



## Dexmedetomidine and clonidine as intrathecal adjuvants to 0.75% isobaric ropivacaine in lower limb orthopaedic surgery

Authors

Dr Khageswar Raut<sup>1</sup>, Assoc Prof, Dr Debasish Swain<sup>2</sup>, Assoc Prof,  
Dr Sidharth Sraban Routray<sup>3</sup>, Assoc Prof

Department of Anesthesiology and critical care, SCB Medical College & Hospital, Cuttack, Odisha, India

Corresponding Author

Dr Debasish Swain

Email: [drkitusraban@gmail.com](mailto:drkitusraban@gmail.com)

### Abstract

**Background and Aim:** Our aim was to compare the analgesic efficacy following intrathecal administration of dexmedetomidine or clonidine as adjuvant with isobaric ropivacaine in lower limb orthopaedic surgery.

**Methods:** Ninety patients of ASA grade I or II, ages between 20-60 years, were randomly allocated to three equal groups, Group R received 2.5ml of isobaric ropivacaine (0.75%) with normal saline as a placebo, group D received 2.5ml of isobaric ropivacaine (0.75%) with 5 µg of dexmedetomidine and Group C received 2.5ml of isobaric ropivacaine (0.75%) with 30 µg of clonidine. All solutions were made up to 3 ml with addition of normal saline. The onset and duration of sensory and motor blockade, time to reach peak sensory and motor level and the sensory and motor regression times were recorded. Time to use first rescue analgesia, hemodynamic changes and side effects were recorded.

**Results:** Time to onset of sensory block and motor block was early in Group D and Group C as compared to Group R. Duration of sensory and motor blockade was prolonged in Groups C and D compared with Group R. The mean regression time to S1 segment was prolonged in Group D, and in Group C compared to Group B. The time to 1st rescue analgesia was significantly prolonged in Group D compared with Group C and group R.

**Conclusion:** The addition of dexmedetomidine to intrathecal ropivacaine prolongs the sensory block and provides prolonged postoperative analgesia when compared to ropivacaine with or without clonidine in lower limb orthopaedic surgeries.

**Keywords:** Clonidine, dexmedetomidine, intrathecal, ropivacaine.

### Introduction

Subarachnoid block is widely used in lower extremity's surgeries due to its safety and simplicity. Many drugs have been used and studied in subarachnoid block. Bupivacaine is the most widely used long acting spinal anaesthetic but it has been associated with cardio toxicity.<sup>1</sup>

Ropivacaine has a high pKa and low lipid solubility which is a s-enantiomer and has been used extensively for epidural and peripheral nerve blocks. It is less cardiotoxic and has a significantly higher threshold for Central Nervous System (CNS) toxicity. The efficacy and tolerability of isobaric Ropivacaine for spinal

anaesthesia in orthopaedic surgery have been demonstrated in several studies.<sup>2</sup> It has shown to produce sufficient surgical anaesthesia and analgesia with reduced side effect. However, Ropivacaine is less potent than Bupivacaine. Its action is slower in onset and short lived.<sup>3</sup> To overcome this, many adjuvants have been added to Ropivacaine intrathecally to potentiate the anesthetic effect. The efficacy and safety of Clonidine, which is a partial  $\alpha_2$  adrenoreceptor agonist, when used intrathecally is well established. Its addition to local anaesthetics prolongs the duration of both motor and sensory spinal blockade. Dexmedetomidine, a highly selective  $\alpha_2$  adrenergic agonist has evolved as a panacea for various applications and procedures in the perioperative and critical care settings.<sup>4</sup> It is also emerging as a valuable adjunct to regional anaesthesia and analgesia in central neuraxial blocks. Hence, the present study is being undertaken to evaluate and compare the effects of Dexmedetomidine and Clonidine as intrathecal adjuvants to Ropivacaine.

## Methods

A prospective randomized comparative study was conducted in SCB Medical College, Cuttack after obtaining permission from hospital ethical committee vide letter no IEC/IRB No 509. The study was done on 90 hospital inpatients (after taking informed consent from patient and patient attendants) who were to be scheduled for lower limb orthopaedic surgeries of age ranging from 20- 60 years between September 2015 to October 2017. 90 patients of physical status ASA I and II were selected on basis of inclusion and exclusion criteria and were randomly allocated into three groups. Each group consists of 30 patients.

