Original Research Article

Comparative study of intrathecal bupivacaine and clonidine combination versus bupivacaine and dexmedetomedine for gynaecological procedures

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Abstract

Background: Gynaecological procedures are often done under regional anaesthesia.Various adjuvants are being used with local anesthetics for prolongation of intraoperative and post-operative analgesia. Dexmedetomidine, a highly selective alpha-2adrenergic agonist, has emerged as a valuable adjunct to regional anesthesia and analgesia.The study was aimed to compare the onset, duration of sensory and motor block, hemodynamic effects, post-operative analgesia, and adverse effects of dexmedetomidine and clonidine with bupivacaine for spinal anesthesia. **Material and Methods:** A total of 50 patients belonging to ASA Grade 1 and 2 undergoing elective gynecological surgery under spinal anesthesia were studied. The patients were allocated in two groups (25 each). Group I bupivacaine + clonidine (B+C) received 17.5 mg of bupivacaine supplemented 45 mcg clonidine and Group II bupivacaine + dexmedetomidine (B+D) received 17.5 mg bupivacaine supplemented 5 mcg dexmedetomidine. The onset time of sensory and motor level, time to reach peak sensory and motor level, hemodynamic changes and side effects were recorded. **Results:** Mean time of onset of sensory block in Group I and Group II were found to be 3.65±0.68 mins and 2.78±0.20 mins respectively (p>0.05). The onset of motor block in Group I was slightly less than Group II. Five patients in Group I B+C and nine patients from group II B+D had significant bradycardia and hypotension. Nausea and vomiting was reported in one case in group I B+C shivering was reported in 1 case of each group. **Discussion:** Use of intrathecal dexmedetomidine as an adjuvant to bupivacaine seems to be an attractive alternative to clonidine for long duration gynecological surgical proceduresdue to its profound intrathecal anesthetic and analgesic properties combined with minimal side effects.

Key Words: Bupivacaine, clonidine, dexmedetomidine, gynaecological procedures.

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Email: shubhanand84@gmail.com
Received Date: 21/01/2017 Revised Date: 10/02/2017 Accepted Date: 14/03/2017
DOI: https://doi.org/10.26611/1015211

Access this article online	
Quick Response Code:	Website: www.medpulse.in
	Accessed Date: 06 April 2017

INTRODUCTION

Anaesthetic techniques have improved drastically over the last few decades. Many techniques and drug regimens have been tried from time to time with varied success, to eliminate the anxiety component during regional anaesthesia[1-2]. Gynaecological procedures such as vaginal hysterectomy, abdominal hysterectomy are often done under regional anaesthesia[3-4]. Spinal anaesthesia with bupivacaine is given routinely for such procedures. The routine doses of bupivacaine are associated with prolonged and intense sensory and motor block and significant sympathetic block. In low doses, bupivacaine limits the distribution of spinal block and yield a comparably rapid recovery, but may not provide an adequate level of sensory block[5].Various adjuvants are being used with local anesthetics for prolongation of intraoperative and post-operative analgesia. Spinal anaesthesia with bupivacaine alone has relatively short duration of action and needs early analgesic intervention

How to cite this article: Madhuri Pramod Lonikar, Shubhada Anand Patil, Mohd. Imran Haroon. Comparative study of intrathecal bupivacaine and clonidine combination versus bupivacaine and dexmedetomedine for gynaecological procedures. *MedPulse International Journal of Anesthesiology.* April 2017; 2(1): 01-05. http://medpulse.in/Anesthsiology/index.php

in the post-operative period. To overcome this disadvantage, the concept of co-induction of anesthesia has come forward by administering selective α_2 agonist like clonidine to reduce the dose requirement of bupivacaine and its adverse effects and prolong analgesia in the post-operative period[6]. Dexmedetomidine, a highly selective alpha-2adrenergic agonist has emerged as a valuable adjunct to regional anesthesia and analgesia[7]. It has become of the frequently used drugs along with routine anaesthetic drugs, due to its haemodynamic, sedative, anxiolytic, analgesic, neuroprotective and anaesthetic sparing effects[8]. Earlier human studies showed that, intrathecal 5 mcg dexmedetomidine would produce longer duration of analgesic effect in spinal anesthesia with minimal side effects[9-12]. In present study, the usefulness of intrathecal bupivacaine and clonidine combination was compared with bupivacaine and dexmedetomedine for gynaecological procedures.

