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Original Research Article

Comparison of Buprenorphine and Dexmedetomidine as Adjuvants to Bupivacaine in Elderly Patients Undergoing Transurethral Resection of Prostate under Spinal Anaesthesia

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Abstract

Transurethral resection of the prostate (TURP) is a commonly performed procedure in elderly male patients. Postoperatively, these patients suffer from bladder spasms associated with using a transurethral balloon to prevent bleeding from the prostatic bed. As a result, anaesthetic techniques that provide postoperative analgesia without jeopardising patient safety must be developed. Spinal anaesthesia is a commonly used technique for these procedures, as this is the quickest and most reliable form of regional anaesthesia. Therefore, a combination of low-dose local anaesthetics along with other adjuvants can prolong postoperative analgesia. This study evaluates the sensorimotor effects of the addition of buprenorphine or dexmedetomidine to low-dose intrathecal bupivacaine in patients undergoing TURP.

Aim and Objective: The aim and objective of the study were to compare and contrast intrathecal Dexmedetomidine and intrathecal Buprenorphine as adjuvants to 0.5% hyperbaric Bupivacaine for TURP surgeries. The two groups were intrathecal Dexmedetomidine and intrathecal Buprenorphine. The two groups were compared in terms of, the time required for the first analgesic request in patients, time to sensory regression to S1 and Duration of motor blockade.

Methodology: It is a prospective quasi-experimental study. The study was conducted on 116 elderly patients (ASA 1 or 2) over 55 years of age undergoing transurethral resection of the prostate under spinal anaesthesia after receiving approval from the institutional ethical committee at the Government Medical College, Thiruvananthapuram. Patients were divided into two groups, Group B 58 patients and Group D 58 patients. Patients in Group B received 60 mcg of buprenorphine with 0.5% bupivacaine 9 mg intrathecally. Patients in Group D received 5 mcg dexmedetomidine with 0.5% bupivacaine 9 mg intrathecally.

Result: The duration of motor blockade was found to be nearly identical in both groups with the highest statistical significance. The duration of analgesia and time to sensory regression to S1 were found to be longer in the dexmedetomidine group than in the buprenorphine group. During the research, both groups had stable and comparable hemodynamics. In comparison to buprenorphine, intrathecal administration of dexmedetomidine as an additive to hyperbaric bupivacaine was associated with fewer side effects.

Keywords: Buprenorphine, Dexmedetomidine, International Association for the Study of Pain, Motor Block, Transurethral resection of the prostate.

Introduction

The International Association for the Study of Pain (IASP) defined pain as "an unpleasant sensory or emotional experience associated with actual or potential tissue damage or described in terms of such damage" [1]. Transurethral resection of the prostate (TURP) is a commonly performed procedure in elderly male patients[2] and postoperatively, these patients suffer from bladder spasm that is associated with the use of a transurethral balloon to prevent bleeding from the prostatic bed or capsule [3,4]. Anaesthetic techniques need to be developed that give postoperative analgesia without compromising patient safety. Spinal anaesthesia is a commonly used technique for these procedures, as this is the quickest and most reliable form of regional anaesthesia. Besides, the patient remains awake during the surgical procedure, enabling early identification of complications of TURP such as transurethral resection syndrome involving osmolar disturbances, fluid overload, or water intoxication.

There are numerous advantages to selecting spinal anaesthesia over general anaesthesia, making it the preferred anaesthetic in modern surgical practice. Many clinical investigations support the hypothesis that neuraxial blockade, either alone or in combination with general anaesthesia, may reduce postoperative morbidity and mortality. It is appropriate for individuals with respiratory illnesses and aids in the prevention of intubation-related complications such as laryngospasm. It also aids in maintaining the patency of the airway and reducing blood loss [4].