- Group R- Received 2.5 ml of 0.75% isobaric Ropivacaine (diluted with normal saline to 3ml)
- Group D- Received 2.5 ml of 0.75% isobaric Ropivacaine with 5 mcg of inj.

Dexmedetomidine. (diluted with normal saline to 3ml)

- Group C- Received 2.5 ml of 0.75% isobaric Ropivacaine with 30 mcg of inj. Clonidine. (diluted with normal saline to 3ml)

## Exclusion criteria

1. Unwillingness of the patients.
2. Patients with cardiac disease and coagulopathy.
3. Infection at the site of injection.
4. Patients with preexisting neurological or spinal deformities
5. Patients allergic to local anaesthetics.
6. Pregnant women or lactating mother.
7. Patient taking ACE Inhibitors, calcium channel blocker,  $\alpha_2$  receptor blocker, anticoagulants

After detailed preanaesthetic examination, all patients were kept fasting for six hours before the procedure and received tablet alprazolam 0.25 mg and tablet ranitidine 150 mg the night before surgery. In the preoperating room peripheral vein was secured and preloading was done with 500 ml ringer lactate solution. After shifting the patient to the operating room monitoring devices were attached which included heart rate, electrocardiograph (ECG), pulse oximetry (SpO<sub>2</sub>), non-invasive blood pressure (NIBP), respiratory rate and the baseline parameters were recorded. Lumbar puncture was performed in sitting position using 25 -gauge Quincke type spinal needle. The intrathecal drug was prepared by a separate anaesthesiologist under strict aseptic conditions. The anaesthesiologist who administered anaesthesia was blinded to the group allocation. Vitals were recorded every 2 minutes up to the 10<sup>th</sup> minute and every 10 minutes thereafter up to 60 minutes. Beyond 60 minutes the vitals were recorded every 15 minutes till the time of discharge from PACU (Post Anaesthesia Care Unit). All the parameters recorded after spinal injection and during surgery were compared with baseline. Changes in these parameters were recorded and mean changes in each group at

different periods of observation was calculated. Onset of sensory block, onset of motor block, duration of sensory block and duration of motor block were noted for inter group comparison. The sensory dermatome level was assessed by pin prick method. The motor blockade was assessed according to the modified Bromage Scale.<sup>5</sup> Bromage 0- Patient able to move hip, knee and ankle. Bromage 1- Patient unable to move hip, but able to move knee and ankle. Bromage 2- Patient unable to move hip and knee but able to move the ankle. Bromage 3- Patient unable to move hip, knee and ankle. Onset of sensory and motor block- Time to reach the T-10 Dermatome and to reach the Bromage 3 level. Duration of sensory and motor block-Time to regression to dermatome S<sub>2</sub> and time to reach Bromage 0 was noted in post operative care unit. All durations were calculated taking the spinal injection time as time zero. Postoperatively, the pain score was recorded by using visual analog pain scale (VAS) between 0 and 10 (0 = no pain, 10 = severe pain), with the vital recordings of the study until the patient was discharged.<sup>6</sup>

IV paracetamol was given as rescue analgesia when VAS was greater than 4. Time of

administering the first dose of rescue analgesia was noted. Sedation was assessed by using Modified Ramsay sedation scale. Side effects including nausea, vomiting, bradycardia, hypotension, respiratory depression, sedation, shivering etc. were assessed both intra-operatively as well as post-operatively.

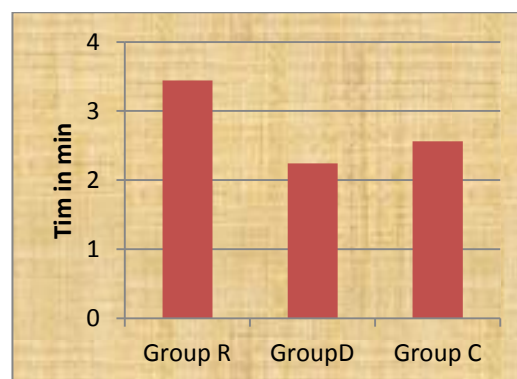
Hypotension is defined as a decrease in systolic blood pressure more than 20% of the baseline value, which was treated by Ephedrine 6 mg i.v or when the SBP was less than 90mmHg and bradycardia is defined as heart rate less than 60/min but atropine 0.6mg i.v was given when heart rate falls below 50/min. Post operatively vital signs, VAS scores and sedation scores was monitored in the recovery room every 15 minutes until the time of regression of sensory block to S<sub>2</sub> dermatome and then patient was shifted to the ward. All the statistical analysis were performed by using SPSS version 21. The various statistical tests that were used in this study were analysis of variance (ANOVA) test, Post hoc test (Bonferroni test) and nonparametric tests like kruskalwallis test. For all statistical analysis p <0.05 was considered statistically significant.

