EVALUATION OF THE EFFECT OF SINGLE BOLUS DOSE OF INTRAVENOUS DEXMEDETOMIDINE IN SPINAL ANAESTHESIA FOR LOWER LIMB SURGERIES.

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ABSTRACT

Introduction

The use of intrathecal adjuvants in spinal anaesthesia in enhancing and prolonging it's action has been well established and is widely used for surgery below the umbilicus. Dexmedetomidine, a selective α_2A receptor agonist is a suitable adjuvant due to its selective activity.

Objectives

To evaluate the effect of a single bolus dose of intravenous dexmedetomidine as an adjuvant in cases undergoing lower limb surgeries under spinal anaesthesia.

Methodology

One hundred patients posted for lower limb surgery under spinal anaesthesia with hyperbaric bupivacaine, were equally divided into two groups. In group D, in addition to spinal, intravenous dexmedetomidine 0.5mcg/kg over 10 min was given whereas group C patients received spinal and intravenous normal saline .

Results

The onset of sensory and motor block was faster in group D (2.09 ± 0.71 min, 3.18 ± 1min)compared to group C (3.5 ± 0.82 min, 6.19 ± 1.87 min) which was statistically significant . The duration of sensory and motor block was also significantly prolonged in Group D (174.5 ± 14.04 min, 133.4 ± 10.42 min) as compared to Group C(138.2 ± 11.51 min, 120.4 ± 8.8 min). The duration of analgesia in Group D (225.3 ±20.11 min)was prolonged when compared to Group C (168.3 ± 15.11).

Conclusion

Intravenous dexmedetomidine as a single bolus dose before spinal anaesthesia can fasten the onset of sensory and motor block, prolongs the duration of sensory and motor block and also increased the duration of analgesia.

KEY WORDS

Adjuvants; analgesia; bupivacaine; dexmedetomidine; lower extremity; pain management; spinal anesthesia.

INTRODUCTION

Post-operative pain still remains the most common type of acute pain and is dreaded by all patients undergoing surgery. Analgesia for post-operative pain control is essential and insufficient post-operative pain control can produce various effects on quality of life, prolong the recovery time and decreases patient satisfaction.[1] Various types of analgesia regimens are used for attenuation of post-operative pain. Insufficient post-operative pain may activate the sympathetic nervous system and hence contribute to increased myocardial oxygen consumption which may further lead to myocardial ischemia and infarction leading to decrease in myocardial oxygen supply.[2] Uncontrolled post-operative pain is a major concern for an anaesthesiologist as the patients are not pain free and are dissatisfied.

Spinal anaesthesia is commonly used for surgeries below the umbilicus.[3] Adjuvants with opioids such as fentanyl, morphine or buprenorphine are sometimes added to improve and enhance the quality and duration of block. The adjuvants added to local anaesthetics prolong the effects of the drug and enhance post-operative pain relief.[4] Non-opioids adjuvants like clonidine and dexmedetomidine also prolong the effects of the drug.[5] Only few studies have shown use of intravenous dexmedetomidine and clonidine to enhance and prolong the effect of spinal anaesthesia.[6] Intravenous adjuvants also decrease the sympathetic tone and stress response to surgery and anaesthesia apart from sedation and analgesia.[7] At the substantia gelatonisa, stimulation of α_2 receptors in the spinal cord leads to inhibition of the release of substance P contributing to their analgesic action.[8]

Dexmedetomidine, a selective α_2 A receptor agonist have shown to be more suitable than clonidine as an adjuvant in spinal anaesthesia and can potentiate its action.[9] The efficacy of intravenous dexmedetomidine in prolonging the action of intrathecal local anaesthetics in addition to providing sufficient post-operative analgesia has been seen in only a few studies.[10] The present study is an attempt to evaluate the effect of single bolus dose of intravenous dexmedetomidine in spinal anaesthesia with 0.5% hyperbaric bupivacaine in patients undergoing lower limb surgeries.

