Original Article

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Comparison of Intrathecal Dexmedetomidine and Fentanyl as Adjuvants to Hyperbaric Bupivacaine: A Randomised Controlled Trial

Anaesthesia Section

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ABSTRACT

Introduction: Subarachnoid block using bupivacaine along with fentanyl is routinely used in regional anaesthesia technique in lower limb and lower abdominal surgeries. However, fentanyl is often associated with various side effects. The use of dexmedetomidine as an alternative to fentanyl in regional blocks is emerging due to minimal adverse effects and prolonged duration of action.

Aim: To compare intrathecal dexmedetomidine and fentanyl as adjuvants to hyperbaric bupivacaine.

Materials and Methods: The prospective, randomised study was performed on 100 patients, divided into two groups. Group I patients were administered with bupivacaine 12.5 mg (2.5 mL)+ fentanyl 25 µg (0.5 mL) whereas group II patients received bupivacaine 12.5 mg (2.5 mL) + dexmedetomidine 5 µg (0.5 mL). Post anaesthesia Heart Rate (HR) and Blood Pressure (BP) were recorded. The onset of sensory and motor block, level of sensory block, time for two segment regression, motor and sensor recovery, duration, quality of analgesia and Visual Analog Scale (VAS) score were recorded. Data were analysed using R Studio V 1.2.5001 software. Wilcoxon signed rank test and independent sample t-test were used to find the difference between mean. The $p<0.05$ was considered statistically significant.

Results: Time for onset of sensory block ($p=0.0027$), motor block ($p<0.001$) and peak sensory block ($p<0.001$) was significantly high in group I patients. Most of the patients of group I had a T8 level of sensory block (38%) while in group II around 36% of patients had T6 level of sensory block. Time for full motor recovery ($p=0.0015$) and sensor recovery ($p<0.001$) was high in group II patients.

Conclusion: Dexmedetomidine is associated with long term motor and sensory block, excellent analgesia and there was less demand for rescue analgesics as compared to fentanyl.

Keywords: Analgesia, Blood pressure, Heart rate, Local analgesia, Spinal anaesthesia

INTRODUCTION

In various regional techniques of anaesthesia, the subarachnoid block is commonly used for lower limb and abdominal surgeries with bupivacaine being a local anaesthetic are commonly performed [1,2]. Various opioid adjuncts are used with bupivacaine for long-lasting intra and postoperative analgesia [2]. Fentanyl is a highly lipophilic short-acting opioid when combined with local anaesthetics, which leads to improved quality and duration of anaesthesia [1]. However, the use of intrathecal fentanyl is associated with unreliable postoperative analgesia or adverse effects such as pruritus, nausea/vomiting and respiratory depression [2,3]. Dexmedetomidine is a selective α2 adrenergic receptor agonist, used for various applications and procedures in the preoperative and critical care setting [4]. The use of dexmedetomidine as an adjunct to regional anaesthesia and analgesia is emerging as it produces fewer side effects [1,5]. Previous studies have shown that intrathecal 5 µg dexmedetomidine with hyperbaric bupivacaine can produce more optimal postoperative analgesia with fewer adverse effects [2,6-9].

Despite few evidences of efficacy of dexmedetomidine as an adjuvant to bupivacaine in spinal anaesthesia, the primary objective of this study was to explore the usefulness of dexmedetomidine as an adjuvant. However, the secondary objective was to compare this α2 adrenergic agonist with the previously established and widely used adjuvant- fentanyl on the spinal block characteristics in patients scheduled for surgery.

MATERIALS AND METHODS

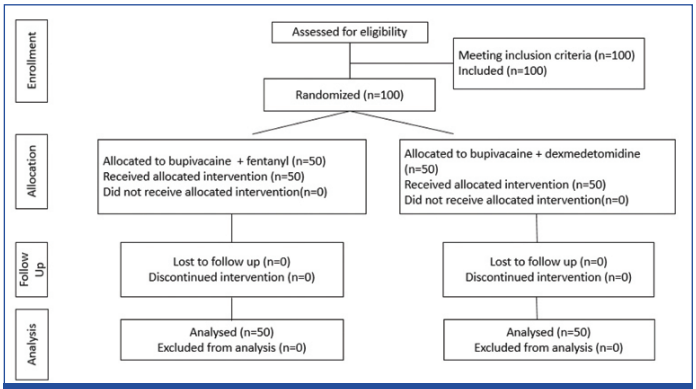
This prospective randomised trial was performed between November 2018-October 2020, Dr. D Y Patil Medical College Hospital and Research centre, Kolhapur, Maharashtra, India following approval by the Institutional Ethics Committee (IEC) (DYPMCK/PG-14/1721/17-18).