## Results

**Table-1:** Demographic parameters

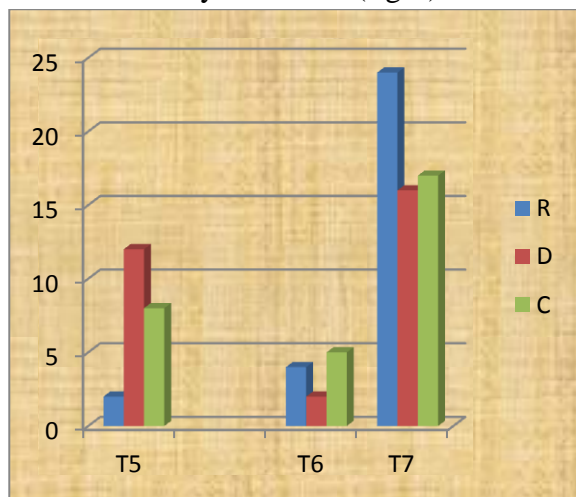
Parameters	Group R	Group D	Group C	P Value
Age(year)	39.13±10.05	43.53±10.41	41.63±9.85	0.24,NS
Weight(kg)	66.87±7.2	66±7.82	64.83±7.5	0.57,NS
Height(cm)	166.47±6.4	164.43±5.92	163.6±5.62	0.16,NS
Duration of surgery(min)	81.7±22.18	82.83±19.4	83.33±20.9	0.95,NS

The demographic parameters of patients in the three groups were comparable and the difference was statistically insignificant. The mean time taken for onset of sensory block was 3.4±0.372 mins in R group, 2.56±0.379 mins in C group and 2.24±0.197 mins in D group. So onset of sensory blockade in group C and in group D was faster compared to the R group and highly significant.( p value <0.001)(fig-1)



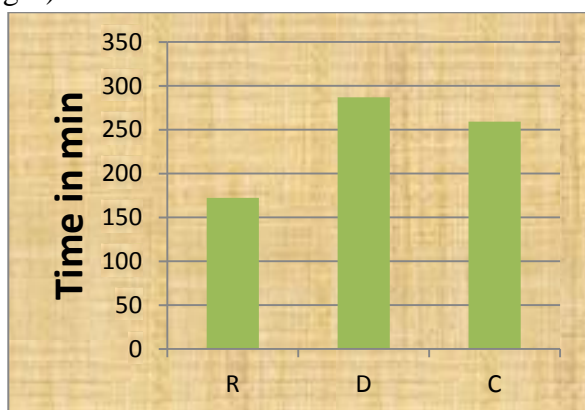
**Fig 1:** Time to achieve T 10 level of sensory block.

Two out of 30 patients in group R, 8 out of 30 patients in group C and 12 out of 30 patients in group D had T5 level of sensory blockade. Four out of 30 patients in group R, 5 out of 30 patients in group C and 2 out of 30 patients in group D had T6 level of sensory blockade. Twenty-four out of 30 patients in group R, 17 out of 30 patients in group C and 16 out of 30 patients in group D had T7 level of sensory blockade. (fig-2)



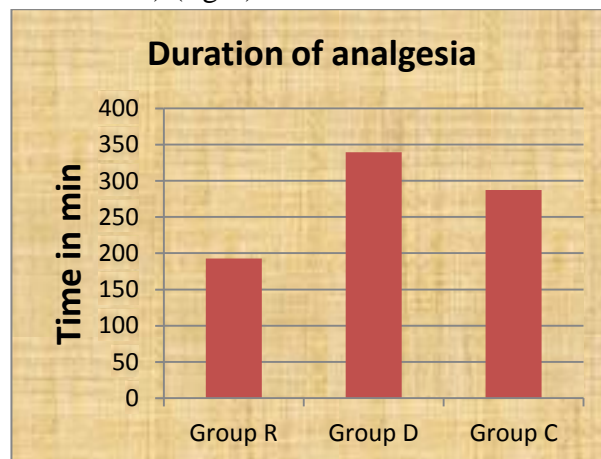
**Fig 2:** Maximum level of sensory blockade achieved

