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Comparative Study of Nalbuphine and Dexmedetomidine as Adjuvant to Intrathecal Bupivacaine in Spinal Anaesthesia

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ABSTRACT

The subarachnoid block is a preferred technique of anesthesia as it is easy to carry out, the onset of action is rapid, better relaxation of muscle and effectual but its duration of action is short. Adjuvants are drugs that increase the efficacy or potency of other drugs when given concurrently. Present study was aimed to compare nalbuphine and dexmedetomidine as adjuvant to intrathecal bupivacaine on spinal anaesthesia Present study was comparative, randomized, interventional study, conducted in patients 21-60 years age, ASA grade I/II, scheduled for elective infraumbilical surgeries under spinal anesthesia. In present study, 60 patients were randomly assigned into Group N (received 3 mL of 0.5% of bupivacaine +0.8 mg of nalbuphine) and Group D (received 3 mL of 0.5% levobupivacaine and 5 µg dexmedetomidine). Early onset of sensory block (2.22±1.12 min vs 3.25±1.24 min), early onset of motor block (4.3±1.3 min vs 6.7±2.62 min), less time to reach maximum level of sensory block (6.2±2.12 min vs 8.3±2.9 min), more total duration of motor block (182.28±31.65 min vs 151.48±38.66 min), late first request for rescue analgesia (281.43±44.57 min vs 211.78±49.88 min) and delayed two segments regression (102.65±21.54 min vs 83.35±25.6 min) was noted in dexmedetomidine group as compared to nalbuphine group and difference was statistically significant. Intraoperative and Immediate post-operative complications such as hypotension, bradycardia, vomiting, pruritis and shivering were more in nalbuphine group but difference was not statistically significant. Dexmedetomidine as adjuvant to intrathecal bupivacaine in spinal anaesthesia had prolonged duration of motor block, prolonged time of two segments regression and reduced demand for rescue analgesics as compared to nalbuphine as adjuvant to intrathecal bupivacaine.

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Key Words

Dexmedetomidine, nalbuphine, bupivacaine, spinal anaesthesia, adjuvant

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INTRODUCTION

The subarachnoid block is a preferred technique of anesthesia as it is easy to carry out, the outset of action is rapid, better relaxation of muscle and effectual. Additionally, reduced recovery time, quick return of patient's average oral intake and safety are its added advantages. Though subarachnoid block is relatively safe, its duration of action is short[1].

Local anesthetic, bupivacaine, is the most common agent used for spinal anesthesia but has relatively short duration of action. Many adjuvants to local anesthetics have been used intrathecally to improve the quality of intraoperative analgesia and prolong it in the postoperative period[2]. Adjuvants are drugs that increase the efficacy or potency of other drugs when given concurrently. They increase the speed of the onset of neural blockade (reduce latency), improve the quality and prolong the duration of neural blockade[3].

Dexmedetomidine is the next generation α2 agonist with highly selective α2-Adrenoceptor agonist. Dexmedetomidine has sedative, anti-anxiety, analgesic, neuroprotective and anesthetic-sparing effects[4]. Dexmedetomidine along with other drugs have been used to increase the duration of analgesia in subarachnoid, epidural and caudal blocks[5,6]. Nalbuphine, a semi-synthetic, mixed agonist-antagonist opioid, has a potential to attenuate the mu-opioid effects and to enhance the kappa-opioid effects. It was synthesized in an attempt to produce analgesia without the undesirable side effects of a μ opioid receptor agonist. Previous studies have shown that epidural or intrathecal administration of Nalbuphine produces a significant analgesia accompanied by minimal pruritus and respiratory depression[7,8]. Present study was aimed to compare nalbuphine and dexmedetomidine as adjuvant to intrathecal bupivacaine on spinal anaesthesia.

MATERIALS AND METHODS

Present study was comparative, randomized, interventional study, conducted under department of anesthesiology and critical care, at Gmers medical college and hospital, Gotri, Vadodara, Gujarat, India. Study duration was of 1 year (January 2022 to December 2022). Study approval was obtained from institutional ethical committee.