METHODOLOGY

A prospective randomized double blind study was conducted in100 patients after ethical clearance from the institutional review committee. Informed and written consent was taken. Patients belonged to ASA I and II, aged 16-60 years and posted for lower limb surgery at Nobel Medical College over a period of one yearfrom August 2018 to August 2019. The sample size of this study was calculated with reference from similar study done in India, for standard deviation (σ) = 2.52 and desirable error (d) = 1[24] We calculated the sample size with 95% confidence interval (Z_1- $a/_2$) = 1.96. So the minimum sample size per group is 50, making a total of 100 for two groups. Patients of ASA III and IV, patients on calcium channel blockers, ACE inhibitors, or clonidine, patients on sedatives, opioids or antidepressants, any allergy to study drugs and contraindications to spinal anaesthesia were excluded from our study.

A total of 100 patients were divided into two groups of 50 each, viz. group D (dexmedetomidine) and group C (control) using sealed envelope technique. Routine pre-anaesthetic check-up was done a day prior to surgery and all patients were explained about the anaesthetic technique and prescribed tab ranitidine 150mg orally on the evening prior to surgery. Nil per oral for at least 8 hours prior to surgery was maintained. After briefing the patients about the procedure in the operative room, an 18G intravenous cannula was inserted in the non-dominant hand and ringer lactate (RL) was infused at a rate of 20ml/kg. Standard ASA monitors were attached. Baseline heart rate, blood pressure, oxygen saturation and ECG were recorded. The anaesthetic nurse was blinded in the randomization schedule and the nurse used an identical syringe to prepare both control and study drug. Using a sealed envelope technique, the patients were randomly divided into two groups. Group D received dexmedetomidine 0.5mcg/kg and group C received normal saline. Both study and control drugs were premixed to a total volume of 30 ml and given intravenously over 10 min as a single bolus dose by an anaesthetist not involved in the study. Under all aseptic precautions spinal anaesthesia was given with 3ml of 0.5 % hyperbaric bupivacaine. After SAB, vitals were recorded every 2 min for first 10 min then every 5 min till the end of surgery and then every 15 min in post anaesthesia care unit (PACU). In our study hypotension was defined as systolic BP<90 mmhg from the baseline. Bradycardia was defined as heart rate <50 beats/min. Hypotension was treated with intravenous fluids and incremental IV mephentermine 6mg. Bradycardia was treated with IV atropine 0.6mg. Oxygen was supplemented via simple face mask at 5L/min.Other side effects like nausea and vomiting were not found in the study.

Sensory blockade was checked in midaxillary line with an alcohol swab. Onset of sensory block and sensory recovery were noted. Sensory blockade was assessed every 2 min for the first 10 min and then every 15 min during surgery and post operatively. Modified bromage scale (0=able to move hip, knee and ankle; 1=unable to move hip but able to move knee and ankle; 2=unableto move hip and knee and but able to move ankle; 3=unable to move hip, knee and ankle) was used to assess the intensity of motor blockade. Onset of motor block and recovery were noted. Motor blockade was assessed every 2 min before the start of surgery and then every 15 min in post anaesthesia care unit. All the duration were calculated considering the time of spinal injection as time zero. Duration of analgesia was considered as time from the onset of sensory block to the time of administration of first rescue analgesics which was administered when the visual analogue scale (VAS) was >3. Throughout the study, the level of sedation was recorded using Ramsay Sedation

Score(RSS).Patients were discharged from PACU after modified bromage scale was zero and sensory regression to S1.

Analysis of data was done using SPSS windows version 21.0 Armonk NY: IBM Corp. Mean, standard deviation and % were calculated and expressed with graphical and tubular presentation for descriptive statistics. For inferential statistics Chi square test and independent t test were applied to find out significant differences between the two groups and other selected variables at 95% confidence interval where p considered as <0.05 was statistically insignificant.

RESULTS

DEMOGRAPHIC DATA

Patients on both side were comparable according to age, gender, weight, ASA physical status as shown on Table no. 1.

