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Evaluation of Intrathecal Dexmeditomedine as an Adjuvant to Hyperbaric Bupivacaine in Gynaecological Surgeries

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Abstract

Background: Intrathecal dexmeditomedine is being used as an adjuvant to the local anesthetic agents. Dexmeditomedine has sedative and analgesic action. This study was carried out with the aim to observe and compare the onset and duration of sensory and motor block, duration of analgesia, hemodynamic changes, level of sedation and side effects between the two groups, i.e. Intrathecal hyperbaric bupivacaine v/s low dose dexmeditomedine and bupivacaine combination in patients posted for routine gynaecological surgeries. *Methods:* This was a prospective randomized controlled double blind study. Sixty adult female patients were divided into two groups. Group (B+D) received intrathecal 0.5% hyperbaric bupivacaine 17.5 mg (3.5 ml) with inj. Dexmeditomedine 10μg in 0.5 ml of normal saline and group (B+S) received Intrathecal 0.5% hyperbaric bupivacaine 17.5mg (3.5 ml) with 0.5 ml of normal saline. The assessment of the parameters like the onset time for sensory and motor block, regression time of the block to two dermatomes, T_{10} dermatome, S_1dermatome, Bromage 0 motor block and the time for request of first rescue analgesic dose was done in both groups. Also, the incidence of untowards side effects like bradycardia, hypotension, shievering and the sedation score in each patient was noted. Statistical analysis was carried out. *Results:* There was no statistical difference in the time of onset of sensory and motor block in both the groups. However, the time for regression of sensory block in the dexmeditomedine group to two dermatomes (188.87±81.79 min), T_{10} dermatome (225.67± 32.51 min), S_1 dermatome (261.80± 79.50 min) and motor block to Bromage scale 0(326.33±76.80 min) was significantly prolonged than in group (B+S)(109.67± 25.31,147.67± 32.12, 180.33± 30.73 &203.67± 28.69 min). The time for first request of rescue analgesic dose was significantly longer in dexmeditomedine group (360.67±80.19 min)than in normal saline group(203.66± 48.75 min). Differential Analgesia (DA) was evaluated as the difference between the time for rescue analgesic dose request and recovery of muscle power to Bromage 0 scale. It was significantly longer in (B+D) group (34.33± 30.11 min), whereas its presence was inconsistent (sometimes absent) in (B+S) group (mean value 10.33±18.94 min). *Conclusion*: Intrathecal dexmeditomedine 10 μg, added to hyperbaric bupivacaine is useful for gynecological surgeries, with minimal and easily treatable side effects and prolonged post-operative analgesia, even after cessation of block (Differential Analgesia). Also, it is helpful to avoid general anesthesia, even if the surgical procedure gets prolonged.

Keywords: Dexmeditomedine; Adjuvant; Intrathecal; Gynecological Surgeries.

Introduction

Intrathecal α_2 adrenergic agonists are being used as adjuvant drugs to the local anesthetic agents [1-2]. Effects of local anesthetic agents are prolonged and the doses are reduced with their use [3]. Again, they have been proved to prolong the effect of sensory and motor block.Dexmeditomedine has sedative and analgesic action when used by intravenous route. It has been proved that Dexmeditomedine has got opoid sparing effect [4]. This study was carried out with the aim to observe and compare the onset and duration of sensory and motor block, duration of analgesia

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(from the injection of the drug to the complete recovery in the post-operative period), hemodynamic changes, level of sedation and incidence of shivering between two groups, i.e, intrathecal Bupivacaine plain v/s low dose of Dexmeditomedine and Bupivacaine combination in the patients posted for routine gynecological procedures.

Materials and Methods

This study was carried out at our institute between January 2017 to March 2017. After the institutional ethical committee approval, our study commenced with informed written consent of each patient for the use of intrathecal Dexmeditomedine and the surgical procedure. Adult female patients undergoing routine gynecological procedures were included in our study. After thorough pre-anesthetic evaluation, patients with anemia (Hemoglobin less than 10 grams%), hypertension under treatment with two antihypertensive drugs, platelet inhibitors, ischemic heart disease, obesity (weight more than 80 kg), chronic obstructive airway disease (on treatment with bronchodilator drugs & abnormal FEV_1 values in spirometry), previous abdominal surgeries (possible intraperitoneal adhesions), features suggestive of probable difficult intubation were excluded from the study. Finally, fifty patients with A S A physical status I and II, between the age group of 35 to 70 years, undergoing Total Abdominal Hysterectomy and the surgery for the prolapsed uterus (Fothergill's repair or Vaginal Hysterectomy) were included in our study. Using a computer generated list of random numbers, patients were randomized and allocated to two groups-

