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A COMPARATIVE STUDY OF EFFICACY OF DIFFERENT DOSES OF DEXMEDETOMIDINE USED AS ADJUVENT WITH HYPERBARIC BUPIVACAINE IN PATIENTS UNDERGOING INFRAUMBILICAL SURGERIES UNDER SPINAL ANESTHESIA

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ABSTRACT

BACKGROUND : Subarachnoid block is commonly used for infraumbilical surgeries. Various adjuvants have been added to prolong the action of intrathecal bupivacaine. Various drugs like Fentanyl, Dexmedetomidine have been added to prolong effect of anesthesia. Dexmedetomidine in different doses have shown varying results.

MATERIALAND METHOD : In this Prospective, Randomized, double blind study, 135 patients divided into three groups(45 each) of age 18-60years and ASA grade I & II undergoing infraumbilical surgeries under spinal anesthesia. Each patient: In group B were given intrathecal 0.5% hyperbaric Bupivacaine(2.5ml); In Group D5 given intrathecal 0.5% hyperbaric Bupivacaine(2.5ml) with 5mcg Dexmedetomidine; In Group D10 given Intrathecal 0.5% hyperbaric Bupivacaine (2.5ml) with 10 mcg Dexmedetomidine.The hemodynamic parameters, onset and duration of sensory and motor block, duration of analgesia were compared between three groups.

RESULT : The mean time of onset of sensory and motor block was lesser in groups where dexmedetomidine was added(**p<0.001**). duration of analgesia was longer in group D10 and group D5 as compared to group B(**p<0.001**). duration of sensory and motor block was longer in group D10 and group D5 as compared to group B(p<0.001). incidence of bradycardia and hypotension was seen in group D10.

CONCLUSION: it is concluded that addition of 5µ Dexmeditomidine to hyperbaric Bupivacaine given intrathecally prolongs duration of sensory, motor block and post operative analgesia. The combination does not have adverse effect.

KEYWORDS : Bupivacaine, Spinal anesthesia, Adjuvents, Dexmedetomidine.

INTRODUCTION

Subarachnoid block is commonly used for surgeries because of its fast onset, less failure rates and cost-effectiveness it is universally accepted for infraumblical surgeries. sometimes it may fall short the duration of surgery requiring supplementation of general anesthesia. Many adjuvants have been used to prolong the spinal effect and also add on to post operative analgesia [1] . Bupivacaine is an amide-type, long-acting local anaesthetic which is a equimolar racemic mixture of R(+) Bupivacaine and S(-) Bupivacaine . Bupivacaine reversibly binds to specific sodium ion channels in the neuronal membrane, resulting in a decrease in the voltage-dependent membrane permeability to sodium ions and membrane stabilization; inhibition of depolarization and nerve impulse conduction; and a reversible loss of sensation(2). It is more potent than Lidocaine(3). There is increasing interest in using various adjuvants to spinal local anaesthetics with the goal of decreasing the dose of local anaesthetics, enhancing the duration of action and decreases side effects of local anaesthetics. Adequate post operative pain management is necessary to facilitate rehabilitation, accelerate functional recovery and enabling patients to return to their normal activity more quickly. Various adjuvants have been used to prolong the action of intrathecal Bupivacaine like Dexmedetomidine (4,5,6) ,Clonidine(7) , Opioids(8) (Fentanyl, Butorphanol), Ketamine, Midazolam, Neostigmine, Magnesium sulphate with varying amount of success. Dexmedetomidine, a new highly selective α2 agonist, dexmedetomidine is approximately 10-fold more α2 selective than clonodine(9). It act on prejunctional and post junctional α2 receptors in dorsal horn of the spinal cord. After activation presynaptic receptors reduces neurotransmitter release, whereas activation of post junctional receptors results in hyperpolarization and reduction of pulse transmission(10). As little as 3µg of dexmedetomidine can prolong motor and sensory block without hemodynamic compromise(5,11) . The present study is being carried out to find a suitable dose of dexmedetomidine which when used as adjuvant to spinal anesthesia along with Bupivacaine (heavy) will enhance block effect and also add on to post operative analgesia. We designed this study to compare the efficacy and associated side effects of varying doses of Intrathecal dexmedetomidine (5µg, 10µg) with 0.5% hyperbaric Bupivacaine - 2.5 ml in patients undergoing infra umbilical surgeries.