Table 1: Demographic Data

Variable	Group D	Group C	p-value
Mean Age ± SD (yrs)	35.44 ± 12.36	35.8 ± 12.67	0.886
Gender (M/F)	40/10	36/14	0.349
Mean weight ± SD (Kg)	58.6 ± 6.13	58.84 ± 5.79	0.841
ASA (I/II)	35/15	39/11	0.362

Spinal Anesthesia

The mean onset of sensory block was faster in dexmedetomidine group (2.09 ± 0.71 min) compared to control group (3.5 ± 0.82 min)which was statistically significant (P < 0.001). The mean duration of sensory block was prolonged in dexmedetomidine group (174.5 ± 14.04 min) compared to control group (138.2 ± 11.51 min)which was statistically significant (P < 0.001) .The mean onset of motor block was faster in dexmedetomidine group (3.18 ± 1 min) compared to control group (6.19 ± 1.87 min)which was statistically significant (P<0.001). The mean duration of motor block was prolonged in dexmedetomidine group (133.4 ± 10.42 min)compared to control group (120.4 ± 8.8 min)which was statistically significant (P < 0.001).In dexmedetomidine group, the mean duration of analgesia (from the time of intrathecal deposition of drug till the administration of rescue analgesia) was 225.3 ± 20.11min. In control group, the mean duration of analgesia was 168.3 ± 15.11min. The duration of analgesia was significantly higher in dexmedetomidine group when compared to control group (p<0.001).

Table 2: Motor and Sensory effects

Mean time in min ± SD Eg: onset of sensory block	Group D	Group C	p-value
Mean onset time of sensory block in min ± SD	2.09 ± 0.71	3.5 ± 0.82	<0.001
Mean duration of sensory block in min ± SD	174.5 ± 14.04	138.2 ± 11.51	<0.001
Mean onset time of motor block in min ± SD	3.18 ± 1	6.19 ± 1.87	<0.001
Mean duration of motor block in min ± SD	133.4 ± 10.42	120.4 ± 8.8	<0.001
Mean duration of analgesia in min ± SD	225.3 ± 20.11	168.3 ± 15.11	<0.001

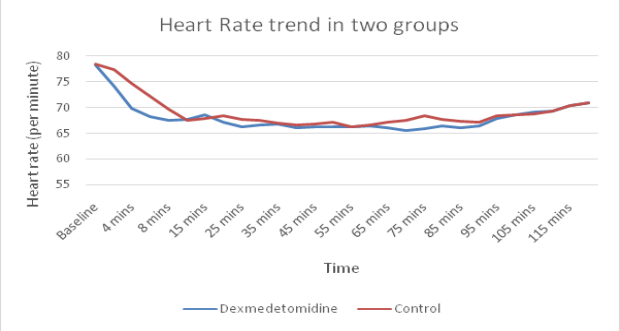

Figure 1: Heart Rate Trend

Only decrease in heart rate and blood pressure were the side effects seen in the patients under study. The lowest HR was 45 bpm in group D. The lowest SBP was 81 mmhg in group D and the lowest DBP was 44 mmhg in group C. Although decrease in heart rate was seen slightly more in dexmedetomidine Group and decrease in blood pressure in control group its distribution was however not statistically significant as shown in the graph 1 and 2.