A. (B+S) group-Hyperbaric Bupivacaine 0.5%-3.5 ml (17.5 mg) with 0.5 ml Normal Saline

B. (B+D) group-Hyperbaric Bupivacaine 0.5% 3.5 ml (17.5 mg) with 10 micrograms of Dexmeditomedine diluted in0.5 ml volume of normal saline.

All the patients were preloaded with 500 ml of Ringer Lactate solution. Under strict aseptic precautions, lumbar puncture was performed in the sitting position at L_3-L_4 level with 23 gauge spinal needle. The syringe was prepared and coded by a third person outside the operation theatre and given to the anesthesiologist performing the lumbar puncture, making the procedure double blind. All the patients were planned in supine position without head up/head down tilt for ten minutes. Immediately 2 liters of oxygen was started with a face mask. The anesthesiologist jotted down the intra operative and post operative data, being blind to the drug combination administered. Patient was shifted from the postoperative room to the wards after complete recovery and recording of all the parameters till the required time.

Considering the time of intrathecal injection as 0, all the durations were noted. Baseline pulse rate, blood pressure and mean arterial pressure were taken at time 0, then every 5 minutes for first half an hour, then every 10 minutes up to first hour, and every half an hour till the discharge from the post operative room.

The sensory and motor blockades were tested every half minute for first 10 minutes. The time for the achievement of T_{10} dermatome sensory block was noted and a minimum of T_8 dermatome block was assured using a bilateral pinprick sensation testing in the mid-clavicular line.

Modified Bromage Scale was used for the assessment of motor blockade as follows-

Bromage 0-The patient is able to make movements at the hip, knee and ankle joints

Bromage 1-The patient is unable to make movements at hip joint, but is able to make movements at knee and ankle joints.

Bromage 2-The patient is unable to make movements at hip and knee joints, but able to make movements at the ankle joints.

Bromage 3-The patient is unable to make movements at any of the hip, knee or ankle joints.

The Modified Bromage Scale was assessed bilaterally. The surgery was allowed to commence after T_8 dermatome sensory block and Modified Bromage Scale score 3 was achieved.

The time to reach the T_{10} sensory dermatome level block, maximum sensory dermatome level block (assessed after 30 minutes), two dermatome sensory level regression time, the time for regression to T_{10} dermatome and time for the regression to S_1 dermatome were noted.The time to achieve Modified Bromage Scale 3 and regressions to Bromage 0 were recorded. The level of sedation was evaluated after 30 minutes and every half an hour thereafter and score was taken as-

0- Alert

1-Occasionally drowsy but easy to arouse

2-Frequently drowsy but easy to arouse

3-Somnolent, but difficult to arouse

Visual Analog Score (VAS 1-100) was used for the assessment of pain in the recovery room every 30 minutes. Need for a rescue analgesic drug was noted with VAS more than 30/100. Intravenous Paracetamol 100 mg infusion was given. Intra operative or post operative incidences of Bradycardia (heart rate ≤ 60 beats per minute) were recorded and treated with inj. IV Glycopyrrolate 0.2 mg or inj. Atropine 0.6 mg. Intra and post operative incidence of hypotension (fall of systolic blood pressure below 90 mm of Hg or more than 30% from the baseline BP) was recorded and treated with one or two doses of IV Mephenteramine 6 mg and 250 ml of Ringer Lactate solution. Intra or post operative incidence of shivering was noted and treated with IV Tramadol0.5 mg/kg and inj. Hydrocortisone 100mg if required.A minimum IV fluid of 1litre of Ringer Lactate and 500 ml of Dextrose-Saline was given to each patient. Blood transfusion was given if necessary (blood losse ≥ 500 ml). All the patients had a follow-up of minimum 7 days till the discharge from hospital. Patients were enquired about post-spinal headache and backache.