An early recovery of gastro-intestinal function after surgery is seen to be an added benefit. Other benefits include a decreased hypercoagulable state associated with surgery, higher tissue blood flow due to sympathectomy, decreased splinting, which improves oxygenation, enhanced peristalsis, and a reduced stress reaction to surgery due to neuroendocrine system suppression [5]. The sympatholytic impact is stronger at increasing levels of blockage, leading to more hazardous complications. Though negative effects cannot be totally eliminated, they can be reduced by using a low dose or a low concentration of a medicine. One of the main disadvantages of local anaesthesia is the short duration of the block. Various adjuvants have been tried and used successfully to overcome this.

Morphine was the first opioid administered intravenously in 1979, and it was quickly followed by other opioids [6,7,8]. Buprenorphine is the lipid-soluble, centrally acting counterpart of the alkaloid thebaine. It has analgesic effects at both the spinal and supra spinal levels [9]. It has been repeatedly demonstrated to increase the duration of anaesthesia [10,11,12]. Dexmedetomidine stimulates the alpha2 adrenergic receptor [9]. It is frequently used as a premedicant, for ICU sedation, and for awake fiberoptic intubation [13, 14]. It was first used intravenously in humans for transurethral prostatic resection [15]. It has nociceptive activity for both visceral and somatic pain and lengthens both sensory and motor blockages.

Aim and Objective

This study aims to learn more about the efficacy of such a combination in our setting, as well as to analyze and compare the following factors in two groups: intrathecal dexmedetomidine and intrathecal buprenorphine as adjuvants to 0.5% hyperbaric bupivacaine for TURP procedures, in terms of: The amount of time

it takes for a patient to ask for their first analgesic. In S1 motor blockade, it's time for sensory regression.

Methodology

It was a prospective quasi-experimental study. The study was conducted on 116 elderly patients (ASA 1 or 2) over 55 years of age undergoing transurethral resection of the prostrate under spinal anaesthesia after receiving approval from the institutional ethical committee at the Government Medical College in Thiruvananthapuram. Before including the patients for the study, all patients were explained about the procedures and a written informed consent was obtained. Patients were divided into two groups of 58 each, Group B and Group D. Patients in Group B received 60 mcg of buprenorphine with 0.5% bupivacaine 9 mg intrathecally. Patients in Group D received 5 mcg dexmedetomidine with 0.5% bupivacaine 9 mg intrathecally. The study was conducted for a period of one year 2020 to 2021. A random sampling technique was used for the study.

Sample size was calculated using the formula N = (za + z1 – β) 2(p1(1-p1) + p2(1-p2)) (p1-p2)2

Where,

P1: Proportion in the first group

P2: Proportion in the second group A: Significance level

1-β: Power

According to the similar study Comparative Effects of Buprenorphine and Dexmedetomidine as Adjuvants to Bupivacaine Spinal Anaesthesia in Elderly Male Patients Undergoing Transurethral Resection of Prostate: A Randomised prospective study

Post-operative analgesia was not required in Group B = 50% Post-operative analgesia was not required in Group D = 75%

P1: 50%

P2: 70%

α: Significance level = 5%

1-β : Power = 80% N= 58 in each group

Inclusion criteria

- Patients 55 years of age and older ASA 1 and 2 patients.
- Patients who undergo elective TURP surgeries

Exclusion criteria:

- Patients who refuse to provide informed consent;
- Infection at the injection site;
- Hypersensitivity to amide local anaesthetics, buprenorphine, or dexmedetomidine.
- Patients with recognised contraindications for spinal anaesthesia
- Patients with coagulation disorders or receiving anticoagulant therapy
- Patients with cardiac illness, heart blockages, and dysrhythmias

Study variables

Exposure variables

- Age
- Weight
- ASA status 1 or 2
- Intervertebral space selected for spinal anaesthesia
- Dose of 0.5% Hyperbaric Bupivacaine, Buprenorphine, Dexmedetomidine

Outcome variables

- Time to first analgesic request
- Level of spinal block
- Duration of motor block
- Time to sensory regression to S1
- Mean arterial pressure
- Heart rate
- Oxygen saturation (SpO_2)
- Nausea
- Vomiting
- Pruritus
- Shivering

