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RESEARCH ARTICLE

COMPARISON OF BUPIVACAINE-DEXMEDETOMIDINE VS BUPIVACAINE-FENTANYL VS BUPIVACAINE -SALINE FOR UNILATERAL SPINAL ANAESTHESIA IN LOWER LIMB SURGERY

Dr. Mamta G. Patel, Dr. Ashka V. Surve, Dr. Arun George, Dr. Mittal S. Patel, Dr. Urvisha A. Mendpara and Dr. Kavan J. Patel

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Abstract

Introduction: Addition of adjuvants like Dexmedetomidine and Fentanyl to hyperbaric Bupivacaine has been proposed to improve the quality of spinal anaesthesia.

Aims and Objectives: The aim of current study was to compare the effects of adding Dexmedetomidine, Fentanyl and saline to low dose hyperbaric Bupivacaine (1 ml, 0.5%) on the properties of unilateral spinal anaesthesia.

Methods and Materials: 120 patients divided into three groups. The spinal anaesthetic agent in each of the three groups was 1 mL bupivacaine 0.5% (5 mg). In groups BD, BF and BS, 5mcg of Dexmedetomidine, 25mg of Fentanyl and 0.5 mL saline were added, respectively. The duration of the motor and sensory blocks in both limbs and the assessment of pain during 24 h after surgery were noted.

Results: Duration of motor and sensory block were significantly longer in the BF and BD groups than the BS group. Mean total number of rescue analgesic required were less in group BD and BF compared to group BS.

Conclusions: Addition of Dexmedetomidine and Fentanyl to low dose Bupivacaine in unilateral spinal anaesthesia increase the duration of the motor, sensory block and post op analgesia.

Introduction:-

Anaesthesia and its developments have always played an important role in the history of medical science. Spinal anaesthesia, which was given for the first time in 1898 by August Bier, is one of the popular and commonly used anaesthesia technique for lower abdominal and lower limb surgeries, due to its well-known advantages like, preservation of consciousness, simple and easy to perform, adequate surgical anaesthesia, minimal interference with blood biochemistry, less blood loss and avoidance of complications of general anaesthesia.

Conventional bilateral spinal anaesthesia has certain side effects such as hypotension, bradycardia, nausea, vomiting and shivering, which can be reduced with either reduction in dose of local anaesthetic drug or unilateral spinal anaesthesia in single limb surgery. Unilateral spinal anaesthesia is a simple and safe technique for unilateral surgery of the lower limbs in which the minimum dose of local anaesthetic is used and adjuvants like opioids or alfa 2 blockers are used to improve the quality of block and to prolong the duration of action. (Manisha et al, 2014) [1]

Corresponding Author:- Dr. Mamta G. Patel

Addition of adjuvants like Fentanyl and Dexmedetomidine to low dose Bupivacaine improves the quality of spinal anaesthesia as it intensifies sensory blockade and prolongs the duration of action without increasing motor blockade or hemodynamic instability (Naseh et al 2019). [2]

Unilateral spinal anaesthesia is performed with the patient in lateral position, rotating the bevel of needle to the bottom and injecting the hyperbaric local anaesthetic agent slowly so that anaesthetic effect can be restricted to one side (Naseh et al 2019). [2] Conventional use of large dose of Bupivacaine in spinal anaesthesia is associated with hemodynamic instability, delayed recovery of motor functions. So we have used low dose 0.5% hyperbaric Bupivacaine i.e. 5mg (1cc)

Bupivacaine is an amide type of local anaesthetic drug with primary action on cell membrane of the axon on which it produces electrical stabilization. Thus, the resting potential is maintained and depolarization in response to stimulation is inhibited and threshold for conductance is increased. Bupivacanie Hydrochloride is available in sterile, isotonic solutions. It may contain sodium hydroxide and/or hydrochloric acid for pH adjustment. Multiple-does vials contain methylparaben 1 mg/mL added as a preservative.