Statistical Analysis

The collected data was compiled in EXCEL sheet and Master sheet was prepared. For analysis of this data SPSS (Statistical Software for social Sciences) software version 20th was used. Qualitative data was represented in form frequencies & percentages. To check association between group and qualitative data chi-square test was applied. Quantitative data was represented in form of mean & SD. To check significance difference between two groups unpaired t-test was applied. P-value was checked a 5% level of significance.

Results

In this study, sixty patients were included, no patient being excluded for any reason. There was no technical difficulty during administration of spinal block. The recovery was uneventful. The difference between the mean time to reach the T_{10} dermatome sensory block between the (B+S) group and the (B+D) group was not significant (P value 0.584). The difference for the time to reach the T_{10} sensory level between the two groups was less in (B+D) group (Mean value 3.80 ± 1.47 minutes) than (B+S) group (Mean value 4.13 ±1.81 minutes), but not statistically significant. The maximum peak sensory level attained with (B+S) group was T_7 in 5 cases,T_6 in 6 cases,T_5 in 0 cases,$T_{4\,i}$ in 2 cases and T_2 in 2 cases; while that with(B+D) group was T_7 in 5 cases,T_6 in 2 cases,T_5 in 3 cases,T_4 in 4 cases and $T_{2\,i}$ in 1 case. With the application of *Chi square test,* the difference in the distribution proved to be not significant statistically. The time for regression of sensory level to two dermatomes was (188.87 ±31.79 minutes) for (B+D) group, while (109.67 ±25.31 minutes) for (B+S) group, which was significantly higher(P <0.0001). Also, the regression time to T_{10} dermatome was(225.67 ± 32.51 minutes) for (B+D)group, while (147.67 ± 32.12 minutes) for (B+S) group; which was statistically significant. Similarly, there was significant difference between regression of sensory level to S_1 dermatome (261.80±39.58 minutes) for (B+D) group and(180.33 ±30.73 minutes) for (B+S) group (P value <0.0001).

All the patients attained Bromage 3 motor blockade, but the group (B+D) could achieve in (4.80 ±2.62 minutes), while the group (B+S) in (4.53 ±2.64 minutes) which was not significant statistically (P value 0.784). The regression time of motor block to Bromage 0 was significantly longer in group (B+D)(326.33 ± 76.85 minutes) than group (B+S) (203.67 ±48.75 minutes), (P value <0.0001).

The time at which the patient demands a dose of rescue analgesic drug (with Visual Analog Score>30) was significantly more in the group (B+D) (360.67 ± 80.19 minutes) than group (B+S)(203.66±48.75 minutes) (p value <0.0001).

The Differential Analgesia (DA) was calculated as the difference between duration of analgesia and duration of complete regression of motor block to Bromage scale 0.Time for Differential Analgesia was significantly longer in (B+D) group (34.33 ± 30.11 minutes) than(B+S)group(10.33 ± 18.94 minutes), (P value=0.014). In the (B+S) group, seven patients had duration of analgesia less than the duration of complete regression of motor block, meaning that the duration of Differential Analgesia was negative.

Table 1: Comparison of Mean Age, Weight & Height in Groups [Unpaired t-test]

	(B+ D) Group Mean± SD	(B+ S) Group Mean± SD	t-value	p-value
Age	46.26±10.23	45.2±6.68	0.338	P=0.738 NS
Weight	56.60±10.74	59.67±9.37	0.229	P=0.774 NS
Height	152.80±10.74	155.00±4.53	1.32	P=0.199 NS

(S-Significant, NS- Not Significant), There was no significant difference in the demographic data between the two groups

Table 2: MAX Level in Groups

MAX Level	(B+ D) Group	(B+ S) Group	*Chi-square value*	*p-value*
T1	00	00		
T2	01	02		
T3	00	00		
T4	04	02	*6.00*	*P=0.199 NS*
T5	03	00		
T6	02	06		
T7	05	05		
Total	15	15		

There was no significant difference in the peak sensory level distribution in the two groups.