Inclusion criteria: Patients 21-60 years age, ASA grade I/II, scheduled for elective infraumbilical surgeries under spinal anesthesia, willing to participate in present study

Exclusion criteria:

- Patients with a history of allergy to local anesthetics
- Patients with local infection at the site of the block
- Pregnant women
- Patients with contraindication to spinal anaesthesia, coagulopathies, previous neurological deficit in lower limb, spinal deformity
- Patients not consented for participation

Study was explained to patients in local language and written consent was taken for participation and study. Patient details such as demographic information, medical/surgical history, clinical examination findings, laboratory investigations (CBC, urine routine and microscopic examination, KFT, LFT, FBSL) were noted. All patients underwent preanesthetic examination, after fitness patients were posted for surgery. One day prior to the surgery, written consent for surgery was obtained.

In operation theatre, the standard monitoring was done and baseline parameters (pulse rate, non-invasive blood pressure, oxygen saturation and respiratory rate) were recorded. Patients received either nalbuphine or dexmedetomidine as adjuvants with Intrathecal Bupivacaine (H) 0.5%, 3 mL as a standard dose. Patients were randomly divided into 2 groups by computer generated numbers.

- Group N patients received 3 mL of 0.5% of levobupivacaine +0.8 mg of nalbuphine comprising a total volume of 3.5 mL
- Group D patients received 3 mL of 0.5% levobupivacaine and 5 μg dexmedetomidine comprising a total volume of 3.5 mL.

Patients and anesthesiologist (the outcomes assessor) who recorded the perioperative data were blinded to the study drugs. After preloading with 10 mL kg^{-1} Ringer lactated solution, spinal anaesthesia was administered under all aseptic precautions, through midline approach. Intraoperatively patient's hemodynamic parameters were periodically recorded. Patients were observed intraoperatively at baseline and at 5, 10 and 15 min, respectively, then at interval of 15 min up to 1 hr and at 30 min till patient is shifted from operation theatre to PACU.

Standard postoperative care was provided. Variables measured were duration of effective analgesia (from the time of intrathecal drug administration to the time of first supplementation with rescue analgesic), postoperatively blood pressure, pulse rate, intensity of pain, spO2, adverse effects such as hypotension, bradycardia, respiratory depression were recorded.

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while

ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi- square test or Fisher exact test as applicable. p-value less than 0.5 was considered as statistically significant.

RESULTS

In present study, 60 patients were randomly assigned into group N (n = 30) and group D (n = 30). General characteristics of study patients such as age (years) , gender (male/female), height (centimeters), weight (kg) and ASA grade (I/II) were comparable in both groups and difference was not statistically significant (Table 1).

In present study, early onset of sensory block (2.22±1.12 min vs 3.25±1.24 min), early onset of motor block (4.3±1.3 min vs 6.7±2.62 min), less time to reach maximum level of sensory block (6.2±2.12 min vs 8.3±2.9 min), more total duration of motor block (182.28±31.65 min vs 151.48±38.66 min), late first request for rescue analgesia (281.43±44.57 min vs 211.78±49.88 min) and delayed two segments regression (102.65±21.54 min vs 83.35±25.6 min) was noted in dexmedetomidine group as compared to nalbuphine group and difference was statistically significant (Table 2).

Intraoperative and Immediate post-operative complications such as hypotension, bradycardia, vomiting, pruritis and shivering were more in nalbuphine group, while nausea was more in dexmedetomidine group but difference was not statistically significant (Table 3).

DISCUSSIONS

Subarachnoid block is a safe, cost effective and easy to perform technique which provides rapid onset and reliable anesthesia along with low risk of infection but has the drawbacks of shorter duration of block and short postoperative analgesia[9]. Excessively soaring regional blocks and toxicity due to local anesthetics are the most common reasons for deaths linked to regional blocks; therefore, decreasing dosage of local anesthetics, adding adjuvants, usage of latest methodology to circumvent inordinate blocks and superior tackling of local anesthetic toxicity are the novel targets for reducing death rate linked to regional anesthesia[10].

Adjuvants are being added to local anaesthetics to increase the quality of intraoperative anaesthesia and also attribute to a prolonged and better anti-nociceptive action in the immediate post-operative period. The anaesthetic and analgesic requirement of local anaesthetics gets reduced by the use of adjuvants because of their analgesic properties and augmentation of local anaesthetic effects[11].

Dexmedetomidine is highly selective α2-Adrenoceptor agonist, when co-administered intrathecally with bupivacaine results in binding to presynaptic C-fibers and post-synaptic dorsal horn nucleus in spinal cord which results in synergistic action to the local anaesthetics effects[12]. The resulting effect may be related to the drug lipophilicity.