Preoperative assessment: After routine preoperative assessment of the patients in the waiting room, basal line readings of the

vital parameters were recorded. In the operating room, appropriate equipment for airway management and emergency drugs were kept ready. The horizontal position of the operating table was checked. Patients were shifted to the operating room and positioned. Once the patient was shifted to the operating room, the electrocardiogram monitoring (leads II and V5), non- invasive blood pressure and pulse oximeter were attached and baseline vitals recorded. Patient was premedicated with midazolam 0.02mg/kg and ondansetron 4mg. Intravenous (IV) access was established, and an infusion of 0.9% NaCl started at a rate of 20 ml/h following an initial bolus of 200 mL. Oxygen was administered @5L/min. The patient was positioned in the right lateral position and lumbar puncture performed under aseptic precautions using either a 23 gauge or a 25-gauge Quincke Babcock spinal needle in the L2/L3 or L3/L4 interspace. Group B Patients received 1.8 ml 0.5% bupivacaine (9mg) and Buprenorphine 0.2 ml (60mcg), Group D Patients received 1.8 ml 0.5% bupivacaine (9 mg) and Dexmedetomidine 0.2 ml (5mcg).

Total volume of the injected solution was 2ml in both groups. After obtaining free flow of cerebrospinal fluid, the study drug was injected intrathecally over a period of 10 seconds. The bevel was directed cephalad during injection of the drug in all patients. The patient was turned supine immediately after performing the block and remained in the supine position until the sensory block reached the highest dermatomal level. Motor block was assessed post operatively using Bromage scale.

The level of sensory block was determined using the hub of a sterile 22-gauge needle in the midline, and dermatomal level assessed every 3 min from completion of injection until the assessed sensory level remained stable for five consecutive assessments. All patients were then placed in the lithotomy position and surgery commenced.

The following parameters were noted.

- Level of sensory blockade
- Duration of motor block
- Time for sensory regression to S1 dermatome.
- Mean Arterial Blood pressure, pulse rate and oxygen saturation were recorded every 3 min for the first 15 min following spinal anaesthesia, and then every 5 min until the end of surgery.
- Hypotension was said to have occurred if the MAP fell less than 65 mmHg and treated with 100% O2, increasing the infusion rate of IV fluids and bolus of mephentermine 3mg/6mg or Ephedrine 3mg/6mg or Phenylephrine 50/100 mcg, Bradycardia was defined as heart rate less than 50/min and was planned to be managed with intravenous atropine in incremental doses.
- Respiratory depression was said to be present if respiratory rate was less than 8/minute and / or Spo2 < 90%. It was planned to be managed with mask ventilation or intubation and IPPV.
- Any discomfort like nausea, vomiting, shivering, pruritus and adverse events such as hypotension, bradycardia respiratory depression and ECG changes were noted.
- Vomiting was planned to be managed with Inj. Ondansetron 4 mg intravenously.
- On completion of surgery, the patient was shifted to the recovery room for observation.
- Patients were transferred to postoperative wards after complete resolution of motor blockade and stabilisation of blood pressure.
- Vital signs and oxygen saturation were recorded until recovery of patients from anaesthesia.
- Injection Diclofenac sodium 75mg was given intramuscularly when the patient

complained of pain in the postoperative period (rescue analgesic)
- Duration of surgical procedure.

Assessment in the Recovery Room

Patient was shifted to the recovery room after completion of surgery. Further testing was performed at 15 min intervals in the recovery room until recovery of the S1 dermatome. All times were recorded from the time of completion of the intrathecal injection. The highest dermatomal level of sensory blockade, and the time to S1 sensory regression were recorded. Motor block was assessed using the Bromage scale (0: No motor block; 1: Hip blocked; 2: Hip and knee blocked; and 3: Hip, knee, and foot blocked). Duration of the motor block was considered until the time when Bromage score returned to 0. Time to the first analgesic request was considered the primary objective of the study.

