Comparison of the Local Anesthetic Effect of Two Doses of Dexmedetomidine , 5µg and 10µg added to Intrathecal Hyperbaric Bupivacaine

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Abstract

Objective: To Ascertain the optimum intrathecal dose of dexmedetomidine along with local anesthetic.

Method: Prospective randomized study, Place and Duration of Study was in the Department of Anaesthesia, FMH College of Medicine & Dentistry, Lahore from1st. February to 31st. July (6 months) 2021. Ninety patients posted for urological, lower abdominal and pelvic general surgical procedures selected for the study were distributed in three groups. All groups comprised 30 patients each. Our facility is providing treatment to infertile males and that was our main study population. We selected ASA1&2 patients between 20 and 60 years. The first group [Control (C)] received only local anesthetic (2 ml. of hyperbaric bupivacaine 0.75%) plus 0.5 ml normal saline. The second group [Dexmedetomidine (D1)] received in addition to local anesthetic 5 micrograms of dexmedetomidine. The third group [Dexmedetomidine (D2)] received in addition to local anesthetic 10 µg of dexmedetomidine. The duration of surgical anesthesia, motor blockade and severity of side effects (hypotension and bradycardia) were noted for all patients in all the three groups. All the groups received 2.5 ml intrathecal injection.

Results: The onset of the blockade was similar in all groups. The duration of block was maximally prolonged in (D2) group. The duration was in between in (D1) group. It was minimum in (C) group.

Conclusion: Intrathecal use of dexmedetomidine with local anesthetic prolonged the sensory and motor blockade and 5 µg was found to be the optimal dose.

Keywords: α2-adrenergic agonist, Dexmedetomidine, Bupivacaine, Lower abdominal surgery

How to cite: *Abaidullah K, Siddiqi KJ, Khan MA, Ahmad M, Awais M. Khalid R. Comparison of the Local Anesthetic Effect of Two Doses of Dexmedetomidine , 5µg and 10µg added to Intrathecal Hyperbaric Bupivacaine Esculapio - JSIMS 2022;18(04):248-252*

DOI: https://doi.org/10.51273/esc22.251846

Introduction

Spinal anesthesia is very popular these days due to its relative safety and economy as compared with general anesthesia. It is especially useful in infraumbilical general surgical, urological, orthopedic, obstetric and gynecological operations. The availability of blunt bevel needles has markedly reduced the incidence of post spinal headache. The problem with spinal anesthesia is its relatively short duration. To overcome this, various adjuvants namely ketamine, clonidine and buprenorphine have been used with local anesthetics intrathecally to cause prolongation of effect. At higher intrathecal doses opioids can cause side effects like pruritus, drowsiness, nausea and vomiting. Ketamine and clonidine also have bad side effects. Nowadays a relatively new drug dexmedetomidine is in use to prolong the duration of effect of intrathecal local anesthetics. It is a specific α2 adrenergic agonist relatively free from these side effects though hypotension and bradycardia can occur.[1]

Dexmedetomidine has been used as a premedicant, and can be used as a sedative in intensive care unit (ICU)

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Submission Date: 02-08-2022
1st Revision Date: 20-08-2022
Acceptance Date: 12-10-2022

setting.[1,2] It causes prolongation of all types of nerve blockade (sensory and motor) and ameliorates both visceral and somatic pain.[3]

There are very few studies in the literature regarding the optimum intrathecal dose of dexmedetomidine.[4] Gupta R et al. used 5 mcg dexmedetomidine along with ropivacaine ,in their study, and found prolonged sensory as well as motor block with minimal hemodynamic change and decreased requirement for rescue analgesics for 24 hours , in comparison with fentanyl.[1] Abdelhamid and El lakany used 5 mcg of dexmedetomidine with local anesthetic intrathecally and encountered prolonged postoperative analgesia and decreased shivering. Those studies depict that usually dexmedetomidine given intrathecally along with local anesthetic prolongs the sensory as well as motor block but increasing the dose more can exhibit troublesome hemodynamic depression. Therefore, we decided to study at our setup the optimum dose producing prolongation of sensory and motor blockade, meanwhile causing negligible hemodynamic disturbances.

Materials and Methods

This prospective randomized study was done in a tertiary care hospital affiliated with medical college. IRB (Institutional Review Board) approval was taken. Sample size was calculated in reference to the study done by Shagufta Naaz et al[(4)]. J Clin Diagn Res 2016 Apr; 10(4): UC 09-UC13. They calculated the sample size using a power analysis of @=0.05 and B=0.8. We selected 90 patients for the study and distributed them randomly in three groups. All the groups comprised 30 patients each. Most of our patients were male by chance as our facility caters for the treatment of infertile males. All the patients had to undergo mainly urological procedures plus some lower abdominal and pelvic general surgical operations.