Dexmedetomidine an imidazole compound is the pharmacologically active dextroisomer of medetomidine that displays specific and selective alfa-2 adrenergic receptor agonism. It has anxiolytic, anaesthetic, hypnotic and analgesic properties. Intrathecal administration produces analgesia by suppressing the release of C-fibers pro-nociceptive neurotransmitters, substance P and glutamate from primary afferent terminals and by hyperpolarization of postsynaptic dorsal horn neurons. An alfa-2 agonist when administered intrathecally or epidurally, provides prolonged analgesic effect without severe sedation due to sparing of supraspinal sites from excessive drug exposure. Dexmedetomidine increases more sensory than motor block duration, as four times the dose is required for inhibition of large myelinated Aα fibers as compared to small unmyelinated C fibres.

Fentanyl is a phenylpiperidine derivative, lipophilic, narcotic, synthetic opioid agonist that is structurally related to meperidine. It is 75 to 125 times more potent analgesic than morphine, acts on μ1 and μ2 opioid receptors. In the spinal cord they are found both on interneurons and primary afferent neurons in the dorsal horn. μ1 receptor stimulation provides analgesia (supraspinal, spinal), euphoria, low abuse potential, miosis, bradycardia and urinary retention. Stimulation of μ2 receptor causes spinal analgesia, depression of ventilation, physical dependence and constipation.

The primary site of action of local anaesthetic is selectively on the nervous tissues at the spinal dorsal root ganglion and anterior and posterior spinal nerve roots. Local anaesthetics block the passage of action potential along the nerve fibre, exclusively at nodes of ranvier of myelinated nerves. The differing diameter of various nerve fibres and varying sensitivity to blockade by local anaesthetic is responsible for zone of differential block such as sympathetic fibres are blocked 3 segments higher than sensory fibres while difference between sensory and motor fibres is 2 segments.

Uptake of local anaesthetic agents is greatest where the CSF concentration of the drug is greatest and this aspect explains the zone of differential blockade. The posterior and lateral spinal cord tracts are heavily myelinated, hence the concentration of local anaesthetics is more in these tracts rather than anteriorly.

Rate of local anaesthetics uptake in various areas and nerves depends upon certain factors, as a result the definite and predictable sequence of neurological blockage is observed as follows, Autonomic and preganglionic fibres>Temperature fibres (cold before warm) > Pin prick fibres> pain fibres conveying pain greater than pin prick >Touch fibres> Deep pressure fibres>Somatic motor fibres>Fibres conveying vibratory and proprioceptive impulses.

Movement of the hyperbaric drug in CSF depends on position of the patient during and immediately after the injection is complete. The initial distribution in CSF of anaesthetics injected through a needle bevel pointing in direction of operative limb that is dependent limb in lateral decubitus position, in unilateral spinal anaesthesia is likely to be greater at the dependent site.

The circulatory changes occur due to sympathetic blockage resulting in hypotension due to sympathetic blockage and decrease in cardiac output. Lack of muscular propulsive force on veins due to motor blockage leads to decrease in venous return. Paralysis of sympathetic nerve supply to adrenal gland causes consequent catecholamine depletion.

Under spinal anaesthesia, lax abdominal wall permits easier movement of diaphragm to compensate any intercostal paralysis. Decreased sensory input to the respiratory center due to deafferentation is responsible for these respiratory changes. The reduction in GFR and effective renal plasma flow, due to hypotension, is only transitory and disappear when blood pressure rises again. The bladder wall, supplied by the parasympathetic system, is paralysed during spinal anaesthesia but the sphincter is not relaxed. Urinary retention may outlast skin analgesia. Engorgement of flaccid penis due to paralysis of nervierigentes (S2-3) is Often the first sign of the onset of successful block. Vasodilatation due to spinal anaesthesia causes heat loss and shivering.

In unilateral spinal anaesthesia with minimum volume and concentration of anaesthetic agents these changes are not significant. We conducted this study to compare and determine the incidence of unilateral block, block characteristics and any untoward effects of using Dexmedetomidine, Fentanyl or Saline(control) as an adjuvant to low dose 0.5% Bupivacaine (5mg) in unilateral spinal anaesthesia for lower limb surgeries of one side.

Materials and Methods:-

This randomized, double blind, control study was carried out after taking permission from the Ethical Research Committee of the institute, in the Department of Anaesthesiology, Govt. Medical College and S.S.G. Hospital, Baroda, between the periods of October 2019 to October 2020.

