# Comparative Evaluation of Bupivacaine and Bupivacaine with Dextmedetomidine in Subarachnoid Block

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#### **Abstract**

Introduction: Since the introduction of spinal anaesthesia in 1898 by Dr. August Bier, who described the intrathecal administration of cocaine, spinal anaesthesia is preferred over general anaesthesia, particularly in surgical procedures of lower abdomen and lower limbs1 (D C Simon et al 2008). The aim of intrathecal local anaesthetic is to provide adequate sensory and motor block necessary for all below umbilical surgeries. Hyperbaric Bupivacaine is the most commonly used intrathecal local anaesthetic. Various adjuvants have been added to Bupivacaine to shorten the onset of block and prolong the duration of block. A number of adjuvants such as clonidine, Midazolam, opioids have been studied to prolong the effect of spinal anaesthesia<sup>3,4</sup> (Elia N.et al 2008, Boussofara et al 2006). Clonidine has side effects like bradycardia, hypotension, dryness of mouth, nausea, respiratory depression, itching, and neurological toxicity. Dexmedetomidine is a new highly selective a, agonist. It is a, agonist drug, when given intrathecally, significantly prolongs the duration of spinal block. Intrathecal a, receptor agonists have been found to have antinociceptive action for both somatic and visceral pain<sup>5</sup> (Al Ghanem SM et al 2009). It is hypothesized that intrathecal 5 µg Dexmedetomidine would produce more postoperative analgesic effect with hyperbaric Bupivacaine in spinal anaesthesia with minimal side effects<sup>5-7</sup> (Al Ghanem, Al Mustafa et al 2009 & Kanazi GE). To see whether the Dexmedetomidine alleviates the side effects of clonidine & Midazolam, we decided to study the efficacy and safety profile of Dexmedetomidine in combination with local anaesthetic in subarachnoid block for below umbilical surgeries.

Keywords: Spinal Anaesthesia; Bupivacaine; Dexmedetomidine.

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#### Introduction

Intrducation not provided.

# Aims & Objectives:

1. To compare the onset & duration of sensory block.

- 2. To compare the onset & duration of motor block
- 3. To evaluate total duration of analgesia.
- 4. To evaluate incidence of intraoperative and postoperative complications.

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#### Material and Methods

Hundred patients were included in this study after getting approval from ethical committee and informed consent from patients. Each group included 50 patients, Group B & Group BD. Group B patients were anaesthetized with hyperbaric Bupivacaine 0.5% 3cc (15mg) + 0.5 cc normal saline and Group BD patients were given hyperbaric Bupivacaine 0.5% 3cc (15mg) + 5 µg Dexmedetomidine. All the basic investigations were done including complete blood count (CBC), Urine exam. 12 lead ECG, Random blood sugar, Blood urea & Sr. Creatinine, LFTs.

The procedure was explained to each patient a day prior to surgery and patients were kept nil per oral after 10 pm on previous night.

On the day of surgery, patient's basic PR & BP was recorded. Patients were secured with IV line and preloaded with 11 RL. Patients were connected to multiparameter. Under all aseptic precautions lumbar puncture was done with Quincke's spinal needle in L3-4 space. Group B patients were given Inj. Bupivacaine 0.5% (3cc) + 0.5 cc Normal saline and Group BD patients were injected Inj. Bupivacaine 0.5% (3cc) + 5µg Dexmedetomidine. The study was double blinded.

All the vital parameters were recorded at 0,3,5,10,15,20,25,30 minutes after spinal anaesthesia and every 10 minutes for one hour, then every 30 min for first two hours and then every 60 min for 9 hours in postoperative period.

Sensory blockade was assessed using 22G needle. Analgesia is defined as loss of sensation to pinprick and anaesthesia as loss of sensation to touch.

Motor blockade was assessed by straight leg raising while lying supine and was graded according to Modified Bromage Scale.<sup>17</sup>

Grade 0 - No Paralysis

Grade 1 - Inability to raise extended legs

Grade 2 - Inability to flex knee, able to move feet only

Grade 3 - Complete paralysis

Onset of motor block was taken as time to achieve Bromage score 1 from the time of intrathecal injection of drug. After 20 min of block the Bromage score was considered as the maximum degree of motor block.