MATERIAL AND METHODS

In this prospective, randomized and double blinded study, a total of 50adult females belonging to American Society of Anesthesiology (ASA) Grades 1 and 2 scheduled for gynecological surgery under subarachnoid block were enrolled after obtaining approval from the Hospital Ethics Committee along with written and informed consent. Patients with contraindication to regional anesthesia, history of significant coexisting diseases like ischemic heart disease, hypertension, impaired renal functions, rheumatoid arthritis, and severe liver disease where excluded from the study. The patients were allocated in two groups (25 each). Group I bupivacaine + clonidine (B+C) received 17.5 mg of bupivacaine supplemented 45 mcg clonidine and Group II bupivacaine + dexmedetomidine (B+D) received 17.5 mg bupivacaine supplemented 5 mcg dexmedetomidine. All patients were examined and investigated a day prior to surgery, and were familiarized with visual analogue scale (VAS) [13]and its use for measuring the postoperative pain. They were advised fasting for 6 h and received alprazolam 0.5 mg as premedication a night before and 0.25 mg in morning on the day of the surgery. In the operation theatre, electrocardiogram (ECG), pulse oximetry, and noninvasive blood pressure were attached and baseline parameters were recorded and monitoring was initiated. Intravenous (IV) access was secured and all patients were preloaded with ringer lactate 10 ml/kg. These patients were randomly assigned using sealed envelope technique to either of the two groups in a double blind manner. The various treatment groups were as per Table 1. The study solutions were prepared in a 5 ml syringe by an anesthesiologist who then handed them over in a coded form to the attending anesthesiologist blinded to the nature of drug given. Subarachnoid block was administered at the L2–3or L3–4vertebral level using 26-gauge spinal needle with patients in the sitting position under all aseptic precautions. Patients were made supine following the block.

Table 1: Grouping of the study population

Group	Drugs given
Group I B+C	Intrathecal bupivacaine 12.5 mg (2.5 ml) + clonidine 30 µg (0.2 ml) + preservative free normal saline (0.3 ml)
Group II B+D	Intrathecalbupivacaine 12.5 mg (2.5 ml) + dexmedetomidine 5 µg (0.05 ml) +preservative free normal saline (0.45 ml)

BC=Bupivacaine clonidine; BD=Bupivacaine dexmedetomidine

The onset and duration of sensory block, highest level of sensory block, time to reach the highest dermatomal level of sensory block, motor block onset, time to complete motor block recovery, and duration of spinal anesthesia were recorded.

Definitions

Onset of sensory block

The onset of sensory block was defined as the time between injection of intrathecal anesthetic and the absence of pain at the T8 dermatome assessed by sterile pinprick every 2 min till T8 dermatome was achieved. The highest level of sensory block was evaluated by pinprick at midclavicular line anteriorly every 5 min for 20 min after the injection, thereafter every 15 min.

Duration of sensory block

The duration of sensory block was defined as the time of regression of two segments in the maximum block height, evaluated by pinprick. The motor level was assessed according to modified Bromage score[14]: Bromage 0, the patient is able to move the hip, knee, and ankle; Bromage 1, the patient is unable to move the hip, but is able to move the knee and ankle; Bromage 2, the patient is unable to move hip and knee, but is able to move the ankle; and Bromage 3, the patient is unable to move the hip, knee, and ankle.

Time for motor block onset

Time for motor block onset was defined as modified Bromage score of 3. Complete motor block recovery was assumed when modified Bromage score was 0.

Duration of spinal anesthesia

The duration of spinal anesthesia was defined as the period from spinal injection to the first occasion when the patient complained of pain in the postoperative period. All durations were calculated considering the time of spinal injection as time zero. Surgery was allowed to commence on achieving adequate sensory block height (T8). Vitals were recorded 5 min before intrathecal injection; 5, 10, 15, 20, and 25 minutes after and subsequently every 15 minutes. Pain scores using VAS were recorded 5 min before intrathecal injection, after the

start of surgery, and subsequently every 15 min till the surgery was over; and thereafter VAS was assessed in the postoperative period. IV fluids were given to maintain the blood pressure. Heart rate (HR) less than 50 beats/min was corrected using 0.6 mg of IV atropine sulfate. The incidence of pruritus, nausea, vomiting, and sedation were recorded. De Kock sedation scale[15] was used: 1 = patient somnolent but responding to verbal commands; 2 = patient somnolent, not responding to verbal commands but responding to manual stimulation; and 3 = patient somnolent, not responding to verbal commands or manual stimulation. Postoperatively, motor block recovery such as modified Bromage score of zero and sensory block regression were assessed every 15 min after completion of surgery till the time of regression of two segments in maximum block in the post-anesthetic care unit (PACU) along with the vitalsigns and VASscores. Anypatientshowing VAS more than or equal to 3 was administered a supplemental dose of IV. tramadol 50 mg. The amount required by the patients in the next 24 h was recorded in the groups.