Patients with age 18 to 60 years of age, ASA – I/II, Elective unilateral limb surgeries like amputation, debridement, tibia and ankle surgeries were included in this study. A thorough pre-operative assessment of the patients and routine (in all cases) and specific investigations (when indicated) were carried out on day before surgery.

Patients with absolute and relative contraindications to spinal anaesthesia (patient refusal, local skin infection, vertebral column abnormalities, bleeding disorders, thyroid disorders, cardiopulmonary disease, neuropathies), history of diabetes, renal or hepatic disease, allergy to local anaesthetics, pregnant and lactating females, Morbid obesity(BMI>29 kg/square metre) were not included in the study.

It is a time bound study. As per hospital record, we were expecting 10 cases per month. Hence in twelve months approximately 120 cases would be there and the cases were divided randomly into three groups of 40 patients each using sealed envelope method.
Group BD (Study group, n=40) Patients received Inj. Bupivacaine 0.5% 1ml+ InjDexmeditomedine 5mcg 0.5ml =1.5ml intrathecally
Group BF (Study group, n=40) Patients received Inj Bupivacaine 0.5% 1ml+ inj Fentanyl 25mcg 0.5ml=1.5ml intrathecally
Group BS(Control group, n= 40)Patients receiving Inj Bupivacaine 0.5% 1ml+ Inj normal saline 0.5ml =1.5ml intrathecally.

All the selected patients were explained in detail about the purpose, procedure of the study and possible side effects, written informed consent was taken and kept nil by mouth overnight.

After taking the patient in operation theatre, a good venous access was secured and preloaded with 5 ml/kg of Ringer's lactate solution. All patients received premedication Inj. Glycopyrrolate 0.2mg i.v and Inj. Ondansetron 4mg iv before induction. Base line pulse rate, blood pressure and oxygen saturation were noted. Patient was placed in lateral position with the limb to be operated on the lower side, with aseptic and antiseptic precautions painting and draping was done. After identification of L3 –L4 intervertebral space, 25G Spinal needle was inserted. After confirmation of free CSF flow, with the bevel of the needle pointing down, study drug was injected over 10-15secs intrathecally according to randomization. Patient was made to remain in lateral position for 10 minutes. Monitoring was started immediately on turning the patient supine. Surgery was allowed once the peak sensory (T12) and motor blockade (Bromage 3) were achieved. In any case, if failure of spinal anaesthesia or supplementation of general anaesthesia was required then that case was excluded from study.

For ensuring blinding, randomly allocated coded syringes of drugs were prepared after taking aseptic and antiseptic and precautions by a fellow anaesthesiologist not involved in performing subarachnoid block or recording of the outcome during intraoperative and postoperative periods. The Patient and the Anaesthesiologist performing subarachnoid block was blinded. The content of the drug was unblinded after 24 hours of performing subarachnoid block.

After induction of anaesthesia, sensory Block was assessed using pin prick method on both operative and non operative limbs for onset of sensory blockade at T12 (in mins), highest sensory level achieved, time to achieve highest sensory level (in mins), two segment regression time from highest sensory level (in mins), time for regression upto level S1 from highest sensory level.

Motor Block was assessed by Bromage scale as, Grade 0 - No blockade or no motor loss, Grade I - Unable to flex hip, Grade II - Unable to flex knee, Grade III - Unable to flex ankle. Onset of motor blockade (time to attain Grade I motor block), maximum motor grade achieved, time to achieve maximum motor grade and duration of motor block (time to return back to grade 0 from maximum motor grade) were also assessed for motor block.

Vital Parameters like pulse rate, blood pressure, oxygen saturation was monitored before blockade and after giving blockade and then 1,3,5,10,15,20,30 minutes after giving spinal blockade and then every 15 minutes till 1 hour then every 30 minutes till the end of surgery and in postoperative period vitals was monitored hourly for four hours.

Sedation was evaluated with the help of Campbell sedation score every 15 minutes after giving spinal anaesthesia as, 1 for wide awake, 2 for awake and comfortable, 3 for drowsy and difficult to arouse, 4 for not arousable.