Post-operative assessment

Post operatively the patients were instructed to tell the staff nurse whenever they felt the need for an analgesic. The staff nurse noted the time to first analgesic request from the patient. Tramadol IV 50 mg and paracetamol IV 1 gm were the postoperative rescue analgesics. Patients were monitored for 24 hours to detect the occurrence of side effects - respiratory depression, nausea, vomiting, dry mouth, urine retention and pruritus. Patients were also enquired about the occurrence of transient neurological symptoms which was described as pain / paraesthesia in the neck, buttocks, legs or pain radiating to lower extremities after initial recovery from spinal anaesthesia within 72 hrs.

Assessment of blockade after spinal anaesthesia sensory block

Following subarachnoid block, sensory block was assessed by loss of sensation to pinprick using 23G sterile needle. The assessment was started immediately after injection and continued every 15 sec till loss of pinprick sensation at T10 level. At 20 minutes after SAB, the dermatomal level of sensory block was noted and this was considered as the maximum level of sensory block.

Motor block

Motor block was assessed using the Bromage score

Duration of motor block was taken as time from initiation of SAB to return of Bromage Score to 1.

Pain and duration of analgesia

At the end of surgery, the degree of pain was assessed using the VAS scale till VAS Score > 4 was reached. Whenever the patient complained of pain, the rescue analgesic, Inj. Diclofenac 75mg intramuscular was given.

Statistical Analysis

Data were analyzed using SPSS. Quantitative data were conveyed as mean ± SD and qualitative data were conveyed as frequency and percentage. An Independent sample t-test of significance was used when comparing the two means. The chi-square test of significance was used to analyze proportions in between 2 qualitative parameters. P-value & amp;lt; 0.05 was considered as significant.

Result

This study included a total of 116 participants, with 58 participants in Group B and 58 participants in Group D. Group B patients were given 1.8 ml 0.5% Bupivacaine (10mg) and 0.2 ml 60 mcg Buprenorphine. Group D patients received 1.8 mL 0.5% Bupivacaine (10 mg) and 0.2 mL 5mcg Dexmedetomidine. The majority (43.1%) of the patients were aged between 61-70 years in the B group and 71-80 years (34.4%) in the D group. The Age distribution was in the range of 55-89 in Group B and 55-83 in Group D. The ‘p’ value for mean age was not statistically significant (p value = 0.112).

Table 1: The above table indicates the age-wise distribution of the B and D group patients

Variables	Characteristics	Group B	Group D	P- value
		Frequency (%)	Frequency (%)	
Age Group	55-60 Years	14(24.1)	10(17.2)	
	61-70 Years	25(43.1)	15(25.8)	
	71-80 Years	8(13.7)	20(34.4)	
	>80 Years	11(18.9)	13(22.4)	0.112
	Mean±SD Years	68.59±9.09	71.87±8.57	
	Range	55-89 Years	55-83 Years	
Total		58(100)	58(100)	

Table 2: The above table indicates the Duration of motor block (in minutes), Time of Sensory regression of S1 (in Minutes) and Time to first analgesic request (min) of the B and D group patients

Variables	Characteristics	Group B	Group D	P- value
		Frequency (%)	Frequency (%)	
Duration of motor block (in minutes)	Range	130-348	131-230	P=0.00***
	Mean±SD	245.66±63.30	243.18±64.39	
Time of sensory regression of S1 (in minutes)	Range	70-230	70-260	P=0.00***
		142.00±49.30	160.33±60.48	
Time to first analgesic request (min)	Mean±SD	410-77	400-76	P=0.00***
		540.96±128.07	558.58±117.17	

There was not much difference in the duration of the motor block in Group B (245.66 ± 63.30) when compared with Group D (243.18 ± 64.69). It was statistically significant (p value = 0.00 < 0.05).

The time of sensory regression to S1 was shorter in Group B (142.00± 49.30) when compared with Group D (160 ± 60.48). It was statistically significant (p value = 0.001 < 0.05). There was a delay in sensory regression of Group D compared to Group B.

The time to first analgesic request was longer for the dexmedetomidine group 558∓117mins and 540∓128mins for the buprenorphine group. The p value was 0.001 which was statistically significant.