Statistical analysis

Data obtained were tabulated and analyzed using Statistical Package for Social Science (SPSS 15.0 evaluation version). Data was expressed as means and standard deviation (SD), medians and ranges, or numbers and percentages.

RESULTS

A total of 50 adult females belonging to ASA) Grades 1 and 2 scheduled for gynecological surgery under subarachnoid block were studied. To make the comparison unbiased, the number of patients under each type of gynecological surgery performed was kept similar among the groups. No statistical difference was seen in patient's demographics or ASA grade and duration of surgery as well (Table 2).

Table 2: Comparison of demographic profile in two groups

Variable	Group I (B+C)	Group II (B+D)	p value
Age (years)	39.0 ±4.2	39.4 ±6.8	> 0.05
Height (cm)	169.6±2.3	170.1±5.6	> 0.05
Weight (kgs)	66.2±7.7	69.4±3.4	> 0.05
ASA Grade (1:2)	28:2	26:4	> 0.05
Duration of surgery (min)	92.6±30.4	94.4±32.5	> 0.05

Abdominal hysterectomy was the commonly performed gynecological surgery in both groups (Table 3).

Table 3: Types of gynaecological procedures

Type of gynecological procedure performed	Group I (B+C)(n=25)	Group II (B+D)(n=25)
Abdominal hysterectomy	11	14
Vaginal hysterectomy	08	07
Laparotomy for ovarian mass	07	06
Tubal recanalization	04	03

Table 4 depicts comparison of sensory and motor block characteristics in both the groups. Mean time of onset of sensory block in Group I and Group II were found to be 3.65±0.68 mins and 2.78±0.20 mins respectively (p>0.05). The onset of motor block in Group I was slightly less (4.12±0.60 mins) than Group II (4.56±0.88 mins), however, the difference was insignificant (p>0.05).

Table 4: Characteristics of spinal anaesthesia

Variable (min)	Group I (B+C)	Group II (B+D)	p value
Time of onset of sensory block	3.65±0.68	2.78±0.20	> 0.05
Time of onset of motor block	4.12±0.60	4.56±0.88	> 0.05
Time to reach max. sensory level	7.68±1.26	7.84±1.64	> 0.05
Duration of sensory block	354.22±33.51	402.11±24.32	< 0.05
Duration of motor block	205.33±36.91	364.20±55.12	< 0.05
Duration of spinal anaesthesia	376±26.1	504.66±10.45	< 0.05

The duration of sensory block in Group I was 354.22±33.51 min and in Group II was 402.11±24.32 min and the duration of motor block in Group I was 205.33±36.91 mins and in Group II was 364.20±55.12mins. Duration of sensory and motor block was significantly prolonged in group I B+D as compared to group II B+C (p<0.05). The duration of spinal anesthesia was shorter in group I B+C as compared to group II B+D (p<0.05) (Table 4). The mean values of mean arterial pressure and HR were comparable between the two groups throughout the intra- operative and post-operative period. None of the patients experienced respiratory distress at any point of time. SpO2 of all the patients were greater than 96% at all the times and did not require additional oxygen in post- anesthesia room. Five patients in Group I B+C and nine patients from group II B+D had significant bradycardia and hypotension which was treated with mephentermine 6 mg IV. Nausea and vomiting was reported in one case in group I B+C shivering was reported in 1 case of each group. However, the rate of complications were statistically insignificant between both the groups. Lower VAS values (<3) were observed in both the groups during the whole duration of surgery. None of the patients required additional analgesics intraoperatively. Post-operative VAS scores and total analgesic requirement in 24 hrs were minimal in Group II B+D (p<0.05).