MATERIALAND METHODS

After approval from ethical committee of the institution and obtaining written and informed consent from patient, the proposed study was carried out in M.L.N Medical college and associated hospital (S.R.N Hospital) over a period of one year from june 2020 to may 2021 after approval from institutional ethical committee and obtaining written and informed consent from all patients.

SELECTION OF CASES One thirty five patients (45 patients in each groups) belonging to American Society of Anaesthesiologists (ASA) physical status I – II, age group 18-60 yrs of either sex posted for elective infraumblical surgery under spinal anesthesia were recruited in the study.

EXCLUSION CRITERIA:

1. Patients refusal.
2. Local infection at site of spinal block.
3. Patients with bleeding disorder(s).
4. Patients with spine deformity.
5. Patients having cardiorespiratory diseases.
6. Patients having endocrine or metabolic disorders.
7. Patients having renal or hepatic impairment.
8. Patients having prior history of drug abuse.
9. Patients having neurologic and psychiatric disease.
10. Emergency cases

GROUPALLOCATION:

Patients were randomly allocated and divided into three groups (45 patients in each group) using computer generated random number table.

Group B	45 Patients	Each patient received Intrathecal 0.5% hyperbaric Bupivacaine 12.5mg (2.5ml).
Group D5	45 Patients	Each patient received Intrathecal 0.5% hyperbaric Bupivacaine 12.5mg(2.5ml) administered with Dexmedetomidine 5µg.
Group D10	45 Patients	Each patient received Intrathecal 0.5% hyperbaric Bupivacaine 12.5mg(2.5ml) administered with Dexmedetomidine 10µg.

BLINDING:

Blinding was achieved by two different anaesthesiologists – one for preparation of the study drug, second for administration of the drug and data collection. Hence the observer and patient, both were unaware of the study drug.

STATISTICALANALYSIS:

The data were entered into Microsoft Excel spreadsheet and then analyzed by SPSS (Statistical Package for the Social Sciences) version 20.0statistical analysis software. Data were summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. ANOVA test was used to analyze the quantitative variables after ascertaining normal distribution of data, and statistical significance is assumed for values of $P < 0.05$. Tukey's honestly significant difference (Tukey HSD) post-hoc test was used to compare among groups if P was found to be statistically significant.

Qualitative data (Demographic variables, Gender and complications) were compared using Chi-square test. Significance was assessed at 5% level of significance. A "p" value of <0.05was considered as significant.

METHODOLOGY:

Pre-anaesthetic visit: One day before surgery, a detailed pre-anaesthetic examination including history, height and weight measurement , systemic examination of cardio vascular, respiratory and central nervous system was done and examination of spine for any deformity or infection was done . Airway assessment was done. Age, weight, height, side of surgery was noted in all patients.

Routine investigations including Complete Blood Count, Blood Grouping , Coagulation profile, Urine routine and microscopy, Random blood sugar, Serum Urea and Creatinine, 12 Lead ECG and Chest X-Ray were done. All patients were instructed for the methods used for measurement of sensory and motor assessments. In addition, patients were instructed regarding scoring their pain using a Visual Analogue Scale from 0 to 10 and to mention the occurrence of nausea, pruritus, dizziness anytime during the stay in operating room or recovery room. All patients were kept nil oral from 12 mid night prior to the day of surgery and received Tab Ranitidine 150mg and Tab. Alprazolam 0.5 mg both orally, as pre-medication on night prior to surgery.

In the operating room:

In the operation theatre, intravenous access was established using an 18 gauge i.v. cannula and intravenous Ringer Lactate start. Patients were attached to standard monitors Pulse Rate (PR), Systolic and Diastolic blood pressure, and peripheral Oxygen Saturation (SpO_2) and baseline parameters were recorded.

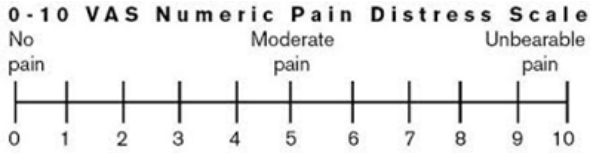
The intrathecal anesthetic solutions was prepared prior to performing the spinal injection by a separate anaesthetist who had no further involvement with the patient. Patients and clinical staff (anesthe siologists, surgeon, and nurses) performing the procedure and making observations were blind to the treatment group. All solutions were prepared under strict aseptic technique using 0.9% normal saline where dilution was required. Once prepared,the solutions were labeled with the Group number.

