has shown similar results. In our study, the patients administered 5μg intrathecal dexmedetomidine reported longer duration of sensory and motor block.

Conclusion

Our conclusion from the study is that dexmedetomidine as intrathecal adjuvant significantly prolongs the sensory and motor blockade of intrathecal hyperbaric bupivacaine without altering the onset of spinal anaesthesia. In equipotent doses dexmedetomidine is more effective as intrathecal adjuvant to hyperbaric bupivacaine than normal saline. Neither normal saline nor dexmedetomidine increases side-effects of spinally administered hyperbaric bupivacaine if given in appropriate doses.

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