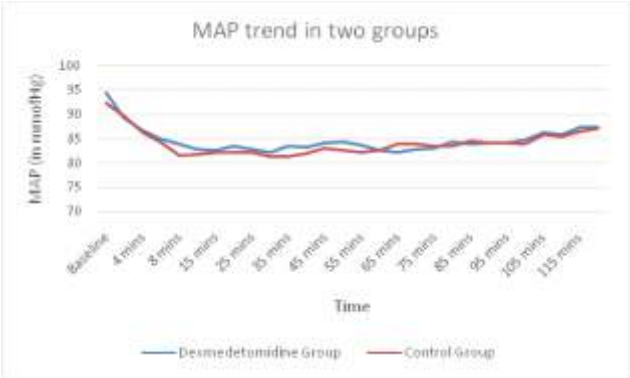

Figure 2: MAP Trend

DISCUSSION

Drugs like epinephrine, phenylephrine, magnesium sulphate, sodium bicarbonate, neostigmine,α_2 agonists like clonidine and dexmedetomidine have been used as adjuvants to local anaesthetics to prolong the duration of spinal anesthesia.[4] Among them clonidine, an α_2 agonist is widely used by oral, intrathecal, and intravenous routes as an adjuvant to prolong the duration of spinal anesthesia.[1] Recent studies have shown the efficacy of both intrathecal and intravenous dexmedetomidine in prolonging the duration of spinal anesthesia.[18] Dexmedetomidine is a more suitable adjuvant to spinal anaesthesia compared to clonidine as it has more sedative and analgesic effects due to more selective α_2A receptor agonist activity.[1] Added advantage of dexmedetomidine is that it does not have any direct effects on the heart. In the coronary circulation, dexmedetomidine causes a dose-dependent increase in coronary vascular resistance and O_2 extraction, but the supply/demand ratio is unaltered.[19] After the administration of dexmedetomidine a biphasic cardiovascular response has been described. A bolus of 1 µg/kg results in a transient increase in BP and a reflex decrease in HR. This initial response is attributed to the direct effects of β-adrenoceptor stimulation of the vascular smooth muscle. This response can be attenuated by a slow infusion over 10 min, which results in stabilization of the HR and BP 10–15% below baseline values.[16] Intravenous and intrathecal injection of dexmedetomidine produces analgesia by acting at laminae VII and VIII of ventral horns of the spinal cord.[17] The drug also acts at locus ceruleus and dorsal raphe nucleus to produce sedation and analgesia.[18] This supra spinal action explains the prolongation of spinal anaesthesia after intravenous dexmedetomidine.

Different doses ranging from 0.2 to 10 µg/kg/h of intravenous dexmedetomidine have been studied in the past.[19] Dexmedetomidine when used in higher doses produces significant hemodynamic instability like hypotension and bradycardia.[20] Aantaa RE et al. concluded that the optimal dose of dexmedetomidine for single dose intravenous premedication in minor surgery appears to be in the range of 0.33 to 0.67 µg/kg.[21] To make the study uniform we selected a dose of 0.5 µg/kg by intravenous route which was administered slowly over a period of 10 minutes prior to administer of spinal anaesthesia. Similar dose was also used before by Jaakola ML et al. and observed moderate analgesia.[22]

In the present study single bolus dose of 0.5µg/ kg of dexmedetomidine has been found to accelerate the onset of sensory block (2.09 ± 0.71 min)compared to control group (3.5± 0.82 min) Similar results were also reported by Harsoor SS et al.[23]and Reddy M et al.[24] who hypothesized that faster onset may be due to α-2 receptor activation induced inhibition of nociceptive impulse transmission. But, Tekin M et al.[11], Elcicek K et al.[25]and Upadhyay S et al.[26] found that time for onset of sensory blockade was not significantly altered by the use of dexmedetomidine.

Statistically significant prolongation of sensory block, i.e in terms of regression of spinal duration (174.5 ± 14.04 min) was observed in the dexmedetomidine group compared to control group (138.2 ± 11.51 min). Almost similar results were also observed by several authors, viz. by Whizar-Lugo V et al.[28], Kaya FN et al.[29], Hong JY et al.[30], Harsoor SS et al.[23], Kubre J et al.[31]and Reddy VS et al.[14] Jorm CM et al attributed this effect to the unique property of dexmedetomidine on locus ceruleus located at the brain stem.[28] Inhibition of locus ceruleus results in disinhibition of the noradrenergic nuclei and applied descending effect on nociception in the spinal cord.[18]

In the present study, the mean time for onset of motor blockade was significantly shorter in dexmedetomidine group (3.18 ± 1 min)when compared to control group (6.19 ± 1.87 min). This result is consistent with Kanazi GE et al.[6], Al-Mustafa MM et al.[32] Esmaoglu A et al.[33] Chandrashekharappa K et al.[34] and Reddy VS et al.[14]who compared dexmedetomidine and clonidine with placebo. However, in studies by Kaya FN et al.[29] and Reddy M et al.[24] the mean time for onset of motor blockade was comparable in dexmedetomidine and control groups which was not statistically significant.