One of the investigators, who was blind to group allocation recorded Pulse rate, Systolic and Diastolic Blood pressure, Respiratory Rate and peripheral O2 saturation (SpO_2) at baseline (i.e. 5 min after stabilization of patient in the operation room), at the time of institution of spinal anesthesia i.e. 0 minute, at every 5 min interval for first 15 minutes and at 15 minute intervals for the rest of surgery.

All the patients were shifted to post anaesthesia recovery room and were observed.

Visual Analogue Scale (VAS) [12]given by Revill in 1976 was used for recording the intensity of pain of the patients. It is an imaginary straight line of 10 cm from 0 to 10. Patients were asked to point out the scale after test drug was given. "0" indicates no pain while "10" denotes worst pain imaginable.

Pain scores were measured at the time of incision and every 15 min thereafter in the operation room and recovery room using visual analogue scale. However, patients were instructed to report pain score of 4 or more at any point of time. Pain score ≥4 was considered inadequate analgesia/anesthesia.



Sensory assessment:

Sensory level was assessed by loss of sensation to pinprick[13] in the midclavicular line bilaterally. Time to reach sensory level of T6 on the operating side was taken as the time of onset of sensory block and this duration was noted.

Motor assessment:

Motor block was assessed based on a **Modified Bromage scale**[14]. Time taken to reach Bromage 3 was taken as the time of onset of motor block.

Bromage 0	**No motor block**
Bromage 1	Inability to raise extended leg, able to move knees and feet.
Bromage 2	Inability to raise extended leg and move knees, able to move feet.
Bromage 3	Complete block of motor limb.

Observed parameters:

1. **Hemodynamic parameters and other vital parameters :**Pulse rate, Mean Arterial Pressure, Peripheral Oxygen Saturation.
2. **Onset of sensory Block :**
3. **Duration of Sensory Block :**
4. **Onset of Motor Block :**Time duration taken from administering spinal anaesthesia to reach muscular paralysis.
5. **Duration of Motor Block :**Time from achieving Bromage 3 to regaining Bromage 0. Recovery of the motor block was considered when the patient has no motor weakness.
6. **Duration of Surgery** was noted.
7. **Duration of analgesia :**Time of establishment of spinal effect to the first request of analgesia.
8. **Side effect**was noted.

OBSERVATION

Table – 1 :Showing patient´s characteristics

Variable	Group B		Group D5		Group D10		ANOVA	
	Mean	SD	Mean	SD	Mean	SD	F	p-value
AGE	36.40	10.54	32.73	7.73	32.33	8.17	2.86	0.061
Weight(kg)	67.64	5.31	68.17	5.25	67.82	5.13	0.12	0.87
Height(cm)	169.04	5.51	168.4	5.46	168.8	4.83	0.12	0.87

- The mean age of group B was maximum (36.40±10.54 yr) and minimum in group D10(32.33±8.17yr). No significant difference was found in mean ages between the groups (p=0.061).
- The mean Weight of group D5 was maximum (68.17±5.25) and minimum in group B (67.64±5.31). No significant difference was found in mean weight between the groups (p=0.87).
- The mean Height of group B was maximum (169.04 ±5.51) and minimum in group D5 (168.4±5.46). No significant difference was found in mean height between the groups (p=0.87).

Table – 2 :Sex Distribution of Cases

SEX	Group B		Group D5		Group D10		chi sq	p-value
	No.	%	No.	%	No.	%		
Male	25	55.6%	23	51.1%	22	48.9%	0.42	0.812
Female	20	44.4%	22	48.9%	23	51.1%		

The male – female proportion of group B, group D5 and group D10 was 55.6% : 44.4%, 51.1%:48.9% and 48.9%:51.1% respectively. No significant difference was found in male - female proportion among the groups (p=0.812).

Table – 3 :Bi-group Comparison of Pulse Rates

PR	Group B vs Group D5	Group B vs Group D10	Group D5 vs Group D10
	p-value	p-value	p-value
Pre Op	0.985	0.132	0.094
0 min	0.852	0.443	0.187
5 min	0.60	**0.030**	**0.040**
10 min	0.110	**0.014**	0.691
15 min	0.471	**0.027**	0.324

30 min	0.384	0.057	0.583
45 min	0.285	0.057	0.708
60 min	0.632	0.075	0.405
75 min	0.275	0.051	0.673
90 min	0.286	0.076	0.779
105 min	0.208	0.117	0.953
120 min	0.169	0.094	0.956

- Between Group B and Group D5 no significant difference was found at any time
- Between Group B and Group D10 significant difference was found at 5 min **(p=0.030)**, 10 min **(p=0.014)** and 15 min **(p=0.027)**.
- The bi-comparisons showed that between Group D5 and Group D10 significant difference was found at 5 min **(p=0.040)**.