Inclusion criteria: Following written informed consent, 100 patients with an age range from 18-60 years of American Society of Anesthesiologists (ASA) grade I and II scheduled to undergo either lower limb, abdominal, gynaecological and/or urological surgeries were included in the study.

Exclusion criteria: Patients with allergy to the anaesthetics, dependent on narcotics, spinal abnormality, skin infection, bleeding disorder, cardiopulmonary manifestations, peripheral neuropathy, and obstetric cases were excluded from the study.

Sample size calculation: Sample size was calculated using R Studio V 1.2.5001 software. The calculated sample size for each group was n=42 and the power of the study was 90%.

Patients were divided into two groups by sealed envelope simple random sampling procedure, each group consisted of 50 patients. Group I patients were anaesthetised with bupivacaine 12.5 mg (2.5 mL)+fentanyl 25 µg (0.5 mL) and group II patients with bupivacaine 12.5 mg (2.5 mL)+dexmedetomidine 5 µg (0.5 mL) [Table/Fig-1].



[Table/Fig-1]: CONSORT chart.

Study Procedure

Patients of both the groups were advised to remain nil per oral for six hours and received diazepam 10 mg and ranitidine 150 mg orally as premedication the night before and in the morning on the day of the surgery. In the operation theatre, electrocardiogram, pulse oximetry and non invasive BP monitors were attached and baseline parameters such as Pulse Rate (PR), BP, were recorded, and monitoring was initiated. Intravenous (i.v.) access was secured, and all the cases were preloaded with 500 mL ringer lactate solution. At the L3-L4 intervertebral space subarachnoid block was administered using a 23-gauge Quincke spinal needle with patients in the sitting or left lateral position under all aseptic precautions. Postanaesthesia vital parameters such as HR, BP and VAS were recorded at different time interval.

Sensory block was tested by the pin-prick method using a hypodermic needle. The onset and duration of sensory block, the highest level of sensory block and the time for two dermatomal segment regression of sensory level were recorded. The onset of sensory block is defined as the time of injection of the drug into subarachnoid space to loss of pin-prick sensation. The duration of sensory block is defined as the time from onset to time of pin-prick sensation to the S1 dermatomal area. The motor block was assessed by the modified Bromage score, which consists of grades such as grade 0 for full flexion of knee and feet, grade 1- just able to flex knees, full flexion of feet, grade 2- unable to flex knee, but some flexion of feet possible and grade 3- unable to move legs or feet [10]. Intra and postoperative pain were assessed by VAS scale and categorised into no pain to slight pain (0-2), mild pain (2-5), moderate (5-7), severe pain (7-9), and worst possible pain (10). Analgesics were given on patient demand and time taken at analgesia required was noted. Postoperative VAS was recorded at 3, 6, and 12 hours. Four point modified Belzarena scale was used to assess the quality of intraoperative analgesia which is characterised as 1- unable to tolerate pain, 2- able to tolerate discomfort with additional analgesia, 3- some discomfort but no additional analgesics required and 4- completely satisfied [11]. Postoperative complications such as hypotension, bradycardia, sedation, nausea, vomiting, and urinary retention were recorded.

STATISTICAL ANALYSIS

Data were analysed using R Studio V 1.2.5001 software. Continuous variables were expressed in mean±standard deviation (Mean±SD) whereas categorical variables were expressed in percentage and frequency. Wilcoxon signed rank test and independent sample t-test were used to find the difference between mean. The $p<0.05$ was considered statistically significant.

RESULTS

The mean age of the patients (N=100) was 41.32±11.48 years. Baseline characteristics of the two groups were well matched as illustrated in [Table/Fig-2].

Characteristics	Group I	Group II	p-value[WT]
Age (years)	42.18±10.45	40.16±12.27	0.46
Height (ft)	5.51±0.43	5.53±0.33	0.5111
Sex (M:F)	26:24	25:25	-
ASA (I:II)	28:22	26:24	-

[Table/Fig-2]: Demographic characteristics of the patients.
[WT]: Wilcoxon signed rank test.

The time taken for the onset of sensory and motor block was significantly high in group I patients when compared with group II patients [Table/Fig-3]. Similarly, time for peak sensory block in group I was significantly higher than group II ($p<0.001$).

Group, I patients had the highest level of sensory block as compared with group II [Table/Fig-4].