Intraoperatively and postoperatively

complications viz. hypotension, variations in the heart rate, nausea, vomiting were noted & treated.

Postoperatively the patients were observed for the duration of analgesia by using VAS score (0 to 10). Zero being no pain and 10 being the most severe pain. Patients were given rescue analgesics once the VAS score exceeds.<sup>5</sup>

The onset of sensory blockade, Maximum sensory blockade, Motor onset, Maximum motor blockade, duration of sensory & motor block and duration of analgesia were noted.

The results of the study were statistically analyzed between the groups using unpaired t test.

P < 0.05 - statistically significant

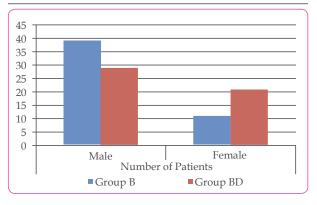
P < 0.01 - statistically highly significant

P > 0.05 - statistically not significant

#### Observations and Results

Table 1: Sex wise distribution.

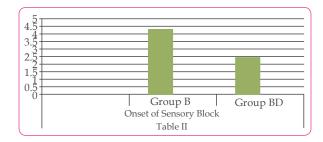
Gender	Number of Patients		Chi Square Test	P value	
	Group B	Group BD			
Male	39	29	2 71	>0.05	
Female	11	21	2.71	>0.05	
Total	50	50			



Sex wise distribution was statistically compared using chi square test and found to be non significant i.e. P > 0.05. (Table 1)

Table II: Onset of Sensory Block.

	Group B		Group BD		P Value
	Mean	SD	Mean	SD	
Onset of Sensory Block in minutes	4.32	±0.61	2.47	±0.29	< 0.05; Significant

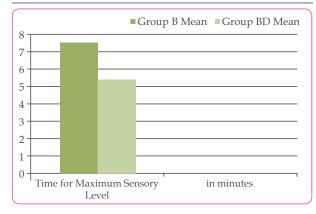


We can see that there is statistically significant difference in the mean duration of onset of sensory block between two groups. (P < 0.05) (Table 2)

Onset of sensory block was significantly faster (P < 0.05) in study group compared to control group.

Table III: Time for Maximum Sensory Level.

	Group B		Grou	p BD	P Value
	Mean	SD	Mean	SD	•
Time for	7.51	±0.27	5.39	±0.31	< 0.05;
Maximum					Significant
Sensory Level					
in minutes					

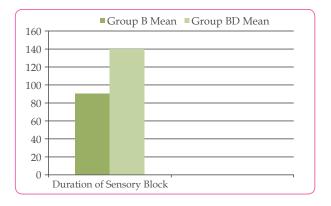


We can see that there is statistically significant difference in the mean duration of maximum sensory level between two groups. (P < 0.05) (Table 3)

It indicates cephalic spread of sensory block occur faster when Dexmedetomidine was added to intrathecal Bupivacaine.

Table IV: Duration of Sensory Block.

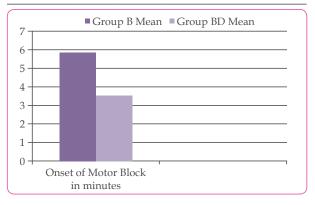
	Group B		Grou	p BD	P Value
	Mean	SD	Mean	SD	
Duration of Sensory Block	90.21	±6.09	139.86	±6.18	< 0.001; Highly Significant



From above graph we come to know that there is statistically significant difference in mean duration of time for regression of two segment sensory blockade between two groups (P < 0.001). It means regression of sensory block was slower in patients those who received intrathecal Dexmedetomidine. (Table 4)

Table V: Time for Onset of Motor Block.

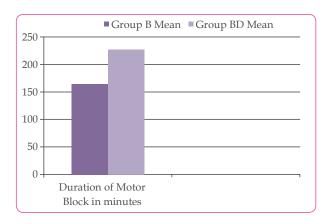
	Group B		Grou	p BD	P Value
	Mean	SD	Mean	SD	
Onset of Motor Block in minutes	5.87	±0.29	3.53	±0.27	< 0.05; Significant



There is statistically significant difference in mean duration of onset of motor block between two groups (P< 0.05). Thus from above results it is clear that onset of motor block is quicker in patients received intrathecal Dexmedetomidine. (Table 5)

Table VI: Duration of Motor Block.