Duration of surgery was noted in minutes. Pain assessment started at the end of surgery at 0 hour and every hourly for first 4 hours then every 2 hourly for next 8 hours and then 4 hourly for 24 hours. It is a 10 cm scale graded from 0-10 in such a way that 0 denotes no pain and 10 denote the most excruciating pain. The patients were asked to mark the point on the scale that corresponded to their level of pain intensity at the time of observation. The duration of effective analgesia was counted from the time of injection of spinal drug to VAS score of 4 or more. At this time, they were given rescue analgesic in the form of inj. Diclofenac aq. (75mg) i.m. Total doses of rescue analgesics required in the first 24 hours of postoperative period were also noted.

The patients were monitored for intra and post operative complications such as, Bradycardia (pulse rate less than 50/minute or less than 20% of pre procedure value), which was treated with Inj. Atropine 0.6 mg i.v. Hypotension defined as systolic blood pressure less than 90mm Hg or less than 20% of pre procedure value was considered as hypotension and was treated with IV fluids, oxygen and i.v. Ephedrine 5mg. Respiratory depression with decrease in SpO2 to less than 95% was defined as hypoxia and treated with supplemental oxygen via Oxygen mask at 4L/min. Nausea and vomiting were treated with Inj. Metoclopramide 10mg iv. Pruritus was treated with antihistamines. For dryness of mouth patients were reassured. Shivering was treated with proper covering of patient. For urinary retention urinary catheterization was done.

Statistical Analysis:
A master chart was prepared to arrange the observed parameters of each and every case. Mean and Standard values were taken out. Analysis of variance (ANOVA) of the data for the various parameters was done using student's paired t- test for intra-group comparison and unpaired t-test for intergroup comparison. The significance of ANOVA was judged as follows, $P > 0.05$ not significant, $P < 0.05$ significant and $P < 0.001$ highly significant.

Results:-

All three Groups were comparable with respect to age, gender, ASA grading and mean duration of surgery, baseline hemodynamic parameters. (Table 1)

The mean time for onset of sensory block at T12 level was as per Table 2. In all three groups, highest sensory level achieved was T10 in majority of patients in all three groups.

Difference in onset of motor blockade (time to attain bromage grade I motor block) was as per Table 3. Time to achieve maximum motor grade and duration of motor block were significantly higher in group BS compared to groups BD and BF.

Intra and postoperative vital parameters and sedation score were comparable in all three groups. The difference among duration of effective analgesia was as shown in Table 4. Number of doses of inj. Diclofenac 75 mg i.m. as rescue analgesia was higher in BS group and the difference between BS-BD and BS-BF was statistically significant with p value of 0.0001.

Discussion:-

Unilateral spinal anaesthesia for lower limb surgeries have many advantages over conventional spinal anaesthesia like longer lasting block in operative limb, reduced incidence of hypotension and faster recovery. The main disadvantage of unilateral spinal anaesthesia is short duration of action which can be overcome by adding adjuvants to local anaesthetic agents.

As per Naseh et al 2019, addition of adjuvants like Fentanyl and Dexmedetomidine to low dose Bupivacaine improves the quality of spinal anaesthesia as it intensifies sensory blockade and prolongs the duration of action without increasing motor blockade or hemodynamic instability. [2] We have observed similar findings in our study.

The time taken to achieve T12 sensory block in our study, is illustrated in Image 1. Similar results were observed by Vinod et al. 2016, Ji Eun et al. 2013 and Farhad et al. 2016. [3,4,5]

In our study we found that in majority of cases, peak sensory level achieved in dependent limb was T10 in all three groups. In nondependent limb in group BD, BF and BS, respectively 3 (7.5%), 2 (5%) and 4 (10%) patients developed sensory block which was below L3 level.

The current study showed that keeping patients in the lateral position for 15 min did not completely prevent the sensory block in the nondependent side and duration of the block in the independent limb were significantly shorter than the dependent limb. The longer the patient in the lateral position, the higher the probability of achieving success in unilateral spinal anesthesia. Since the distance between the neural roots in the lumbar region is about 10-15mm, even by injecting hyperbaric drugs and the patient being in the lateral position, the drug can distribute in upward direction for 30-60 min. Our findings are in consonance with Naseh et al, 2019, Vinod et al, 2016 and Tapas et al, 2014. [2,3,6]

In our study the mean time taken for two segment dermatomal regression and regression to S1 level was longer with use of dexmedetomidine or fentanyl as adjuvants compared to saline which shows prolonged duration of blockage. Naseh et al,2019, Vinod et al,2016 and Farhad et al,2016 have also found same results with adjuvant use.[2,3,5] The quality of sensory block was improved by the addition of Dexmedetomidine and Fentanyl.