Table 3: The above table indicates the Highest dermatomal level reached and Adverse effects of the B and D group patients

Variables	Characteristics	Group B	Group D
		N (%)	N (%)
Highest dermatomal level reached	T6	16(27.5)	26(44.8)
	T8	16(27.5)	17(29.31)
	T10	26(44.8)	19(32.7)
Adverse effects	Yes	9(15.5)	5(8.6)
	No	49(84.4)	53(91.3)
Adverse effects	Nausea	6	1
	Bradycardia	1	4
	Hypotension	2	0
Total		**58(100%)**	**58(100%)**

The highest dermatomal level i.e.; T6 was reached in 42% of patients receiving dexmedetomidine and 27% of patients receiving buprenorphine.

The incidence of nausea was higher in buprenorphine compared to dexmedetomidine. And incidence of bradycardia was higher in the dexmedetomidine group.

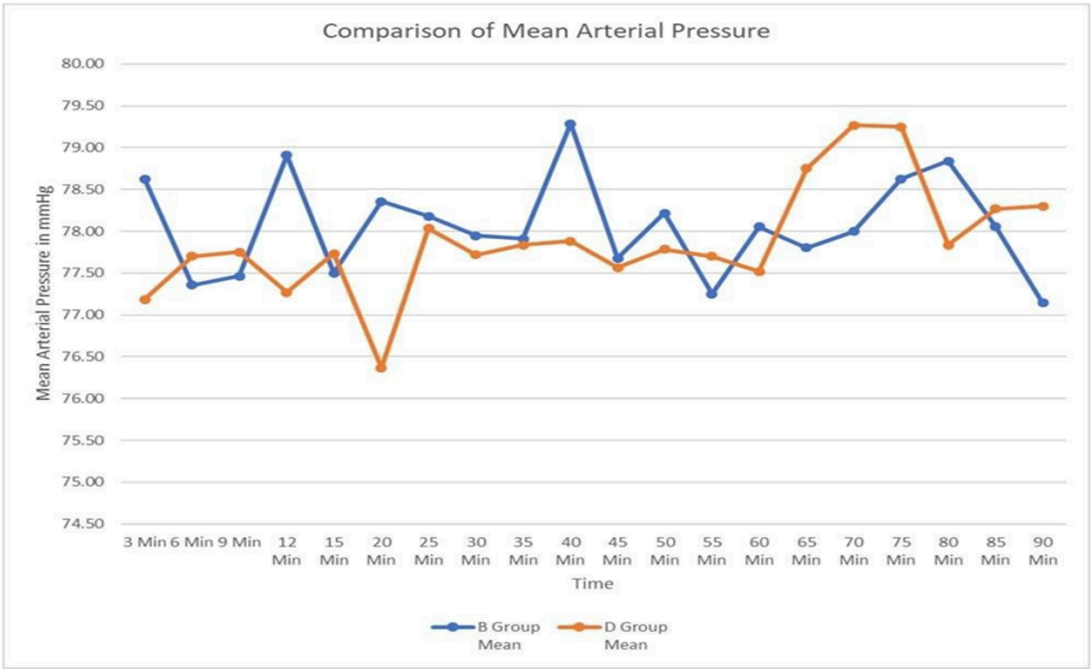

Figure 1: Comparison of mean arterial pressure

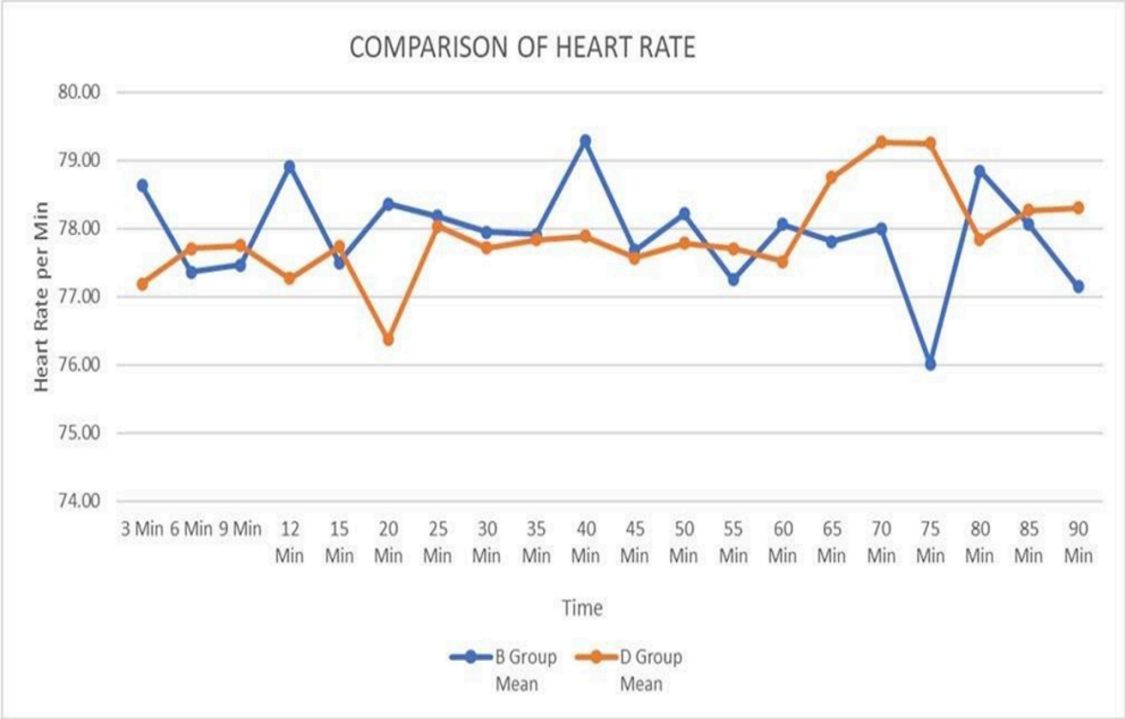

Figure 2: Comparison of heart rate

Figure 1 and 2 indicate the Mean arterial pressure and heart rate of the patients

The mean arterial pressure and Heart rate was monitored from preoperative basal to 90th minute of the procedure and continued postoperatively also (11 intervals). None of the intervals had statistical significance.

Discussion

Subarachnoid block with bupivacaine is the commonly used technique for transurethral resection of prostate. However, a single intrathecal injection of bupivacaine alone provides analgesia for only 2 – 2.5 hours. Most patients require further analgesia during the postoperative period. This prospective study was conducted in Government medical college, Thiruvananthapuram with an aim to compare the effects of intrathecal Dexmedetomidine and Buprenorphine as an adjuvant to 0.5% hyperbaric bupivacaine.