	Group B		Grou	P Value	
	Mean	SD	Mean	SD	
Duration of	164.32	±3.45	227.1	±1.76	< 0.001
Motor Block					
in minutes					

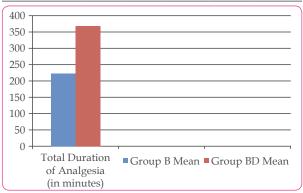


In present study, the mean duration of motor block i.e. time for regression to Bromage 0 in Group BD (Dexmedetomidine group) was 227.1±1.76 min as compared with Group B in which it was 164.32±3.45 min. (Table 6)

There is statistically significant difference in mean duration of time for regression to Bromage 0 i.e. duration of motor block between the two groups (P < 0.001).

Table VII: Total Duration of Analgesia.

	Group B		Grou	P Value	
	Mean	SD	Mean	SD	
Total Duration of Analgesia in minutes	222.54	14.68	368.74	11.72	< 0.001



In present study we found that mean duration of sensory analgesia was 222.54  $\pm 14.68$  min in Group B as compared to 368.74  $\pm 11.72$  min in Group BD. (Table 7)

There is statistically significant difference in mean duration of analysesia between two groups (P < 0.001).

Thus there was significant prolonged duration of sensory analgesia in Dexmedetomidine group i.e. in Group BD as compared to control group (P<0.001).

# Intraoperative and postoperative complications

In our study, intraoperative and postoperative complications were observed such as inadequate level of analgesia, bradycardia, tachycardia, hypotension, high level of block etc.

Only two patients in Group B and 4 in Group BD had bradycardia. Two patients in Group B and 3 patients in Group BD had hypotension.

There was no statistically significant difference of intraoperative & postoperative complications between both the groups with p value as >0.05.

## Discussion:

Dexmedetomidine Hydrochloride, a newer agent within the class of  $\alpha_2$  adrenoreceptor agonist delivers clinically effective sedation with analgesic property for use in intensive care unit setting. Additionally it has ability to eliminate or reduce the need for other analgesic medications. There is no evidence of respiratory depression with Dexmedetomidine. Because of its selective  $\alpha_2$  receptor activity, use of Dexmedetomidine has modest and predictable haemodynamic effects, making it a popular sedative and analgesic drug in intensive care unit. 18

Dexmedetomidine is now being used outside the ICU in variety of clinical settings including sedation and adjunct analgesia in the operating room, sedation in diagnostic procedures and for other applications such as withdrawal / detoxification amelioration in adult and paediatric patients.<sup>19</sup>

Animal studies have been used intrathecal Dexmedetomidine at a dose ranged 2.5 – 100  $\mu$ g. The largest dose of intrathecal Dexmedetomidine 100  $\mu$ g was used in a sheep model, where a 7 day follow up showed no neurological deficit in the studied animals.<sup>20</sup> In human studies, dose ranged 3-5  $\mu$ g 5,8,9,10,21. The dose of Dexmedetomidine used in subarachnoid block ranged 3-5  $\mu$ g in various studies showing effective clinical & safety profile. Hence, in this study, we used 5  $\mu$ g preservative free Dexmedetomidine with 15  $\mu$ g hyperbaric Bupivacaine intrathecally in Group BD.

Present study was undertaken to evaluate the effect of addition of Dexmedetomidine in subarachnoid block along with 0.5% Bupivacaine (H) on sensory, motor, haemodynamic and analgesic parameters both intraoperatively and postoperatively. It was compared with routine standard technique using 0.5% Bupivacaine (H) for spinal anaesthesia.

Our study included 100 patients between 15-45 years of either sex with ASA grade I and II posted

for elective surgeries below umbilicus. The patients having contraindications were excluded from study. Patients were divided into two groups (each 50) i.e. control group (Group B) and study group (Group BD) depending upon drugs used.