Table 3: Comparison of Mean Time to reach T_{10} block & Bromage 3 motor blockade [In Minutes] in Groups [Unpaired t-test]

	(B+ D) Group Mean± SD	(B+ S) Group Mean± SD	t-value	p-value
Time to reach T_{10} block	3.80±1.47	4.13±1.81	0.554	P=0.584 NS
Bromage 3 motor blockade	4.80±2.62	4.53±2.64	0.277	P=0.784 NS

Table 4: Comparison of Indices of recovery time in Groups [Unpaired t-test]

	(B+ D) Group Mean± SD	(B+ S) Group Mean± SD	t-value	p-value
Time to reach 2 Dermatome regression	188.87±31.79	109.67±25.31	7.55	P<0.0001 S
Regression Time to T10	225.67±32.51	147.67±32.12	6.11	P<0.0001 S
Regression Time to S_1Dermatome	261.80±39.58	180.33±30.73	6.29	P<0.0001 S
Time to reach Bromage 0 motor block	326.33±76.85	203.67±28.69	5.72	P<0.0001 S
Time for rescue analgesic	360.67±80.19	203.66±48.75	6.48	P<0.0001 S
Time of Differential Analgesia (DA)-	34.33±30.11	10.33±18.94	2.61	P=0.014 S
Sedation Score	0.733±0.70	00	4.04	P<0.0001 S

Table 5: Adverse Effects in Groups [Chi-square test]

Adverse Effects	(B+ D) Group	(B+ S) Group	*Chi-square value*	*p-value*
Bradycardia	04(26.7%)	07(46.7%)	1.29	P=0.256 NS
Hypotension	09(60.0%)	05(13.3%)	2.14	P=0.143 NS
Shivering	05(33.3%)	07(46.7%)	0.556	P=0.456 NS

Throughout the intra operative and post operative period, the mean value of Heart Rate (HR) was (65 beats/minute) in the group (B+D) and (68 beats/ minute) in the group (B+S). It was not significant (P value >0.0001).

Similarly, the Mean Arterial Pressure (MAP) was observed as (84 mm of Hg) in (B+D) group and (89 mm of Hg) in (B+S) group, the difference being insignificant (p value>0.0001).

All the patients had peripheral oxygen saturation more than96% all the time, every patient received oxygen 2 liters /minute by a nasal cannula in the intra and post operative period.

(9) patients received inj. Mephenteramine 6 mg once in the (B+D) group and (5) patients in the (B+S) group which was statistically not significant (P value>0.0001). (4) patients in group(B+D) needed to be given inj. Atropine/ Glycopyrrolate for Bradycardia while (7) patients in the group (B+S) needed the same, which was not significant (P value>0.0001). Shivering occurred in (5) cases in (B+D) group, and (7) cases in (B+S) group; which was not significant (p value>0.0001). It was treated with 0.5-1 mg/kg dose of inj. Tramadol. The highest level of Sedation Score was (2) in (5) cases in the (B+D) group, while it was (0) in all the cases in the (B+S) group, being significantly higher in (B+D) group

(P value <0.0001).In the seven day post operative follow up of all the cases, onset of the new symptoms like headache, backache, buttock or leg pain was never observed.

Discussion

There are many adjuvants used with the local anesthetic agents like Epinephrine, Adenosine, Magnesium sulphate, Neostigmine, Pentazocine, Fentanyl, Ketamine or Clonidine to prolong the duration of anesthesia and post-operative analgesia. But the side effects of these adjuvants have made their use limited. Intrathecal α_2 adrenergic agonists have antinociceptive action for both somatic and visceral pain (Shah et el) [4]. From this group, Clonidine has been used to potentiate the effects of local anesthetics allowing reduction in the dose requirement without causing respiratory depression (Bakshi U) [5]. Dexmeditomedine is an α_2 agonist approved by FDA in 1991 for use in humans. Intrathecal Dexmeditomedine has been shown to be effective in nociception, visceral as well as neuropathic pain; and its neurological safety has been proven for up to ten years for post-operative anesthesia follow-up (Mayank Gupta [6], Yektas et el [7], kimura et el [8], Yaksh TL et el [9], Liu HJ et el [10]. A small intrathecal dose of Dexmeditomedine (3 µg) used in combination with Bupivacaine for spinal anesthesia has been shown to produce a shorter onset of motor block and prolongation in the duration of sensory and motor block with hemodynamic stability and lack of sedation (Al Mustafa MM et el [11]). In our study ,the dose of Dexmeditomedine was chosen as 10 µg, based on the observations of the previous studies. Mayank Gupta et el [6] have observed that addition of 10 µg of Dexmeditomedine to intrathecal Bupivacaine significantly prolongs the duration of sensory block, motor block and Differential Analgesia in patients undergoing lower abdominal surgeries without increase in the incidence of side effects.