Nalbuphine semi-synthetic opioid with agonist at kappa receptor and antagonist at mu receptor. It activates caudate perhaps by disinhibition and initiates pain enhancing connectivity with other regions.

Table 1: General Characteristics

Characteristics	Group D (n = 30)	Group N (n = 30)	p-value
Age (years)	43.37±12.75	41.13±11.95	0.65
Gender			
Male	17	16	0.79
Female	13	14	
Height (centimeters)	163.1±6.81	160.8±10.6	0.72
Weight (kg)	65.4±11.9	66.3±10.9	0.61
ASA grade			
I	19	20	0.63
II	11	10	

Table 2: Characteristics of sensory and motor block

Characteristics	Group D (n = 30)	Group N (n = 30)	p-value
Onset of sensory block (min)	2.22±1.12	3.25±1.24	0.033
Onset of motor block (min)	4.30±1.3	6.70±2.62	0.045
Time to reach maximum level of sensory block (min)	6.20±2.12	8.30±2.9	0.046
Total duration of motor block (min)	182.28±31.65	151.48±38.66	<0.001
First request for rescue analgesia (min)	281.43±44.57	211.78±49.88	<0.001
Time of two segments regression	102.65±21.54	83.35±25.6	<0.001

Table 3: Intraoperative and Immediate post-operative complications

Complications	Group D (n = 30)	Group N (n = 30)
Hypotension	1	1
Bradycardia	1	2
Vomiting	1	2
Nausea	2	1
Pruritis	1	2
Shivering	1	2

Pronociceptive effect of nalbuphine is abolished by blockade of this connectivity[13]. The technique of intrathecal opioid administration along with local anaesthetics has been studied extensively. Rationale for the combination of opioids and local anaesthetics is that these two types of drugs eliminate pain by acting at two different sites. Local anaesthetics act at the nerve axon, whereas opioids act at the receptor site in the spinal cord[14,15].

Singh *et al.*[16] noted that onset of sensory and motor blocks was faster in group LD (Dexmedetomidine) (2.31±0.66 and 6.24±0.45 min) compared to Group LN (Nalbuphine) (4.33 ± 0.66 and 7.00±0.45 min). Total duration of effective analgesia (402.50±9.79 vs. 294.63±8.95) and total duration of motor block (289.67±5.94 vs. 251.87±8.48 min) were significantly prolonged in Group LD than in Group LN. There was no significant difference in hemodynamic changes and adverse effects between the groups. The addition of 5 µg dexmedetomidine to intrathecal 0.5% isobaric levobupivacaine as adjuvant is associated with prolonged sensory and motor blockade with better perioperative analgesia compared to 0.8 mg nalbuphine.

Gantasala *et al.*[17] noted that duration of analgesia was 320.26±89.52 min for dexmedetomidine (D) whereas it was 222.23±25.43 min for nalbuphine (N) with a $p<0.05$. No side effects were noted. A dose of 5 mcg dexmedetomidine as an adjuvant seems to be optimal for providing postoperative analgesia with better hemodynamic stability.

Khare *et al.*[18] noted that patients in group DB (Dexmedetomidine) had a significantly prolonged duration of analgesia as compared to group NB (nalbuphine). The early onset of sensory and motor blockade was noted in group DB ($p<0.05$). The duration of motor blockade was significantly prolonged in group DB ($p<0.05$). Patients in both groups showed no significant difference in haemodynamic changes and incidence of side effects ($p>0.05$). Dexmedetomidine as an intrathecal adjuvant was found to have prolonged sensory and motor block and provide good quality of postoperative analgesia and stable haemodynamics with minimal side effects as compared to nalbuphine.

Dexmedetomidine provides stable hemodynamic conditions, good quality of intra operative analgesia and prolonged post operative analgesia with minimal side effects[19]. Limitations and shortcomings of present study were small sample size, for elective surgery patients only and from single hospital. Studies with larger number of participants are required to generalize the results and also the patient-to-patient variability of pain perception.

CONCLUSION

Dexmedetomidine as adjuvant to intrathecal bupivacaine in spinal anaesthesia had prolonged duration of motor block, prolonged time of two segments regression and reduced demand for rescue analgesics as compared to nalbuphine as adjuvant to intrathecal bupivacaine. Dexmedetomidine seems to be a better choice as Intrathecal adjuvant with Bupivacaine for lower abdominal surgeries.

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