Ji Eun et al,2013 and Farhad et al,2016, have observed that onset time of motor blockage is significantly higher without adjuvants, similar findings were observed in our study. [4,5] (Image 2) We have also observed that cases with maximum Bromage score less than 3, surgery was completed successfully without any supplementation. No motor block was noted in nondependent limb in any of the three groups. Naseh et al. 2019 and Tapas et al. 2014 have found similar results. [2,6]

Addition of adjuvants also increase the mean duration of motor block. Our study and other studies like Naseh et al. 2019, Vinod et al. 2016 and Farhad et al. 2016 have observed same findings. [2,3,5].

Dexmedetomidine group has shown prolonged analgesia in the studies conducted by Farhad et al, Ji Eun et al which was similar to our study [4].

In group BS requirement of rescue analgesic was frequent as illustrated in Image 4. Naseh et al, 2019 also has observed reduced frequency of use of rescue analgesic when adjuvants are used in spinal anaesthesia. [2]

Other than one patient who developed pruritus in Group BF which was treated with antihistamines, no complications were observed in all the three groups in intra or post-operative period.

Tables:-

GROUP	GROUP BD	GROUP BF	GROUP BS	P VALUE	
Ageinyears (Mean±SD)	38.25±8.07	39.57±8.29	39.40±7.62	BD-BS	>0.05
				BF-BS	>0.05
				BD-BF	>0.05
Gender(male:female)	31:9	29:11	27:13		
ASA grade (I:II)	29:11	26:14	27:13	BD-BS	>0.05
				BF-BS	>0.05
				BD-BF	>0.05
Mean duration of Surgery(minutes)	59.58±13.58	61.42±10.25	57.32±09.23	BD-BS	>0.05
				BF-BS	>0.05
				BD-BF	>0.05

Table 1:- Demographic data.

SR.NO	PARAMETER	GROUPBD (Mean±SD)	GROUPBF (Mean±SD)	GROUPBS (Mean±SD)	PVALUE
1	Onset of sensoryblock at T12(minutes)	2:05±0.07	2:06±0.007	2:09±0.007	BD-BF,>0.05 BD-BS<0.05 BF-BS<0.05
2	Highest sensory level achieved				
	T8 level	7(17.5%)	8(20%)	7(17.5%)	
	T10	27(67.5%)	29(72.5%)	30(75%)	
	T12	6(15%)	3(7.5%)	3(7.5%)	
3	Time to achievehighest sensory level(minutes)	3:47±0.08	3.49±0.008	3.53±0.05	BD-BF,>0.05 BD-BS<0.05 BF-BS<0.05
4	Time oftwosegment regression from highest level of block(minutes)	62.75±9.54	64.62±13.27	56.125±11.03	BD-BF,>0.05 BD-BS<0.05 BF-BS<0.05
5	Time to regresssensoryblock up to 1dermatome from highest level of block(minutes)	98.12±11.65	99.37±12.36	77.37±10.54	BD-BF,>0.05 BD-BS<0.05 BF-BS<0.05

Table 2:- Asessment of sensory block.

SR NO	PARAMETER	GROUPBD (Mean±SD)	GROUPBF (Mean±SD)	GROUPBS (Mean±SD)	PVALUE
1	Onsetofmotorblockade(minutes)	3:47± 0.22	3:49± 0.21	3:53± 0.28	BD-BF,>0.05 BD-BS,<0.05 BF-BS,<0.05
2	Maximummotorblockade achieved(BROMAGESCALE)				
	BROMAGE1	3(7.5%)	2(5%)	4(10%)	
	BROMAGE2	8(20%)	7(17.5%)	9(22.5%)	
	BROMAGE3	29(72.5%)	31(77.5%)	27(67.5%)	
3	Time toattain maximummotor block(minutes)	4:58± 0.02	4:59± 0.23	5:06± 0.21	BD-BF,>0.05 BD-BS, <0.05 BF-BS,<0.05
4	Duration ofmotor block (minutes)	77:55±10.54	79:32±10.36	58:19±9.70	BD-BF,>0.05 BD-BS,<0.05 BF-BS,<0.05

Table 3:- Asessment of motor block.