Table – 4 :Bi-group Comparison of Systolic Blood Pressure

SBP	Group B vs Group D5	Group B vs Group D10	Group 5 vs Group D10
	p-value	p-value	p-value
Pre Op	0.068	0.180	0.890
0 min	0.219	0.960	0.129
5 min	0.751	**0.004**	**0.030**
10 min	0.584	**0.010**	0.121
15 min	0.256	**0.006**	0.276
30 min	0.389	0.081	0.673
45 min	0.355	0.063	0.645
60 min	0.055	0.205	0.809
75 min	0.067	0.368	0.647
90 min	0.197	0.205	1.000
105 min	0.169	0.236	0.982
120 min	0.748	0.109	0.397

- Between Group B and Group D5 no significant difference was found at any time.
- Between Group B and Group D10 significant difference was found at 5 min (**p=0.004**), 10 min **(p=0.010)** and 15 min (**p=0.006**).
- The bi-comparisons showed that between Group D5 and D10 significant difference was found at 5 min (**p=0.030**).

Table – 5 :Bi-group Comparison of Diastolic Blood Pressure

DBP	Group B vs Group D5	Group B vs Group D10	Group 5 vs Group D10
	p-value	p-value	p-value
Pre Op	0.066	0.180	0.890
0 min	0.222	0.960	0.129
5 min	0.754	**0.006**	**0.040**
10 min	0.590	**0.016**	0.132
15 min	0.344	**0.020**	0.346
30 min	0.340	0.080	0.674
45 min	0.355	0.064	0.625
60 min	0.060	0.212	0.819
75 min	0.060	0.372	0.657
90 min	0.188	0.210	1.200
105 min	0.170	0.212	0.972
120 min	0.764	0.100	0.327

- Between Group B and Group D5 no significant difference was found at any time.
- Between Group B and Group D10 significant difference was found at 5 , 10 and 15 min.
- The bi-comparisons showed that between Group D5 and D10 significant difference was found at 5 min.

Table –6: Bi-group Comparison of Duration of Surgery and Duration of Analgesia

Variable	Group B vs Group D5	Group B vs Group D10	Group 5 vs Group D10
	p-value	p-value	p-value
Duration of Surgery (MIN)	0.989	0.477	0.395
Duration of Analgesia(MIN)	**<0.001**	**<0.001**	**<0.001**

The bi-comparisons showed that between Group B and Group D5 significant difference was found in duration of analgesia (p<0.001).

Significant difference in duration of analgesia too showed significant differences for rest other group pairs.

Table – 7 :Bi-group Comparison of Duration of Sensory and Motor Block

Variable	Group B vs Group D5	Group B vs Group D10	Group D5 vs Group D10
	p-value	p-value	p-value
Duration of sensory block(MIN)	**<0.001**	**<0.001**	**0.008**
Duration of Motor Block (MIN)	**<0.001**	**<0.001**	**<0.001**

- The bi-comparisons showed that between Group B and Group D5 significant difference was found in duration of sensory (p<0.001) and duration of motor block (p<0.001).
- Between Group B and Group D10 significant difference was found in duration of sensory (p<0.001) and duration of motor block (p<0.001).
- Between Group D5 and Group D10 significant difference was found in duration of sensory (p=0.008) and duration of motor block (p<0.001).

Table – 8 : Intergroup Comparison of Complications

COMPLICATIONS IF ANY	Group B		Group D5		Group D10		chi sq	p-value
	No.	%	No.	%	No.	%		
None	45	100.0%	45	100.0%	37	82.2%	17.01	**0.002**
Bradycardia	0	0.0%	0	0.0%	2	4.4%		
Bradycardia and hypotension	0	0.0%	0	0.0%	6	13.3%		

Among the complications, in group D10, Bradycardia was observed in 2 cases while Bradycardia and hypotension were found in 6 (13.3%) cases. The significant difference was found in proportion of complications among the three groups (p=0.002)