The time for two-segment regression was significantly slower in group II (139.22±7.45 min) when compared with group I (83.32±8.71 min) ($p<0.001$). Significantly higher time for full motor recovery ($p=0.0015$) and sensory recovery ($p<0.001$) was observed in group II patients. Duration of analgesia, quality of intraoperative analgesia and VAS score is shown in [Table/Fig-5].

The onset of action	Group I (seconds)	Group II (seconds)	p-value
Sensory block	137.5±12.16	131.86±8.92	0.0027[PT]
Motor block	230.68±16.75	216.42±12.94	<0.001[WT]

[Table/Fig-3]: The onset of sensory and motor block.
PT: Paired t-test, WT: Wilcoxon signed rank test

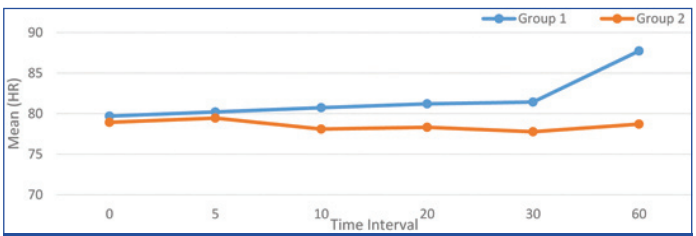
Level of sensory block	Group I N (%)	Group II N (%)
T4	00 (00)	03 (06)
T5	00 (00)	04 (08)
T6	04 (08)	18 (36)
T7	06 (12)	14 (28)
T8	19 (38)	10 (20)
T9	12 (24)	01(02)
T10	09 (18)	00 (00)

[Table/Fig-4]: Highest levels of sensory block.

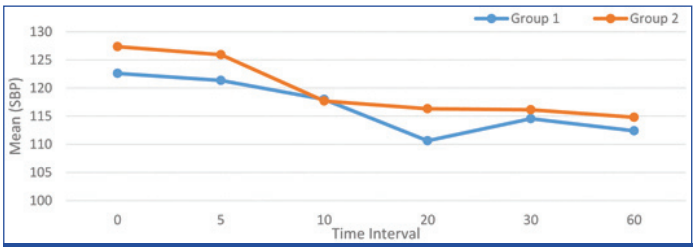
Variables	Group I	Group II	p-value
Duration of analgesia			
Duration of complete analgesia (min)	167.32±24.66	240.2±17.45	<0.001[PT]
Duration of effective analgesia (min)	212.6±20.32	326.84±35.69	<0.001[PT]
Time of first rescue analgesia (min)	219.42±25.96	352.84±54.33	<0.001[PT]
Quality of intraoperative analgesia			
Point 1	00 (0%)	00 (0%)	-
Point 2	12 (24%)	00 (0%)	-
Point 3	5 (10%)	03 (6%)	-
Point 4	33 (66%)	47 (94%)	-
VAS score			
Intra operative	0.62±0.7180	0.2±0.4	<0.001[PT]
3 hours	0.94±0.79	0.46±0.54	<0.001[PT]
5 hours	3.68±0.99	1.66±0.65	<0.001[PT]
12 hours	4.32±1.33	2.72±1.27	<0.001[PT]

[Table/Fig-5]: Duration analgesia, quality of analgesia, and VAS score.
PT: Paired t-test; VAS: Visual analog score

The groups were not differing significantly with respect to HR at any interval except at 60 min ($p=0.0025$) [Table/Fig-6]. No significant difference was observed in diastolic BP in both groups. Significant reduction in systolic BP was observed in group II patients compared with group I at 0 minute ($p=0.03$), 10 minutes ($p=0.02$), 20 minutes ($p=0.009$), 30 minutes ($p=0.003$), and 60 minutes ($p=0.004$) [Table/Fig-7].



[Table/Fig-6]: Heart Rate (HR) at different time interval (min).



[Table/Fig-7]: Systolic Blood Pressure (SBP) at different time interval (min).

DISCUSSION

Subarachnoid block is one of the commonly used regional technique of anaesthesia using bupivacaine and fentanyl [1,2]. However, dexmedetomidine is emerging as adjuvant alternative to fentanyl due to its less adverse effect and prolonged duration of action [1,5]. This study was conducted to assess the efficacy of the intrathecal dexmedetomidine bupivacaine in regional anaesthesia compared to a conventional drug such as fentanyl and bupivacaine.