Inclusion criteria was male and female patients aged 20-60 years and American society of anesthesiologists class 1 and 2. Extremes of ages and BMI were avoided in the study. In similar studies, similar demographic profiles were encountered.[4] Exclusion criteria was patients with hypertension, cardiac disease, coagulation disorders and β blocker therapy etc. Computer-generated random number sequencing was used for randomisation. All the groups received 2.5 ml volume intathecally. This comprised 2ml of 7.5% bupivacaine plus 0.5 ml normal saline. The arrangement was made that in groups D1 and D2, after adding dex. the volume of normal saline was such that total volume of the injectate was 2.5ml. The first group (C) received only 15 mg of heavy bupivacaine intrathecally only. The second group (D1) received the same amount of heavy bupivacaine plus 5 μg of dexmedetomidine. Third group received the same amount of heavy bupivacaine plus 10 μg of dexmedetomidine.

All the patients fasted for 6 hours for solids but were allowed clear fluids upto 2 hours before surgery. On arrival in the operation theatre, intravenous access was taken and all the patients received lactated ringer's solution 10ml/kg. Patients, wellbeing was monitored using non- invasive blood pressure, pulse oximetry, and ECG. Under strict aseptic precautions, using 25-gauge pencil point blunt bevel needle, subarachnoid block was established in the sitting position at 3-4 lumbar interspace. Hyperbaric bupivacaine was taken in 3cc. disposable syringe (2ml= 15mg) and dexmedetomidine in the insulin syringe 5 or 10 micrograms according to the group allocation. The available ampule of dexmedetomidine over the counter contains 200 micrograms in 2 ml. Dexmedetomidine was added to the 3cc.syringe of heavy bupivacaine. 2.5 ml volume was ensured in all the patients in all the groups by adding normal saline. The intrathecal injection time of the drug was labeled zero time and subsequently all the time calculations were done in reference to that. Sensory checking with the pin prick method was done with 23 G hypodermic needle, every minute, to find out the time for the onset of block, for the maximum block and the highest dermatomal level until all were recorded. Hemodynamics were checked every 2 minutes initially, for 10 min. then every 5 min. thereafter. Analgesia was checked every 30 min. until patient started feeling pain, both intra and postoperatively. Modified bromage scale was used for motor blockade assessment. This scale assesses the intensity of motor block by the patient's ability to move his lower extremities. Bromage score 1 is complete block (unable to move feet or knees). Bromage 2 is almost complete block (able to move feet only). Bromage 3 is partial block (just able to move knees). Bromage 4 is detectable weakness of hip flexion while supine (full flexion of knees). Motor blockade grossly coincided with the duration of analgesia. It was taken as hypotension if the fall in SBP 30% or more from the pre-induction level and treatment was done with intravenous crystalloids, colloids and ephedrine. It was labelled bradycardia if heart rate decreased to<50 beats per minute and was treated with intravenous glycopyrrolate 0.4 mg. Anal-

gesic fortification with other drugs was not done. Anxious patients were given 1mg. of Midazolam. Analgesia time was considered from the time of intrathecal injection to the first dose of the rescue analgesic due to pain. Nalbuphine 4 mg intravenous, was our rescue analgesic until the pain subsided to an acceptable level.

Results

Most of our patients were males (88 males as compared to 2 females only). The age of the patients ranged from 20 to 60 years. The weight of most of the patients ranged from 75–80 kilograms (Table 1). Most of our patients had microsurgical varicocelectomy operation.

The onset of the sensory block was almost 5 minutes or less in all the groups. Maximum block established in 10 minutes or even less in all the groups. Duration of analgesia/motor blockade was maximum (more than 200 min.) in the D2 group. It was least (less than 100 min.) in the control (C) group and in between in the D1 group (133 min.). Hemodynamic stability was more in the control group where only 1 patient became unstable, i.e. either had bradycardia or hypotension. In the D1 group 26 patients (28.9%) remained stable and only 4 patients (4.4%) became unstable. In the D2 group 23 patients (25.6%) remained stable and 7 patients (7.8%) showed either bradycardia or hypotension (Table 2). Data was analyzed using SPSS-23. The first table shows descriptive statistics of the patients. As regards gender, frequency and percentages are given whereas mean and standard deviation are used to illustrate age and weight. In the second table, Kruskal Wallis H test was used for the variables barring hemodynamics where Chi Square test was used.