RESULT

Demographic data and clinical characteristics were comparable among the three groups in respect of age, height, weight, sex and baseline vital parameters in terms of Pulse rate, Mean Arterial Pressure, Oxygen saturation with no statistically significant difference (p> 0.05) **(Table- 1,2)**

The mean duration of surgery was similar between the three groups with no statistically difference (p=0.362)**[Table 6]**

The duration of analgesia was longer in group D10(352.89±29.24 minutes) and group D5(330.91±31.93minutes) as compared to group B (144.38±16.20minutes) and the result was statistically significant (p<0.001)**. [Table 6]**

The duration of sensory block was longer in group D10(308.22±30.06 minutes) and group D5 (292.56±26.51minutes) as compared to group B(170.87±14.49 minutes), and the result was statistically significant(p=0.001).**[Table-7]**

The duration of motor block was longer in group D10 (329.22±28.40 minutes), and group D5 (306.53±24.99minutes) as compared to group B (157.00±13.53minutes), and the result was statistically significant (p<0.001). **[Table 7]**

The incidence of bradycardia was found in group D10(17.7%) as compare to D5 and group B which was statistically significant (p=0.002**) [Table 8]**

The incidence of hypotension in group D10 (13.3%) was more as compare to group D5 and group B but the incidence is statistically significant (p<0.002)**[Table 8]**

DISCUSSION:

In this prospective , randomized, double blind study in patient scheduled for infraumbilical surgery, we compared the dose dependent effect of 5 µg and 10µg of dexmedetomidine added to 12.5 mg of intrathecal bupivacaine on the onset time, duration of motor and sensory block, duration of analgesia and associated side effects if any. We choose 5µg and 10µg of dexmeditomidine in comparision with plain bupivacaine so that in addition to prolongation of analgesia by dexmeditomidine, its dose dependent side effect may be confirmed with minimal side effects[67].

A study was done by **Kanazi et al**[15] including 60 patient undergoing TURP or bladder tumour under spinal anesthesia reported shorter

onset time of sensory and motor block but longer sensory and moter regression times in bupivacaine given with dexmedetomidine (3µg) as compared with bupivacaine alone. They showed that mean time to sensory regression to s1 was 303±75 minute.

Safiya I Shaikh, Rohini Dattatri[16]:
the aim of this study was to investigate the effects of intrathecal administration of dexmedetomidine 5µg and 10µg, as an adjuvents to bupivacaine heavy 0.5%, on the onset and duration of sensory and motor block,the hemodynamic stability,the duration of analgesia and the occurrence of any side effects. they concluded that dexmedeto midine added to bupivacaine heavy intrathecally has dose dependent favourable effects on the onset and regression of sensory and motor block, they also found that heart rate, blood pressure accessed at various time intervals showed no statistically significant difference, Our study also has same findings.

Jamlia RH et al[17]. The purpose of this study was to evaluate the onset and duration of sensory and motor block as well as operative analgesia and adverse effects of dexmedetomidine given intrathecally with hyperbaric 0.5% bupivacaine or hyperbaric 0.5% bupivacaine alone for spinal anaesthesia. Patients in group D(pt received intrathecal hyperbaric bupivacaine 15 mg +5µg dexmedetomidine)had significant longer sensory and motor block times than patients in group S(pt. received intrathecal hyperbaric bupivacaine 15 mg) . the mean time of sensory regression to S1 was 306±21.8 min in group D and 192±9.9 min in group S (P 0.0000). The regression time of motor block to reach modified Bromage 0 was 236±16.6 min in group D and 162.5±7.5 min in group S (P 0.0000). also found that dexmedetomidine has a dose dependent effects on onset and regression of motor and sensory block and time to rescue analgesia with minimal side effects, when used as an adjuvant to intreathecal bupivacaine

A study done by R Rajan et al.(2018)[18] they compared the onset and duration of sensory and motor block, analgesia time and adverse effects along with the hemodynamic changes, folowing intrathecal administration of dexmedetomidine with bupivacaine heavy total 120 patient of ASA class 1 and 2 and age group between 18 -60 yrs selected and divided randomly in three groups (40 patient in each group) selected. Group B received: hyperbaric bupivacaine 15 mg with normal saline as a placebo, group D received bupivacaine heavy 15 mg with 5 µg dexmedetomidine. They concluded that addition of 5µg dexmeditomidine to intrathecal bupivacaine heavy prolongs the motor and sensory block and prolong the post operative analgesia when compared to bupivacaine alone with preserved hemodynamic stability in lower abdominal and lower limb surgeries.