The time taken for sensory blockade regression to S2 level were 172 ± 33.5 minutes in group R, 286.6 ± 50.21 minutes in group D and 258.83 ± 20.93 minutes in group C. Intergroup analysis revealed a statistically significant difference amongst group R and D and group R and C. These values also significantly differ between group D and group C (P <0.05). Duration of sensory blockade was longer in group D than group C. (fig-3)

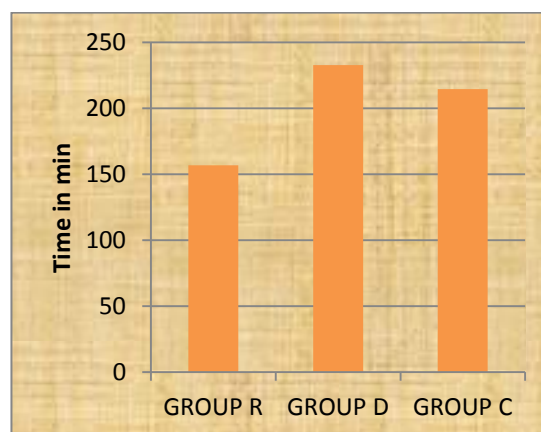


**Fig 3:** Time taken for sensory blockade regression to S2 level

The duration of analgesia was 192.66±18.18mins in R group, 339.5 ±28.80 mins in D group and 287.16±14.60 mins in C group. So duration of analgesia in group D and in group C was longer compared to the group R and highly significant.( p value <0.001) (fig-4)

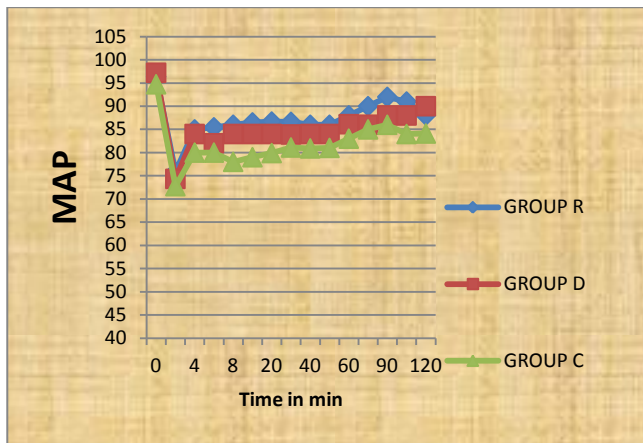


**Fig 4:** Comparison of duration of analgesia



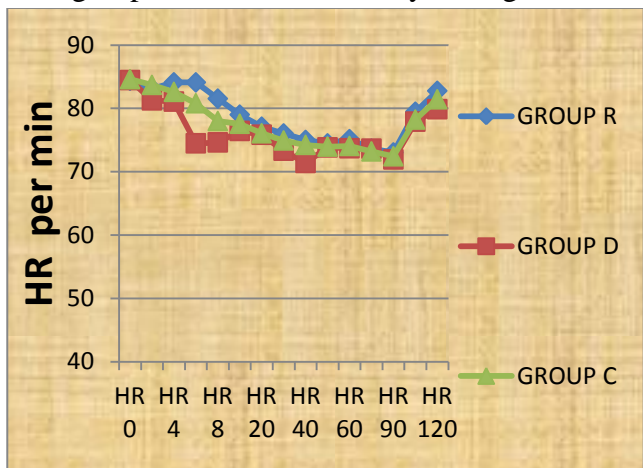
**Fig 5** Time taken for motor block regression to Bromage 0

The mean time taken for motor block regression to Bromage 0 was 156.66±102 mins in R group, 232.76±23.10 mins in D group and 214.43±21.82 mins in C group. So duration of motor blockade in group D and C was longer compared to the group R and highly significant.( p value <0.001) (fig-5)