The demographical characteristics (age and height) of the patients was similar in both the groups and were comparable with previous reports [2,12]. The dexmedetomidine as an adjuvant to bupivacaine is an attractive alternative to fentanyl + bupivacaine for long duration surgical procedures as it is associated with various factors such as- early onset and long term motor and sensory block, long duration of analgesia, low VAS score and higher time for peak sensory block. Study conducted by Paul A et al., also revealed the similar findings [13]. In contrast with these findings, the study of Mahendru V et al., and Rahimzadeh P et al., suggests an insignificant difference in the onset of sensory and motor block [2,14]. The variance in the result was may be due to the use of isobaric bupivacaine (in their studies), the difference in the definition of onset time and differences in patient positioning as in sitting position increased gravity-induced peripheral blood pooling causes hypotension and may influence onset of blocks [2,15].

The highest levels of sensory block in group I and II were T6 (8%) and T4 (6%), respectively. Similar results were observed in previous studies [2,14,16]. Significantly prolonged two sensory segment regression in group II was observed which was similar to the previous reports [2,6,7,9]. Moreover, higher time for full motor recovery ($p=0.0015$) and sensor recovery ($p<0.001$) was observed in group II patients which was comparable with the study of Mahendru V et al., and Thada B et al., [2,17]. The prolonged duration of sensory and motor block could be due to the synergistic action of bupivacaine in the presence of dexmedetomidine which produces action by binding with motor neurons in the dorsal horn [2,16].

Previous studies suggested that bupivacaine and dexmedetomidine treated patients showed delayed requirement of rescue analgesia, improved analgesic efficacy as well as dose-dependent prolongation of motor and sensory block with the decreased analgesic requirement [2,7,9,13]. Similarly, in the current study, duration of complete analgesia, duration of effective analgesia and time for first medication was significantly high in group II. Here, four-point modified Belzarena scale was used to assess the quality of intraoperative analgesia (1- unable to tolerate pain; 2- able to tolerate discomfort with additional analgesia; 3- some discomfort but no additional analgesics required, and 4- completely satisfied) [11]. Authors noted high quality of analgesia in 94% of patients of group II and 66% in group I as they were completely satisfied. These findings were unique points noted in this study. Pain was assessed by VAS, it consist of line anchored at one end by a label such as 'no pain' and at other end 'worst pain imaginable' or pain as bad as can be' [18]. Intraoperative VAS score in group I was significantly higher than group II which was similar to previous reports [19]. These findings suggest that dexmedetomidine adjuvant to bupivacaine produces excellent and long-lasting analgesic action. The most common adverse effect associated with the use of $\alpha 2$ adrenergic receptor agonist is bradycardia and hypotension [20]. Similarly, in this study decreased diastolic BP was observed in group II at a different time interval. A level of or higher level of anaesthesia is the reason for the hypotension and bradycardia. The cause of hypotension during high level of anaesthesia is the blockade of the cardiac sympathetic nerve [21].

Limitation(s)

The study limits due to lack of control group to study systemic effect of dexmedetomidine and fentanyl. Moreover, this study contributes to the information on dexmedetomidine as an attractive adjuvant bupivacaine. Hence, further studies that compare the i.v. and intrathecal effect of dexmedetomidine considering a control group is recommended.

CONCLUSION(S)

Dexmedetomidine 5 µg provides rapid onset and high duration of sensory and motor block and can provide excellent and long lasting analgesic action. Intrathecal dexmedetomidine can be considered as an alternative to fentanyl in surgical procedures as it produces profound intrathecal anaesthesia and analgesia with minimal adverse effects.

REFERENCES

[1] Verghese T, Dixit N, John L, George R, Gopal S. Effect of intravenous dexmedetomidine on duration of spinal anaesthesia with hyperbaric bupivacaine-A comparative study. Indian J Clin Anaesth. 2019;6:97-01.

[2] Mahendru V, Tewari A, Katyal S, Grewal A, Singh MR, Katyal R. A comparison of intrathecal dexmedetomidine, clonidine, and fentanyl as adjuvants to hyperbaric bupivacaine for lower limb surgery: A double blind controlled study. J Anaesthesiol Clin Pharmacol. 2013;29:496-02.

[3] Cowan CM, Kendall JB, Barclay PM, Wilkes RG. Comparison of intrathecal fentanyl and diamorphine in addition to bupivacaine for caesarean section under spinal anaesthesia. Br J Anaesth. 2002;89:452-58.

[4] Grewal A. Dexmedetomidine: New avenues. J Anaesthesiol Clin Pharmacol. 2011;27:297-02.