Group B received Inj. Bupivacaine 0.5% (heavy) 15mg (3cc) + Normal saline 0.5 cc

Group BD received Inj. Bupivacaine 0.5% (heavy) 15mg (3cc) + Inj. Dexmedetomidine 5µg (0.5cc)

In present study, in Group B 39 patients were males and 11 were females while in Group BD 29 were males and 21 were females.

Sensory Block parameters: (Table no. II, III & IV)

# *Time of onset of sensory block:*

In present study mean time for onset of sensory block was 2.47±0.29 min in Group BD, which was quicker as compared to 4.32±0.61 min in Group B. Onset of sensory block was significantly faster (p<0.05) in study group as compared to control group.

Regarding onset of time our findings are similar to study conducted by R. Brinda et al.,<sup>16</sup> who carried out study on 100 patients who were undergoing elective lower abdominal surgery. Group A(n=50) received hyperbaric Bupivacaine 0.5% + normal saline and Group B was given 0.5% Bupivacaine 15mg + 5 μg Dexmedetomidine. Time to sensory block to reach T10 dermatome was 4.60(0.70 min in Group A and 2.07(0.47) min in Group B. Quicker onset of sensory block in patients of Dexmedetomidine group in present study is also comparable with studies carried out by Nazima Memon et al 15, Veennah Chatrath et al. 13 Our findings were also similar to Sunil B.V. et al.,<sup>22</sup> who studied 90 patients in three groups of each.<sup>30</sup> Each group received intrathecally either 15mg hyperbaric Bupivacaine alone (Group B) or 10 μg (Group D10) or 5 µg Dexmedetomidine added to 15 μg hyperbaric Bupivacaine. The sensory block onset time to reach T10 in group B was 4.7±1.1 min, group D5 3.5±0.8 min and group D10 3.1±0.5 min.

In conclusion, addition of Dexmedetomidine prolonged the sensory block significantly when used with hyperbaric Bupivacaine intrathecally in a dose dependent manner. It supports the addition of Dexmedetomidine up to  $10~\mu g$  with Bupivacaine in spinal anaesthesia.

Our findings were contradictory to study conducted by Feroz Ahmad Dar et al.,<sup>14</sup> Sangeeta Agrawal Bansal et al.,<sup>12</sup> who found no difference in time of onset using 5 µg Dexmedetomidine.

Time for Maximum Sensory Block and Maximum Sensory Level achieved: (Table III)

In our study time to achieve maximum sensory block was 5.39±0.31 min in Group BD as compared to 7.51±0.27 min in Group B. Time to achieve maximum sensory block was significantly lower (p<0.05) in Dexmedetomidine group as compared to control group. It indicates cephalad spread of sensory block occur faster when Dexmedetomidine was added to intrathecal Bupivacaine. This finding was similar to that of study carried out by R. Brinda et al.,<sup>16</sup>

However our finding was contradictory to finding of Sangeeta Agarwal Bansal et al.,<sup>12</sup> and Feroz Ahmad Dar et al.,<sup>14</sup> who found no such difference regarding time to achieve maximum sensory block.

In present study maximum sensory block achieved was T4 in both groups, Group BD & Group B. This finding was comparable to study conducted by Veena Chatrath et al., <sup>13</sup> found similar dermatomal level of maximum sensory block achieved in patients who received intrathecal Dexmedetomidine.

Duration of Sensory Block (Time for Two Segment Regression): (Table IV)

In our study, mean time for two segment regression from maximum sensory dermatomal level in Group BD was 139.86±6.18 min which was much significantly longer (p<0.001) than that of Group B in which it was 90.21±6.09 min.

It means regression of sensory block was slower in patients those who received intrathecal Dexmedetomidine.

Our result is comparable with the study conducted by Nazima Memon et al.,<sup>15</sup> and Hala E A Eid et al.,<sup>11</sup>

Motor Block Parameters: (Table No. V & VI)

Onset of Motor Block: (Table No. V)

In present study mean time of onset of motor block was significantly quicker (P<0.001) i.e. 3.53±0.27 min in Group BD as compared to 5.87±0.29 min in Group B.

This result was comparable to R. Brinda et al., <sup>16</sup> who found mean time of onset of motor block 2.30±0.45 min in Dexmedetomidine group (5 mcg) as compared to 6.57±0.49 min in control group.