The study included 116 male patients belonging to the age >55 years of ASA grade 1 and 2 scheduled to undergo Trans urethral resection of prostate.

Kanazi GE et al [14] have used 3 µ g dexmedetomidine in their study and said to have comparable equipotent effect with clonidine. Hala EA Eid et al [16] studied the effects of dexmedetomidine on a dose related manner (control, 10 µ g and 15µ g) and confirmed the prolongation of duration of analgesia.

Many studies have chosen 5µ g of dexmedetomidine as an additive to intrathecal hyperbaric bupivacaine and proven efficacy [6,17]. Hence in our study we chose 5µ g dexmedetomidine as an additive to hyperbaric bupivacaine.

Few studies have been conducted with a higher dosage of buprenorphine. Capogna et al [18], Mahima Gupta et al [19] and Sapkal Praveen S et al [20], have chosen 60µ g of buprenorphine as an additive to intrathecal bupivacaine and showed to have a significant prolonged duration of analgesia along with nausea and vomiting that were not statistically significant.

Duration of analgesia

Duration of analgesia was taken from the time of intrathecal injection of drugs to the first supplementation of rescue analgesic when a patient complained of pain. In our study, the mean duration of analgesia was 540.9 minutes in the buprenorphine group and 558.5 minutes in the dexmedetomidine group.