DISCUSSION

Management of intra and post-operative painhas been revolutionized since the understanding of its neurobiology and pharmacology of the available drugs for the control of pain[16]. Various drugs have been tried in the subarachnoid space along with local anaesthetics with the aim of improving the duration of post-operative analgesia[17]. Spinal anaesthesia is the most commonly used technique in developing country like India as it is rapid onset, technically easy administration and economical technique[18]. Intrathecal α_2 receptor agonists have been found to have anti-nociceptive action for both somatic and visceral pain. Clonidine is a selective partial agonist for α2-adrenoreceptors and it increases the duration of sensory and motor spinal block when added to spinal local anaesthetics. This effect of clonidine is dose dependent and doses of more than 75 µg intrathecal clonidine is accompanied by excessive sedation, hypotension and bradycardia[19]. Local anesthetics act by blocking sodium channels. Alpha-2 adrenoreceptor agonists act by binding to the presynaptic C-fibers and post-synaptic dorsal horn neurons. They produce analgesia by the depressing release of C-fiber transmitters and by hyperpolarization of post-synaptic dorsal horn neurons[20]. The complementary action of local anesthetics and alpha-2 adrenoreceptor agonist accounts for their profound analgesic properties. The prolongation of motor block of spinal anesthetics may be the result of binding of alpha-2 adrenoreceptor agonists to the motor neurons in the dorsal horn[20]. Dexmedetomidine when used intravenously during anaesthesia reduces opioid and inhalational anesthetics requirements[21]**.** It has about ten times higher affinity for 2- adrenoreceptor than clonidine. It is useful in blunting haemodynamic responses in perioperative period due to its central sympatholytic effect and successfully used in intravenous doses varying from 0.25 to 1 mcg/kg for attenuating intubation responses[22]. In present study, time of onset of sensory blocks was similar in both groups. Al-Ghanem *et al*[10] also observed no difference in the onset time in patients receiving dexmedetomidine (7.5±7.4 mins) and fentanyl (7.4±3.3 mins) as adjuvant to isobaric bupivacaine (p=0.95).The intrathecal 5 mcg dexmedetomidine shown prolonged duration of motor block.When compared to the duration of motor block in Kanazi *et al*[9] study (250±76 mins) and in Al-Ghanem *et al* study (240±64 mins)[10]. Hala EA Eid *et al*[23]observed dose dependent prolongation of motor and sensory blockade with reduced analgesic requirement with increasing dosage of intrathecal dexmedetomidine. Doses varying from 3 to 15 mcg have been used as adjuvant to bupivacaine for spinal anaesthesia. There has been dose-dependant prolongation of analgesia.It is observed in various studies that dexmedetomidine as an epidural adjuncts prolong the motor and sensory block duration time and post-operative analgesia without any additional morbidity[24,25]. Both dexmedetomidine and clonidine provide good quality of intra-operative analgesia and hemodynamic stability. Intrathecal dexmedetomidine and clonidine added to bupivacaine reduce both visceral and somatic pain in present study. The analgesia was significantly better in Group II B+D as compared to Group I B+C and it was statistically significant. Al-Ghenam *et al*[10] and Mahendru *et al*[26] study shows that the use of intrathecal dexmedetomidine as an adjuvant to bupivacaine seems it to be an attractive alternative to fentanyl and clonidine for long duration surgical procedures. Bradycardia and hypotension are the major side effects observed following dexmedetomidine infusion. Bradycardia is attributed to reflex response for transient hypertension during initial part of infusion. Subsequent decrease in heart rate is due to decrease in central sympathetic outflow. Hypotension is attributed to decreased central sympathetic outflow. In the present study, these side effects were not significant due to small doses of intrathecal dexmedetomidine and clonidine with local anesthetics were used. To conclude, the use of intrathecal dexmedetomidine as an adjuvant to bupivacaine seems to be an attractive alternative to clonidine for long duration gynecological surgical procedures due to its profound intrathecal anesthetic and analgesic properties combined with minimal side effects.

ACKNOWLEDGEMENTS

We express our deep sense of gratitude to the Management, JIIU Trust and Dr. Amarnath B. Solapure, Dean, IIMSR Medical Collage, Badnapur, Jalna, Maharashtra. We also deeply acknowledge the help and support of Dr. Sudhir Bhope, Prof. and Head, Dept. of Anesthesia and Dr. A. M. Khadri, Medical Superintendant, Noor Hospital, Badnapur and my Patients.

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Source of Support: None Declared
Conflict of Interest: None Declared