[5] Mantz J, Josserand J, Hamada S. Dexmedetomidine: New insights. Eur J Anaesthesiol. 2011;8:03-06.

[6] Kanazi GE, Aouad MT, Jabbour-Khoury SI, Al Jazzar MD, Alameddine MM, Al-Yaman, et al. Effect of low-dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. Acta Anaesthesiol Scand. 2006;50:222-27.

[7] Al-Mustafa MM, Abu-Halaweh SA, Aloweidi AS, Murshidi MM, Ammari BA, Awwad ZM, et al. Effect of dexmedetomidine added to spinal bupivacaine for urological procedures. Saudi Med J. 2009;30:365-70.

[8] Al Ghanem SM, Massad IM, Al-Mustafa MM, Al-Zaben KR, Qudaisat IY, Qatawneh AM, et al. Effect of adding dexmedetomidine versus fentanyl to intrathecal bupivacaine on spinal block characteristics in gynaecological procedures: A double blind controlled study. Am J Appl Sci. 2009;6:882-87.

[9] Gupta R, Verma R, Bogra J, Kohli M, Raman R, Kushwaha JK. A Comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to Bupivacaine. J Anaesthesiol Clin Pharmacol. 2011;27:339-43.

[10] Bromage PR. A comparison of the hydrochloride and carbon dioxide salts of lidocaine and prilocaine in epidural analgesia. Acta Anaesthesiol Scand Suppl. 1965;16:55-59.

[11] Shilpashri AM, Roychoudhury P, Girish KM. Comparative study of 0.5% bupivacaine and 0.5% bupivacaine with clonidine (30 µg) for spinal anaesthesia. J Evol Med Dent Sci. 2015;4(71):12385-97.

[12] Kamal MH, Ibrahim JH, Saaed AA, Zayed MS, Magdy M. Comparison of intrathecal dexmedetomidine and fentanyl as adjuvants to levobupivacaine in parturients undergoing elective cesarean sections. Med J Cairo Univ. 2017;85:593-600.

[13] Paul A, Nathroy A, Paul T. A comparative study of dexmedetomidine and fentanyl as an adjuvant to epidural bupivacaine in lower limb surgeries. J Med Sci. 2017;37(6):221.

[14] Rahimzadeh P, Faiz SH, Imani F, Derakhshan P, Amniati S. Comparative addition of dexmedetomidine and fentanyl to intrathecal bupivacaine in orthopedic procedure in lower limbs. BMC Anaesthesio. 2018;18:62.

[15] Shahzad K, Afshan G. Induction position for spinal anaesthesia: Sitting versus lateral position. J Pak Med Assoc. 2013;63:43409.

[16] Ravipati P, Isaac GA, Reddy PN, Krishna L, Supritha T. A comparative study between intrathecal isobaric Ropivacaine 0.75% plus Dexmedetomidine and isobaric Ropivacaine 0.75% plus fentanyl for lower limb surgeries. Anaesth Essays Res. 2017;11:621-26.

[17] Thada B, Khare A, Sethi SK, Meena S, Verma M. Comparison of dexmedetomidine and fentanyl as intrathecal adjuvants to 0.5% hyperbaric bupivacaine for total abdominal hysterectomy under subarachnoid block: A prospective randomised double-blind study. Anaesthesia, Pain & Intensive Care. 2017;21:65-72.

[18] Hala EA, Shafie MA, Youssef H. Dose-related prolongation of hyperbaric bupivacaine spinal anaesthesia by dexmedetomidine. Ain-Shams J Anaesthesiol. 2011;4:83-95.

[19] Jain N, Mathur PR, Soni P, Patodi V, Sethi SK, Mathur V. A comparative clinical study of intrathecal bupivacaine 2.5 mg with dexmedetomidine 5 µg versus intrathecal bupivacaine 2.5 mg with fentanyl 25 µg on the duration of labor analgesia using combined spinal epidural technique. J Obse Anaesth Crit Care. 2019;9:24.

[20] Eisenach JC, De Kock M, Klimscha W. α2-Adrenergic agonists for regional anaesthesia: A clinical review of clonidine (1984-1995). Anaesthesiology: The Journal of the American Society of Anaesthesiologists. 1996;85:655-74.

[21] Maruyama K, Nishikawa Y, Nakagawa H, Ariyama J, Kitamura A, Hayashida M. Can intravenous atropine prevent bradycardia and hypotension during induction of total intravenous anaesthesia with propofol and remifentanil? J Anaesth. 2010;24:293-96.

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