Thus from above results it is clear that along with faster onset of sensory block, onset of motor block is also quicker in patients who received intrathecal Dexmedetomidine.

Duration of Motor Block: (Time for regression to Bromage 0): (Table No. VI)

In present study the mean duration of motor block in Group BD was 227.1±1.76 min which was significantly prolonged (P<0.001) as compared to Group B in which it was 164.32±3.45 min.

Results of our study are comparable with the study carried out by R. Brinda et al.<sup>16</sup> The mean time for regression of motor block to Bromage 0 was 141.56±15.29 min in control group and 229.98±14.26 min in Dexmedetomidine group.

Our results were also comparable with the study carried out by Veena Chatrath et al13 who found that the mean duration of motor blockade was 318.36±9.374 min in Dexmedetomidine group as compared to only 146.94±9.713 min in control group(P<0.05). Similar results were observed by Sunil B.V. et al22 in which mean duration of motor block was 225±23.3 min in Dexmedetomidine group (5mcg) as compared to 149.4±17.5 min in control group.

Duration of Analgesia: (Table No. VII)

In present study we found that the mean duration of sensory analgesia was 222.54±14.68 min in Group B as compared to 368.74±11.72 min Group BD.

The mean duration of sensory block was prolonged in our study comparable to most of the previous studies carried out by R. Brinda et al., <sup>16</sup> Nazima Memon et al., <sup>15</sup>

Our findings are similar to that of study conducted by Veena Chatrath et al., <sup>13</sup> who studied 'comparative evaluation of Bupivacaine alone versus Bupivacaine and Dexmedetomidine for spinal anaesthesia in infraumbilical surgeries'. They concluded that addition of Dexmedetomidine to Bupivacaine leads to early onset of sensory and motor block with prolonged duration and patient remained pain free for longer period with decreased demand for rescue analgesia in the postoperative period as compared with Bupivacaine.

# Intraoperative and postoperative complications

In our study, intraoperative and postoperative complications observed were inadequate level of analgesia, bradycardia, tachycardia, hypotension, high level of block.

Intraoperatively two patients had bradycardia in Group B and 4 in Group BD which was treated by Atropine. Hypotension found in 2 patients in Group B and 3 patients in Group BD, treated with Ringer's Lactate solution and Mephenteramine.

There was not a single patient with inadequate level of analgesia, tachycardia and high level of block. Our findings were similar to findings of Sunil B.V. et al.,<sup>22</sup> R.Brinda et al.,<sup>16</sup> Nazima Memon et al.,<sup>15</sup> who also found minimal intraoperative complications.

There was no statistical difference of intraoperative and postoperative complications between both the groups (p>0.05). Results of our study are similar with the studies carried out by Sunil B.V. et al.,<sup>22</sup> Veena Chatrath et al.,<sup>13</sup> Nazima Memon et al.,<sup>15</sup> R.Brinda et al.,<sup>16</sup> in respect of onset of sensory block, onset of motor block, duration of sensory block, duration of motor block, duration of analgesia, intraoperative and postoperative complications.

# **Summary**

The present study titled 'Comparative evaluation of Bupivacaine and Bupivacaine with Dexmedetomidine in subarachnoid block' was prospective, randomized, double blind study included 100 patients belonging to ASA grade I or II of either sex with age between 15-45 years posted for elective for below umbilical surgery.

Control group Group B received Inj. Bupivacaine 0.5% 15mg + Normal Saline 0.5cc while Study group Group BD received Inj. Bupivacaine 0.5% 15mg + Inj. Dexmedetomidine 5mcg (0.5cc).

Pulse rate, systolic and diastolic blood pressure, respiratory rate and SpO2 were monitored intraoperatively and in postoperative period for 9 hours after spinal anaesthesia. Other parameters observed i.e. sensory and motor block parameters, analgesia time and VAS score and subjected to statistical analysis.

The demographic data such as age, sex, height and weight were comparable in both groups and has no influence on outcome of the study.