CONCLUSION

in our study we have found, that addition of dexmedetomidine to bupivacaine (heavy) given in intrathecal spinal anesthesia prolongs duration of sensory and motor blockade, Dose of 5µg of dexmedetomidine was free of any major complication as compared to 10µg dexmedetomidine. It is therefore concluded that a combination of bupivacaine(heavy) along with 5µg dexmedetomidine can safely given in infraumbilical surgery.

REFERENCES

1. Saadalla AT, Khalifa OA.Influence of addition of dexmedetomidine or fentanyl to bupivacaine lumber spinal subarachnoid anesthesia for inguinal hernioplasty. Anaesth Essays Res 2017;11:554-7.
2. National Center for Biotechnology Information. PubChem Database. Bupivacaine, CID=2474, https://pubchem.ncbi.nlm.nih.gov/ compound/Bupivacaine
3. Yano T, Ibusuki S, Takasaki M. A comparison of intracellular lidocaine and bupivacaine concentrations producing nerve conduction block in the giant axon of crayfish in vitro. AnesthAnalg. 2006 Jun;102(6):1734-8.
4. Shukla D, Verma A, Agarwal A, Pandey HD, Tyagi C. Comparative study of intrathecal dexmedetomidine with intrathecal magnesium sulfate used as adjuvants to bupivacaine. J AnaesthesiolClin Pharmacol2011;27:495-9.
5. Kanazi GE, Aouad MT, Jabbour-Khoury SI, et al:Effect of low dose dexmedetomidine or clonidine on the characteristic of bupivacaine spinal block , ActaanaesthesiolScand 2006,50(2):222-227.
6. Brull R, Abdallah F: the facilitatory effects of perineural dexmedetomidine on neuraxial and peripheral nerve blockade :a systemic review and meta analysis . Br J Anaesth2013, 110:915-925.
7. Dobrydnjov I, Axelsson K, Samarutel J, Holmstrom B. Postoperative pain relief following intrathecal bupivacaine combined with intrathecal clonidine. ActaAnaesthesiolScand 2002; 46:806–14.
8. Morgan M.The rational use of intrathecal and extradural opioids. Br JAnaesth1989;63:165-88.
9. Shah A, Patel I, Gandhi R. Haemodynamic effects of intrathecal dexmedetomidine added to ropivacaine intraoperatively and for postoperative analgesia. Int J Basic ClinPharmacol 2013;2:26-9.
10. James C. Eisenach, Marc De Kock, Walter Klimscha; α2-Adrenergic Agonists for Regional Anesthesia: A Clinical Review of Clonidine (1984 - 1995). Anesthesiology 1996; 85:655–674
11. Abdallah FW, Brull R. Facilitatory effects of perineural dexmedetomidine on neuraxial and peripheral nerve block: a systematic review and meta-analysis. Br J Anaesth. 2013 Jun;110(6):915-25
12. D. Gould et al. Visual Analogue Scale (VAS). Journal of Clinical Nursing 2001; 10:697-706
13. Curatolo M, Petersen-Felix S, Arendt-Nielsen L, Zbinden AM: Epidural epinephrine and clonidine: Segmental analgesia and effects on different pain modalities. Anesthesiology 1997; 87: 785–94
14. Bromage PR. A Comparison of the hydrochloride salts of lignocaine and prilocaine for epidural analgesia. Br J Anaesth.1965.37:754-761:
15. 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. ActaAnaesthesiolScand; 2006; 50:222-7.
16. Shaikh SI, Dattatri R. Dexmedetomidine as an adjuvant to hyperbaric spinal bupivacaine for infra-umbilical procedures: A dose related study. Anaesth Pain Intensive Care. 2014;18:180–5. [Google Scholar]
17. Jamliya RH , Deshmukh V , Rajesh C ,Maliwad J, Shah BJ , MinaxiH.Effect of adding dexmedetomidine in intrathecal bupivacaine versus intrathecal bupivacaine alone on spinal block charecteristics in orthopaedic lower limb procedures. Res J Pharm BiolChemSci 2013;4:1340-1346
18. Rajan R, Gosavi S N, Dhakate V, Ninave S. A comparative study of equipotent doses of intrathecal clonidine and dexmedetomidine on characteristics of bupivacaine spinal anesthesia. J Datta Meghe Inst Med Sci Univ 2018;13:4-8