PARAMETER	GROUPBD Mean+SD	GROUPBF Mean+SD	GROUPBS Mean+SD	PVALUE
Duration ofeffective analgesia (minutes)	248.52+16.94	235.92+15.94	134.32+12.52	BD-BF, P<0.05 BD-BS, P<0.001 BF-BS,P<0.001

Table 4:- Duration of effective analgesia.

Images:

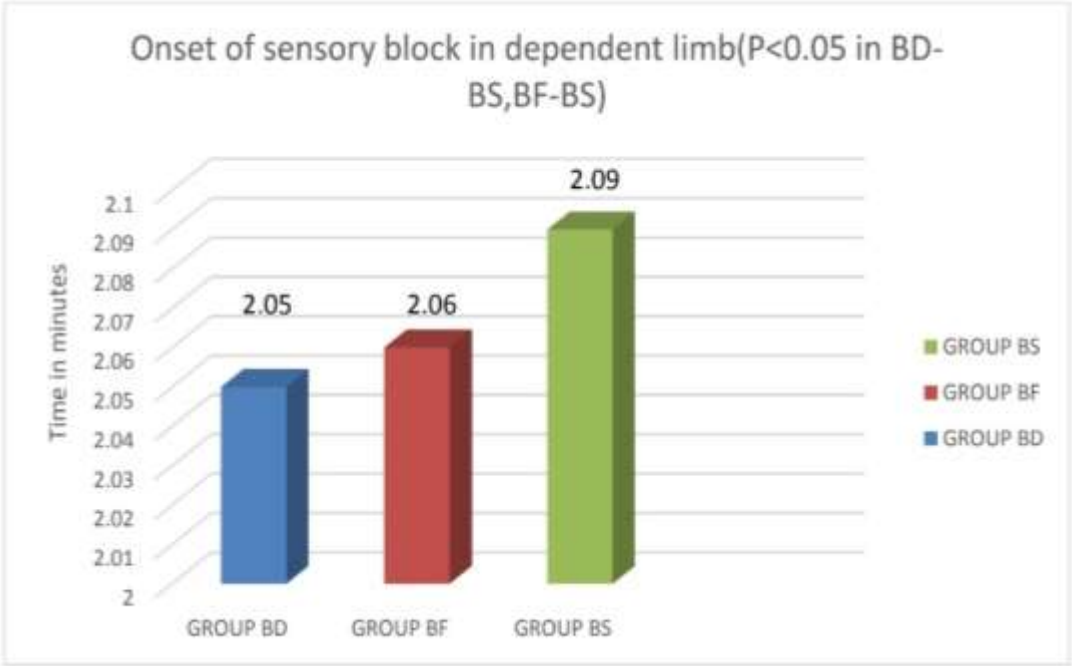

Image 1:- Comparison of onset of sensory block in dependent limb.