- 1. There was no significant difference in mean duration and type of surgery between both groups (p<0.05).
- 2. Mean time for onset of sensory block was significantly less 2.47±0.29 min in Group BD as compared to that of Group B 4.32±0.61 min (p<0.05).
- 3. Mean time for onset of motor block was significantly less 3.53±0.27 min in Group BD as compared to that of Group B 5.87±0.29 min (p<0.05).
- 4. Maximum sensory dermatomal level achieved

was equal i.e. T4 in Group B & BD.

- 5. Mean time for two segment regression was significantly longer (p<0.001) i.e. 139.86±6.18 min in Group BD compared to 90.21±6.09 min in Group B.
- 6. Mean duration of motor blockade in Group BD was 227.1±1.76 min which was significantly prolonged (P<0.001) as compared to Group B in which it was 164.32±3.45 min.
- 7. Mean duration of sensory analgesia was significantly prolonged (P<0.001) i.e. 368.74±11.72 min in Group BD than in Group B i.e. 222.54±14.68 min.
- 8. There was minimal variation in mean pulse rate during intraoperative and postoperative period in both groups from baseline readings (P>0.05).
- 9. Fall in systolic and diastolic blood pressure was not more than 15% of baseline readings in both the groups with haemodynamic stability.
- There were minimal intraoperative and postoperative complications in both the groups and difference was statistically not significant (P>0.05).

### Conclusion

After this study we came to the following conclusion that 0.5% hyperbaric Bupivacaine (15mg) with Dexmedetomidine (5mcg) in subarachnoid block.

- 1. leads to significantly quicker onset of sensory block as compared to 0.5% hyperbaric Bupivacaine.
- 2. leads to significantly quicker onset of motor block as compared to 0.5% hyperbaric Bupivacaine.
- 3. leads to prolonged duration of sensory block as compared to block as compared to 0.5% hyperbaric Bupivacaine.
- 4. leads to prolonged duration of motor block as compared to block as compared to 0.5% hyperbaric Bupivacaine.
- 5. leads to prolonged duration of analgesia as compared to block as compared to 0.5% hyperbaric Bupivacaine.
- 6. leads to minimal intraoperative and postoperative complications as compared to block as compared to 0.5% hyperbaric Bupivacaine.
- 7. leads to favourable haemodynamic stability

without any significant side effects making patients more comfortable in postoperative period.

Therefore addition of 5mcg Dexmedetomidine to 15 mg of 0.5% hyperbaric Bupivacaine in subarachnoid block can be considered safe and as effective as higher doses, minimizing the complication. It is useful in subarachnoid block for below umbilical surgeries where prompt onset and prolonged duration of postoperative analgesia is needed.

Result of our study matches with the result of studies of Nazima Memon et al., <sup>15</sup> Sunil B.V. et al., <sup>22</sup> R.Brinda et al., <sup>16</sup> & Veena Chatrath et al. <sup>13</sup>

Dexmedetomidine produces early onset of prolonged duration of sensory and motor block as well as prolonged postoperative analgesia with minimal side effects. Hence it can be used as an adjuvant to Bupivacaine in subarachnoid block for below umbilical surgeries requiring long time with excellent quality of spinal anaesthesia in postoperative period.

#### Reference

- DC Simone, R. Maria, A Casati, C Caterina, F Guido. Spinal anaesthesia: an evergreen technique. Acta Biomed 2008; 79: 9-17.
- Alahuhta S, Kangas-Saarela T, Hollmén Al, Edström HH. Visceral Pain during caesarean section under spinal and epidural anaessthesia with Bupivacaine. Acta Anaesthesiol Scand 1990;34:95-8.
- 3. Elia N, Culebras X, Mazza C, Sciffer E, Tramér MR. Clonidine as an adjuvant to intrathecal local anaesthetics for surgery: Systematic review of randomized trials. RegAnaesth Pain Med. 2008;33:159-67
- Boussofara M, Carlés M, Raucoules-Aimé M, Sellam MR, Horn JL. Effects of intrathecal midazolam on postoperative analgesia when added to a Bupivacaine-clonidine mixture. RegAnaest Pain Med. 2006;31:501-5.
- Al-Ghanem SM, Massad IM, Al-Mustafa MM, Al Zaben KR, Qudaisat IY, Qatawneh AM and Abu-Ali HM. Effect of Adding Dexmedtomidine versus Fentanyl to Intrathecal Bupivacaine on Spinal Block Characteristics in Gunaecological Procedures: A Double Blind Controlled Study. Am J Appl Sci 2009;6:882-7.
- 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 procedure. Saudi Med J. 2009;30:365-70