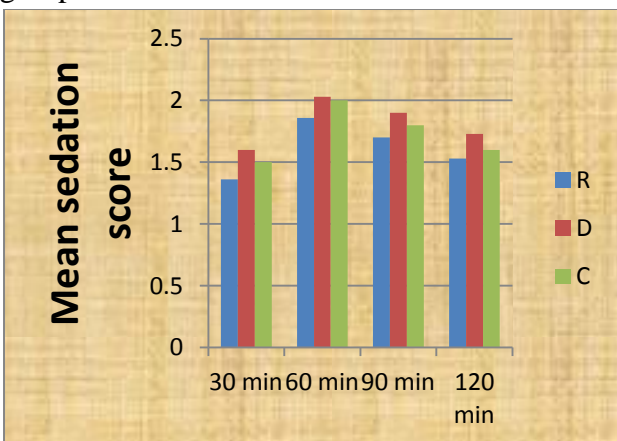
**Fig 6-** Comparison of mean blood pressure in 3 groups

The preoperative mean blood pressure was  $96.36 \pm 2.64$  mm Hg,  $97.2 \pm 9.14$  mm Hg,  $94.72 \pm 7.8$  mm Hg in group R, D and C respectively. Fall in mean blood pressure was comparable in all three groups and was statistically not significant.



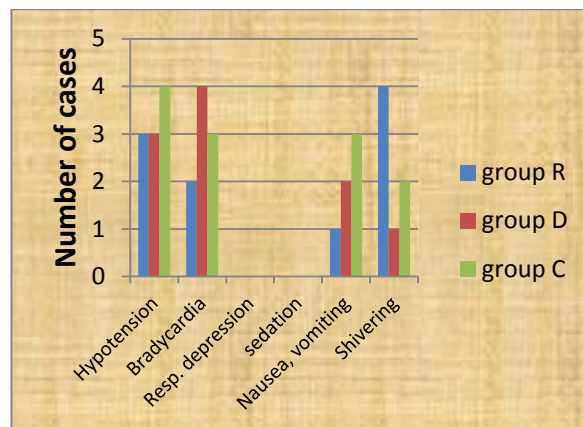
**Fig 7 :** Comparison of Heart rate among the 3 groups

Figure 7 shows the variation in heart rate in three groups.



**Fig 8 :** Comparison of mean sedation score among the three groups

Although the mean sedation score in Group D and Group C was higher than Group R at different time but it was statistically insignificant.(fig-8)Figure 9 shows incidence of side effects among the three groups and their statistical comparison.



**Fig 9 -** Comparison of side effects between 3 groups

**Discussion**

Ropivacaine is a new long-acting, enantiomerically pure (S-enantiomer), amide local anaesthetic with a high pKa and low lipid solubility.<sup>7</sup> It is considered to block sensory nerves to a greater degree than motor nerves. Because of sensory motor dissociation Ropivacaine may be a favourable local anaesthetic for day-case surgery and may result in earlier postoperative mobilization than bupivacaine.

While Clonidine has been used as an adjuvant to local anaesthetic agents for intrathecal purposes with successful results, there are only a few studies available for Dexmedetomidine for such studies and hence there is a need to compare its effectiveness as a spinal adjuvant to ropivacaine.<sup>8,9</sup>

In our study, all patients receiving either drugs achieved adequate level of anaesthesia. Mean time needed for sensory blockade at T10 was  $156.4667 \pm 33.78$  s in Group RD and  $185.2000 \pm 35.17$  s in Group RF. The results are clinically and statistically significant.

Our results are consistent with El-Attar et al.<sup>12</sup> study where he compared intrathecal dexmedetomidine and fentanyl as additives to