Table 1: *Descriptive statistics of the patients (n=90)*

Variable	Group C	Group D1	Group D2
Gender			
Male	30 (100%)	30 (100%)	28 (93.3%)
Female	-	-	2 (6.7%)
Age (years)	36.53±10.96	36.66±8.47	36.26±8.40
Weight (kg)	78.53±12.62	77.36±7.95	78.23±10.47

Table 2: *Characteristics of sensory and motor blockade (Time in min.)*

Characteristic	Control (C)	D1	D2	P Value
Onset of sensory block	4.43±1.16	3.36 ± 1.12	3.30± 0.79	0.0001
Maximum block (sensory+motor)	8.63±2.73	6.50±1.19	6.36 ± 1.27	0.0001
Highest sensory level	T8 (T6-T8)	T8 (T6-T8)	T6 (T4-T8)	
Duration of analgesia/ Motor blockade	95.3±35.0	133.6±35.6	214.8 ± 31.4	0.0001
Rescue analgesia (minutes)	104.0± 44.3	153.5±38.9	235.6 ± 38.3	0.0001
Highest pain score	3.1±1.5	2.3±0.7	2.0 ± 0.6	0.013
Haemodynamics				
Stable	29 (%)	26	23	0.056
Unstable	1	4	7	

Discussion

To prolong the analgesia and anaesthesia in operations done under spinal anaesthesia has been hitherto a difficult proposition. Dexmedetomidine is presently of tremendous help in this regard. Very little amount (5-10 µg of dexmedetomidine added to the local anesthetic, say Bupivacaine) can literally double the duration of analgesia.

Dexmedetomidine is a highly specific α2adrenergic agonist.[1] The sedative cortical analgesic effects of dexmedetomidine are caused by the hyperpolarization of noradrenergic neurons. Norepinephrine release is inhibited in the medullospinal noradrenergic pathway.[5-7] This triggers the formation of new neurotransmitters that consequently decrease histamine secretion producing hypnosis that resembles normal sleep, making dexmedetomidine a promising and efficient sedative.[8] The decreased activation in the descending noradrenergic pathway, which regulates nociceptive transmission, stops passage of pain signals and analgesia is produced.[7] At spinal cord level, increased activity in both α2-C and α2 – A adrenergic receptors, present in the dorsal horn neurons, especially lamina II, produces effective analgesia.[6,9,10] The sympatholytic effect due to stimulation of central α2 adrenergic receptors resulting in hypotension and bradycardia is beneficial in the attenuation of stress response of surgery.[10,11]

Recent studies have demonstrated that intrathecal dexmedetomidine significantly decreases postoperative analgesic requirements.[12] Different dose finding studies,[13,14] have been conducted in the past to find the optimal dose. The studies evaluating intrathecal dexmedetomidine do not demonstrate any neurological deficits produced by it, in the dose range 2.5 – 100 mcg. Some studies, however have shown that dexmedetomidine could have adverse effects on myelin sheath in human beings.[15] Kanazi et al. used 3 mcg of dexmedetomidine intrathecally with local anesthetic and found quicker onset of

motor block and prolongation in the duration of sensory and motor block with hemodynamic stability. Al - Mustafa et al. used 5 & 10 mcg of dexmedetomidine with bupivacaine intrathecally in urological cases and found prolonged analgesia and motor blockade in a dose dependent manner. Hala EA Eid et al. in their study using 10 and 15 mcg of dex. with 3ml of 0.5% heavy bupivacaine encountered good and prolonged analgesia.[16] Shagufta Naaz et al. in their study even used 20 mcg dose of dexmedetomidine. In our study, in agreement with previous studies, the control group, i.e. that without dexmedetomidine had the shortest time of anesthesia and analgesia. Onset of sensory and motor blockade was somewhat delayed as compared to dex. groups (study groups). In study groups, the onset of blockade was quicker with 10 mcg dex. dosage as compared to that with 5mcg dex. respectively D2 and D1 groups in our study. Time to reach maximum blockade was also less whereas the height of the block was more in dex. groups especially in D2 group (10 mcg dex. group). Hemodynamics remained stable in the control group whereas there was some bradycardia &hypotension in the D1 and D2 groups, more in the later. All this complies with the findings of the previous studies. Presently, more research is required to establish the safety, efficacy and optimum dosage of intrathecal dexmedetomidine.

Conclusion

The addition of 5µg of dexmedetomidine to 15 mg of hyperbaric bupivacaine for the subarachnoid block has caused a significant increase in the duration of the block in patients undergoing urological and lower abdominal surgery without causing adverse effects on cardiovascular stability.

Conflict of Interest *None*

Funding Source *None*

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Authors Contribution

KA: Conceptualization of Project
KJS: Data Collection
MAK: Literature Search
MA: Statistical Analysis
MA: Drafting, Revision
RK: Writing of Manuscript