The mean duration of motor block was prolonged in dexmedetomidine group (133.4 ± 10.42 min) compared to control group (120.4 ± 8.8 mins) but not as long as that of sensory block. Similar prolongation of motor blockade was reported in previous studies conducted by Hong et al.[30] and Kubre J et al.[31] Similarly, Tekin M et al.[11], Whizar-Lugo V et al.[28], Al Mustafa MM et al.[32], Elcicek K et al.[25]and Santpur MU et al.[35] also found that complete resolution of motor blockade was significantly prolonged in the dexmedetomidine group where they used loading and infusion dose of dexmedetomidine. But they used larger dose of bupivacaine. The mechanism of motor block produced by α_2-agonist is unclear but some evidence showed that clonidine may produce direct inhibition of impulse conduction in the large, myelinated A α fibers and the 50% effective concentration (EC50%) measured was found to be approximately fourfold of that in small, unmyelinated C fibers.[32] The same mechanism may be applicable to dexmedetomidine, which explains the more sensory than motor block prolongation in dexmedetomidine group compared to control group. Contrary to the above studies, Kaya FN et al.[29], Reddy VS et al.[14] reported no significant prolongation in the duration of motor block with dexmedetomidine group though sensory block was prolonged which they thought that like clonidine motor and sensory block was concentration dependant and sensory fibres might be more inhibited than motor fibres at the same concentration of drugs.

The duration of analgesia i.e. time from the onset of sensory block to the time of administration of first rescue analgesia in dexmedetomidine group (225.3 ± 20.11min)was more compared to control group (168.3 ± 15.11 min) which was statistically significant. The observation was also consistent with the study done by Hong JY et al.[30], Harsoor SS et al.[23], Reddy M et al.[24] and Reddy VS et al.[14] Similarly, Al-Mustafa

MM et al.[32], Kaya FN et al.[29] and Kubre J et al.[31] also found that the time to first request for postoperative analgesic was significantly prolonged and the 24 hrs mean requirement of analgesics was significantly less in the dexmedetomidine group, which they attributed to the action at spinal, supra-spinal, direct analgesic and/or vasoconstricting actions on blood vessels.

Hemodynamic parameters HR, SBP, DBP and MAP were stable during the study period. Although the incidence of decrease in heart rate was more in the dexmedetomidine group (12%) compared to control group (4%) but was not statistically significant (p=0.140). The result of the present study correlates well with the result published by Kubre J et al.[31] The lower HR observed in dexmedetomidine group could be explained by the postsynaptic activation of $\alpha_2$adrenoceptors in the CNS, which results in a decrease in sympathetic activity and circulating levels of catecholamines. Studies done by Aantaa RE et al.[21]also support these finding. Intraoperative and postoperative bradycardia and hypotension were also observed by Tekin M et al.[11], Al Mustafa MM et al.[32] and Hong JY et al.[30]with dexmedetomidine, but they used the drug throughout the procedure by continuous intravenous infusion.

In the present study no statistically significant hypotension and bradycardia were observed in both the groups. The incidence of side effects like hypotension and bradycardia requiring treatment were comparable in both the groups and was not statistically significant. These findings were consistent with findings of Reddy VS et al.[14] and Reddy M et al.[24]

CONCLUSION

We conclude that dexmedetomidine 0.5 µg/kg bolus infusion prior to subarachnoid block with hyperbaric bupivacaine quickens the onset of sensory and motor block, prolongs the duration of sensory and motor, prolonged duration of analgesia with minimal changes in hemodynamic profile and acceptable side effects thereby making dexmedetomidine an effective adjuvant for spinal anaesthesia.

RECOMMENDATIONS

This study has shown that IV dexmedetomidine is a useful adjunct for spinal anesthesia with hyperbaric bupivacaine. However, its use in children and elderly patients need further evaluation. The cost factor of dexmedetomidine should also be considered during its use.

LIMITATION OF THE STUDY

1. Patients with ASA physical status grade I and II were only involved in this study. So these results might not be applicable in patients with higher grades.
2. The sample size of the study was small and was carried out at only one institution which was too small for broad generalization.
3. Extremes of age were not included in this study. Result may vary in children and elderly patients.
4. Emergency lower limb surgeries were not included in this study.

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CONFLICT OF INTEREST

None

FINANCIAL DISCLOSURE

None

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