It is not well understood how intrathecal α_2 adrenergic agonists prolong the sensory and motor block (Dattatri [12]).The local anesthetic acts by blocking the sodium channels, while α_2 agonists are supposed to block the pre-synaptic c fibers and post-synaptic dorsal horn neurons. They depress the release of c- fiber transmitters and cause hyperpolarisation of post-synaptic dorsal horn neurons. The direct impairment of release of excitatory amino acids release by spinal interneurons might be leading to prolonged motor block (Shaikh et el [12], Hala EA et el [13]). Intrathecal Dexmeditomedine exhibits its facilitatory and nociceptive effect by a dual mechanism of inhibiting the release of neurotransmitters by acting in the pre-synaptic α_2 A receptors and by hyperpolarizing the post-synaptic neurons [6,25]. Inhibition of motor neurons in the dorsal horn of the spinal cord might prolong the motor blockade [25]. However, ED_{50} of Dexmeditomedine for sensory C fibers being 2.5 µg and motor Aβ fibers more than10µg [26], the dose of intrathecal Dexmeditomedine was selected as 10µg.

Eid et el [24] have used higher doses (15µg),but were associated with higher sedation scores and highly prolonged duration of spinal block, which was unnecessary in our study, hence higher doses of Dexmeditomedine were not selected. Intrathecal Dexmeditomedine has been shown to be effective in nociceptive, visceral as well as neuropathic pain and its safety has been proved for up to ten years [6,8,9,10]. It was observed by Shaikh S.L. and Dattatri R [12]. That addition of Dexmeditomedine (5 to 10 µg) to hyperbaric Bupivacaine intrathecally produced a rapid onset of sensory and motor block, prolonged the duration of sensory and motor block and the time for the requirement of the first analgesic significantly in a dose dependent manner. Hemodynamic parameters were found to be comparable and stable with minimal side effects.

Similarly, a dose dependent effect on the onset and regression of sensory and motor block and the time for requirement of first dose of rescue analgesic was observed along with lower VAS scores and minimal side effects by Tarbeeh [14] and Jamliya R.H. [15]. Time for regression of sensory level (430.05±89.13 minutes), time for requirement of first dose of analgesic (459.8±100.9 minutes) and the duration of motor blockade (323.05±54.58 minutes) was observed by Nethra S.S. et el [16]; when 5 µg of Dexmeditomedine (in 0.5 ml of normal saline) was added to 6 mg (1.2 ml) Bupivacaine which were significantly prolonged as compared to Bupivacaine 6 mg (1.2 ml) with 0.5 ml normal saline. The values given for dexmeditomedine group were, Time for regression of sensory level (301.10 ±94.86 min),Time for the requirement of first dose of analgesic (321.85 ±95.08 min) and the duration of motor block (220.10 ±63.61 min). All of these values are comparable with our study module. However, in our study, as the dose of Bupivacaine was chosen as17.5 mg and Dexmeditomedine as 10 µg, longer durations were observed.

Kim J. E. et el [17] used 3 µg Dexmeditomedine with 6 mg hyperbaric Bupivacaine and compared with same dose of Bupivacaine with normal saline

for the elderly male patients undergoing Transurethral Prostatectomy. It was found that the peak level was similar in both the groups. However, a faster onset time for the peak sensory level, longer duration of spinal block, time for the regression to two sensory dermatomes was higher with the Dexmeditomedine group as compared to the control group. The mean time for first analgesic request was longer in the Dexmeditomedine group (487 min) as compared to the control group (345 min). Recovery from the motor block was delayed. As the study was carried out in elderly patients, longer duration of analgesia than that in our study could be explained. Kanazi et el [18] compared the combination of 12mg of Bupivacaine with 3 µg of Dexmeditomedine with equal dose of Bupivacaine with normal saline. Significantly shorter onset of motor block was observed with Dexmeditomedine. In the Bupivacaine with Dexmeditomedine group, sensory regression time to two dermatomes (122 ±37 min), regression to S_1 dermatome (303 ±75 min) and the motor recovery to Bromage scale 0 (256 ±76 min)was observed as compared to the Bupivacaine with saline group as, sensory regression time to two dermatomes (80 ±28 min), time to S_1 dermatome regression (190 ±48 min) and motor regression time to Bromage scale 0 (163 ±42 min). These effects were noted without any significant hemodynamic instability or sedation. As higher dose of dexmeditomedine (10 µg) was used in the present study, the durations observed must have been longer.