- 7. Kanazi GE, Aouad MT, Jabbour-Khoury SI, Al Jazzar MD, Alameddine MM, Al-Yaman R et al. Effect of low dose Dexmedetomidine or clonidine on the characteristics of Bupivacaine spinal block. Acta Anaesthesiology Scand.
- 8. Ibrahim F.A. Khalifa. Comparative study of adding intrathecal Dexmedetomidine versus Sufentanil to heavy Bupivacaine for postoperative analgesia in patients undergoing inguinal hernia repair. Benha Medical Journal 2009; 26: 207-19
- 9. Rajni Gupta, Jaishi Bogra, Reetu Verma, Monica Kohli, Jitendrakumar Kushwaha, Sanjivkumar et al. Dexmedetomidine as an intrathecal adjuvant for postoperative analgesia. IJA 2011; 55: 347-51
- Rajni Gupta, Jaishi Bogra, Reetu Verma, Monica Kohli, Rajesh Raman, Jitendrakumar Kushwaha et al. A comparative study of intrathecal Dexmedetomidine and Fentanyl as an adjuvants to Bupivacaine. JOACP 2011; 339-343
- 11. Hala E A Eid, Mohammed A Shafie, Hend Youssef. Dose related prolongation of hyperbaric Bupivacaine Spinal anaesthesia by Dexmedetomidine. Ain Shams J Anaesthesiol 2011; 4: 83-95
- 12. Bansal S, Bansal V. A randomized controlled double blinded prospective study of the efficacy of low dose Dexmedetomidine as an adjuvant to intrathecal Bupivacaine in hysterectomies. Int J Med Sci Public Heal [Internet] 2014; 3(7):876.
- 13. Attri J, Bansal P, Chatrath V, Kaur G, Khetarpal R. Comparative evaluation of Bupivacaine alone versus Bupivacaine and Dexmedetomidine for spinal anaesthesia in infraumbilical surgeries. Ain-Shams J Anaesthesiol [Internet] 2015; 8(1):83.

- 14. Feroz Ahmed Dar 1. The effects of Dexmedetomidine added to Spinal Bupivacaine for lower limb surgery. IOSR J Dent Med Sci {Internet}. 2014; 13(4):17-20.
- 15. Memon N, Pathak RG. Evaluation of effect of adding Dexmedetomidine to hyperbaric Bupivacaine in Spinal anaesthesia. 2015; 4(5): 355-9.
- 16. Brinda R, Sowmya SV, Shankar R. Effect of addition of Dexmedetomidine to Bupivacaine versus Bupivacaine alone in spinal anaesthesia for elective lower limb surgery. Int J Med Applied Sci. 2015; 4(1): 288-93.
- 17. Bromage PR. A comparison of the hydrochloride and carbon dioxide salt of lidocaine and Prilocainein epidural analgesia. Acta Anaesthesiol Scand 1965; 16: 55-69.
- 18. Annals of Pharmacology 2007; 41: 245-55
- 19. Toshio Ashno, Shuji, Shuichiro, Hiroyuki Shimonaka and Hioki Lida. Antinociception by epidural and systemic α2 adrenoreceptor agonists and their binding affinity in rat spinal cord and brain. Anaesth Analf 2000; 90: 400-07.
- 20. Eisrnach J, Shafer S, Bucklin B, Carswell J. Pharmacokinetics and pharmacodynamics of intraspinal Dexmedetomidine in sheep. Anaesthesiology 1994; 80: 1349-59.
- 21. Morgsn M. The Rationale use of intrathecal and extradural opioids. Br J Anaesth 1989; 63:165-88.
- 22. Sunil BV, Sahana KS, Jajee PR. 'Dexmedetomidine as an adjuvant withhyperbaric Bupivacaine for spinal: anaesthesia: a double blind controlled study'. Journal Evaluation of Medical and Dental Sciences 2013; Vol 2, Issue 40, October 07; Page: 7604 7611.