The duration of analgesia in the Buprenorphine Group was 540.9 minutes whereas in the study conducted by Mahima Gupta et al [19] it was 289.66 ±68.94. But the mean duration of analgesia in the studies conducted by Shaikh and Kiran et al [10] and Capogna et al [18] was 475 minutes and 430 minutes. This similarity may be due to the geriatric population involved in all of the studies cited above. The duration of analgesia in the dexmedetomidine group in the study conducted by Mahima Gupta et al [19] was 493 minutes and the study conducted by Shah et al [21] was 474 minutes. The duration of analgesia was significantly prolonged in the study done by Rajni Gupta et al [11] (478 minutes). In our study, the mean duration of analgesia was 558.5 minutes in the dexmedetomidine group which was similar to above mentioned studies. Also, the study done by Eid et al [16] showed that duration of analgesia with dexmedetomidine Group was proportional to its dose. In this study, the Dexmedetomidine group had prolonged duration of analgesia compared to Buprenorphine group. Mahima Gupta et al [19] have shown similar results. The prolonged analgesic action of intrathecal α2 agonist is by decreasing the release of Cfibres neurotransmitters and by causing hyperpolarization of neurons in the postsynaptic dorsal horn

Duration of motor block

The duration of motor block was taken from time of intrathecal drug administration to the time taken to attain modified Bromage 3. The mean duration of motor block in the Buprenorphine group was 245.66 minutes and in the Dexmedetomidine group was 243.18 minutes (p value 0.00).

In the study conducted by Mahima Gupta et al [19] the duration of the motor block in the dexmedetomidine group was 413.4 minutes and the study conducted by Rajni Gupta et al [11], where the duration of the motor block was 421 minutes. This may be due to the low drug volume used in our study. The mean duration of motor block in buprenorphine group is 245.66 minutes, whereas the duration of motor block in Mahima Gupta et al [19] study was 205.17 minutes which is significantly lower than our study. This could be explained by the population taken into consideration for our study.

In our study itself, there was not much difference in the duration of motor blockade in the dexmedetomidine and buprenorphine group. However, compared to the parent study where the duration of motor blockade without any adjuvants was 177 56.9, the findings in our study are statistically significant.

Haemodynamic stability

Al-Ghanem et al [22] in their study noted that the use of intrathecal dexmedetomidine to be associated with decrease in blood pressure and heart rate.

In the present study, it was noted 4 cases of bradycardia and nil cases of hypotension in the dexmedetomidine group whereas 1 case of bradycardia and 2 cases of hypotension in buprenorphine group. They were managed successfully with the use of atropine 0.6 mg I.V and ephedrine in incremental doses of 6 mg. Bradycardia at 0- and 5-minute intervals in the dexmedetomidine group had statistical significance. Mahima Gupta et al [19] in their studies also incidence of bradycardia was more in the dexmedetomidine group. Dexmedetomidine causes bradycardia but the effect is more prominent when administered intravenously and with a higher dose [24]

Adverse events

The incidence of nausea and vomiting were more in the buprenorphine group as compared to the dexmedetomidine group which is similar to the study conducted by Mahima Gupta et al [19]. Capogna et al [18] also observed a greater number of nausea and vomiting in the buprenorphine group. Similar observations were seen by Sapkal et al [20]. Talke et al [23] in their study observed that α2 adrenergic agents have anti shivering properties. In the present study we have not encountered any case of shivering. This is in contrast to Mahima Gupta et al [19] study where the incidence of shivering was more in the dexmedetomidine group when compared to buprenorphine group. In the present study the SPO2 was in the range of 97 – 100 % without oxygen supplementation. No incidence of respiratory depression, pruritus and ECG changes were found in both the groups

Conclusion

The duration of motor blockade was found to be nearly identical in both groups with the highest statistical significance.The duration of analgesia and time to sensory regression to S1 were found to be longer in the dexmedetomidine group than in the buprenorphine group. During the research, both groups had stable and comparable hemodynamics. In comparison to buprenorphine, intrathecal administration of dexmedetomidine as an additive to hyperbaric bupivacaine was associated with fewer side effects.

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