bupivacaine and concluded that dexmedetomidine has faster sensory onset compared with fentanyl and local anesthetic when injected intrathecally. Our results were similar to the studies done by Mahendru et al.,<sup>10</sup> Gupta et al.,<sup>11</sup> El-Attar et al.,<sup>12</sup> and Safari et al.<sup>13</sup> who concluded that intrathecal dexmedetomidine is associated with prolonged sensory block when compared to other adjuvant. Mahendru et al. studied intrathecal dexmedetomidine, clonidine, and fentanyl as adjuvants to hyperbaric bupivacaine for lower limb surgery. They found that when dexmedetomidine and fentanyl were added as adjuvants, duration of analgesia was prolonged and maximum height of sensory block achieved was T6 in both groups. Gupta et al.<sup>11</sup> studied intrathecal dexmedetomidine and fentanyl as adjuvants to bupivacaine. They concluded that duration of analgesia was prolonged and the maximum height of sensory block achieved was T5 with dexmedetomidine and T6 with fentanyl as adjuvant to local anesthetic. Al-Mustafa<sup>14</sup> observed dose dependent prolongation of motor and sensory blockade with decreased analgesic requirement with increasing dose of intrathecal dexmedetomidine. In a study conducted by Hala E A Eid et al.,<sup>15</sup> significant prolongation of the duration of spinal blockade was seen by intrathecal dexmedetomidine as an adjunct to hyperbaric bupivacaine. Dexmedetomidine reduced postoperative pain scores and provided longer analgesic duration. Kanazi et al.<sup>16</sup> and Al Ghanem et al.<sup>17</sup> concluded that dexmedetomidine and clonidine added to bupivacaine produced a similar prolongation in the duration of the motor and sensory block, with preservation of hemodynamic stability. All these studies are in agreement with our study.

### Conclusion

Dexmedetomidine with Ropivacaine provided an early onset of sensory and motor blockade and prolonged the duration of analgesia when compared to clonidine.

### References

1. Elia N, Culebras X, Mazza C, Schiffer E, Tramèr MR. Clonidine as an adjuvant to intrathecal local anesthetics for surgery: Systematic review of randomized trials. *Reg Anesth Pain Med.* 2008; 33:159–67.
2. Chung CJ, Choi SR, Yeo KH, Park HS, Lee SI, Chin YJ. Hyperbaric spinal ropivacaine for cesarean delivery: A comparison to hyperbaric bupivacaine. *Anesth Analg.* 2001;93:157–61
3. Kakunje R, Sethuramachandran A, Parida S, Bidkar PU, Talawar P. Effects of adding low-dose clonidine to intrathecal hyperbaric ropivacaine: A randomized double-blind clinical trial. *Anesth Essays Res.* 2016;10:38–44
4. Gautier P, De Kock M, Huberty L, Demir T, Izydorczic M, Vanderick B. Comparison of the effects of intrathecal ropivacaine, levobupivacaine, and bupivacaine for Caesarean section. *Br J Anaesth.* 2003;91:684–9.
5. Wahedi W, Nolte H, Klein P. Ropivacaine for spinal anesthesia. A dose-finding study. *Anaesthesist.* 1996;45:737–44.
6. Sagioglu G, Sagioglu T, Meydan B. The effects of adding various doses of clonidine to ropivacaine in spinal anesthesia. *Eurasian J Med.* 2009;41:149–53.
7. Gupta R, Bogra J, Verma R, Kohli M, Kushwaha JK, Kumar S. Dexmedetomidine as an intrathecal adjuvant for postoperative analgesia. *Indian J Anaesth.* 2011;55:347–51.
8. Martin E, Ramsay G, Mantz J, Sum-Ping ST. The role of the alpha2-adrenoceptor agonist dexmedetomidine in postsurgical sedation in the intensive care unit. *J Intensive Care Med.* 2003;18:29–41
9. Kalso EA, Pöyhiä R, Rosenberg PH. Spinal antinociception by dexmedetomidine, a highly selective alpha

- 2-adrenergic agonist. *Pharmacol Toxicol.* 1991;68:140–3.
10. 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; 29:496–502.
11. 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.
12. El-Attar A, Aleem MA, Beltagy R, Ahmed W. A comparative study of intrathecal dexmedetomidine and fentanyl as additives to bupivacaine. *Res Opin Anesth Intensive Care.* 2015;1:43–9.
13. Safari F, Aminnejad R, Mohajerani SA, Farivar F, Mottaghi K, Safdari H. Intrathecal dexmedetomidine and fentanyl as adjuvant to bupivacaine on duration of spinal block in addicted patients. *Anesth Pain Med.* 2016;6:e26714.
14. 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.
15. Hala E A Eid MD, Mohamed A Shafie MD, Hend Youssef MD. Dose-related prolongation of hyperbaric bupivacaine spinal anesthesia by dexmedetomidine. *Ain Shams Journal of Anesthesiology* 2011; 4:83–95.
16. 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;50:222–7.
17. 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 gynecological procedures: A double blind controlled study. *American Journal of Applied Sciences* 2009; 6:882–7.