As the dose of Dexmeditomedine chosen was higher in our study, sedation effect was significant as compared to control group, but the alterations in the hemodynamic parameters were acceptable and treatable with small doses of Atopine/Glycopyrrolate and vasopressors like Mephenteramine. Alarming situations like severe bradycardia or severe hypotension never occurred during our study course. Mayank Gupta et el [6] evaluated the concept of Differential Analgesia (DA).It was the duration of analgesia(time for the request of rescue analgesic)after complete regression of motor block to Bromage scale 0. In their study, the mean duration of DA was 147 minutes for bupivacaine with 10 µg dexmeditomedine.

These values are comparable to the values in our study. The mean duration of DA in our study was (34.33) minutes. However, the duration of Differential Analgesia was zero or negative in some patients of (B+S) group; indicating that it is a property mainly attributed to dexmeditomedine. A prolongation of the duration of DA is associated with a dual advantage of minimizing the untoward sequel of post-operative pain (delayed wound healing, depressed immune functions, prolonged hospitalization, risk of neuro-sensitization and hence, chronic pain);as well as that of prolonged motor blockade (reduced mobilization, deep vein thrombosis and pulmonary embolism etc) (Ramsay MAE [19]).

The median sensory block onset time was (3.80 ± 1.40) minutes in our study, Mayank Gupta et el [6] observed it as 3 minutes, which is comparable. Halder et el [22] also observed similar findings. The highest peak sensory level observed in our study was T_2. Group (B+D) had one patient as compared to (B+S) group(2), being statistically insignificant. Similarly, a decrease in motor block onset time was observed in (B+D) group (4.80 ± 2.62 minutes) as compared to (B+S) group (4.53±2.64) which is statistically insignificant (P value =0.784). Similar findings were observed by Mayank Gupta et el [6]. Samantray et el [20] have reported no significant difference in sensory or motor blockade onset time with addition of Dexmeditomedine to hyperbaric Bupivacaine. This can be attributed to number of variables such as demographic profile, definition of onset time (T_8 v /s T_{10}), volume of intrathecal injection, volume of the diluents used (0.1 v /s 0.5 mi), thereby affecting the concentration and the baricity of Bupivacaine, position of the patient (sitting v/s lateral) and individual pain sensitivity of patients (Gupta et el [6]).

The incidence of bradycardia was (26.7 %) in (B+D) group and (46.7%) in (B+S) group which was statistically insignificant (P value=0.256). However, the heart rate was never less than 55 beats/minute and easily reversed with 0.2 mg of inj. Glycopyrrolate. The incidence of hypotension was (60%) in (B+D) group and (13.3 %) in (B+S) group which was statistically insignificant (P value=0.143). Mayank Gupta et el [6] observed the incidence of bradycardia as 20% and hypotension as 30% which is similar to our observations. (as the higher dose of bupivacaine, 17.5 mg must have produced maximum sympatholysis, therefore addition of Dexmeditomedine might have made insignificant difference. Incidence of shivering was (33.3%) in (B+D) group as compared to (46.7%) in (B+S) group; which is statistically insignificant (p value=0.456).

Nausea, vomiting and urinary retension were not observed in any patient in our study. The sedation score was observed as 0 (14 cases), 1 (12 cases) and 2 (4 cases) in the (B+D) group, while 0 in all the cases in the (B+S) group; the difference being statistically significant. Mayank Gupta et el [6] have found the highest sedation score as 2 seen in 40% of patients

within 10μg of Dexmeditomedine group, which is in coherence with our study as well as Tewari et el [21] and Nethra S et el [16].

Conclusion

To conclude, 10 μg of intrathecal dexmeditomedine as an adjuvant to hyperbaric bupivacaine significantly prolongs the duration of sensory block, motor block and analgesia, but the onset of sensory and motor block is not hastened.

There is significant difference in the duration of Differential Analgesia when dexmeditomedine is added to bupivacaine. There is prolonged post-operative analgesia which is highly advantageous in patients posted for gynaecological surgeries, which are lower abdominal. Also, incidence of side effects was not significant with dexmeditomedine. Sedative and analgesic action of dexmeditomedine is sufficient to prolong the dose of rescue analgesic drug.

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