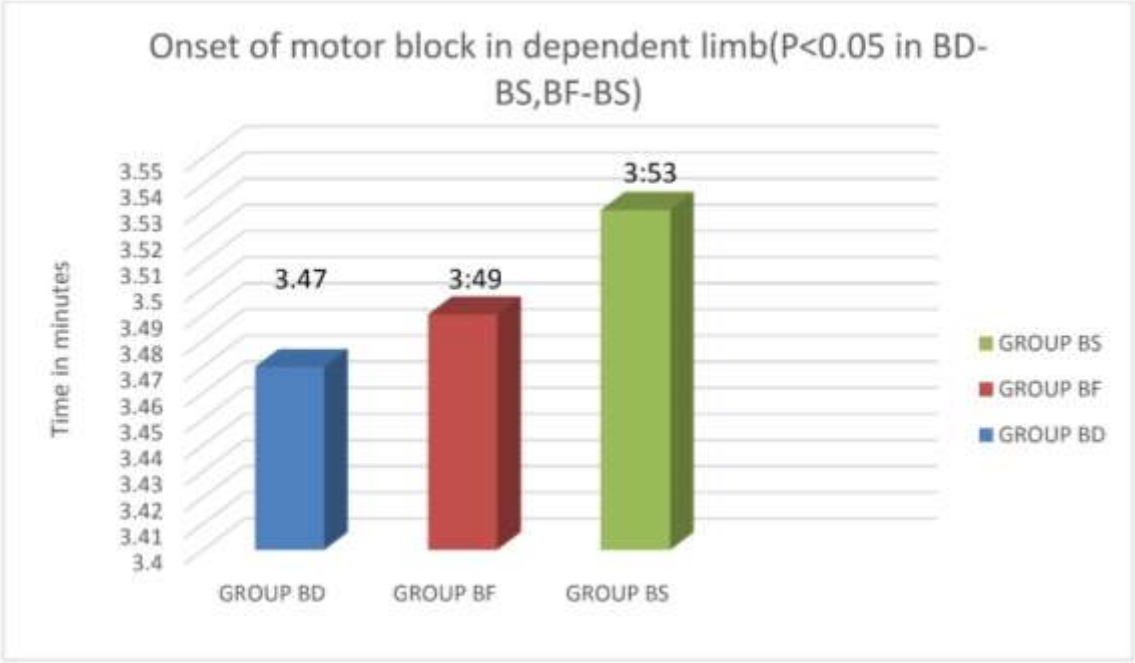

Image 2:- Comparison of onset of motor block in dependent limb.

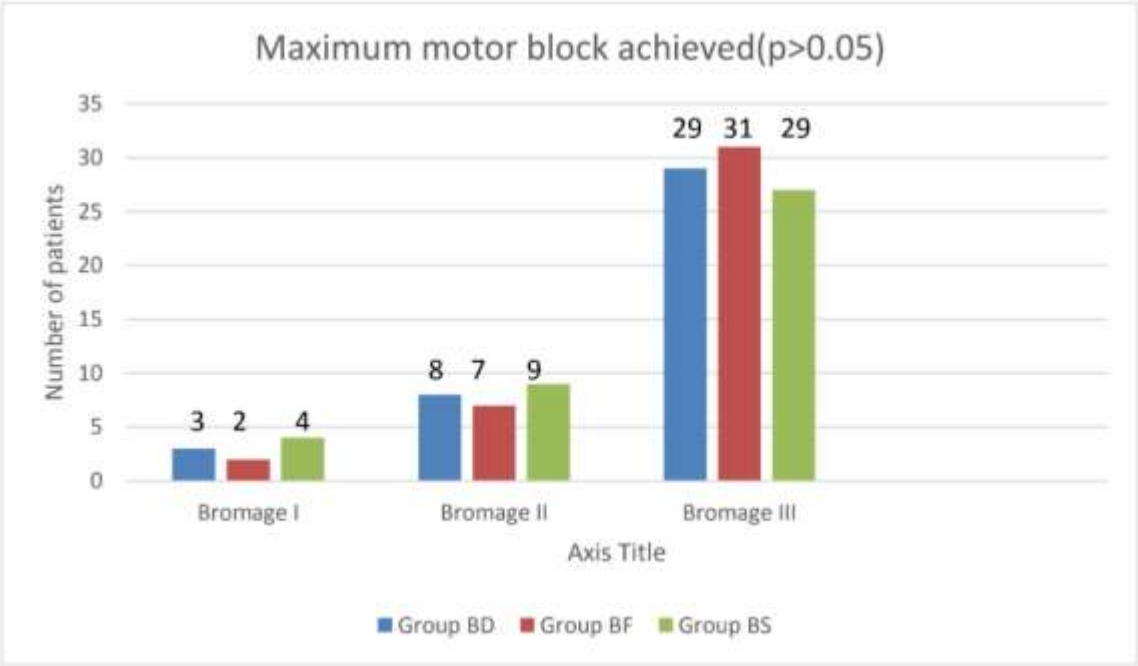

Image 3:- Comparison of maximum motor block achieved in dependent limb.

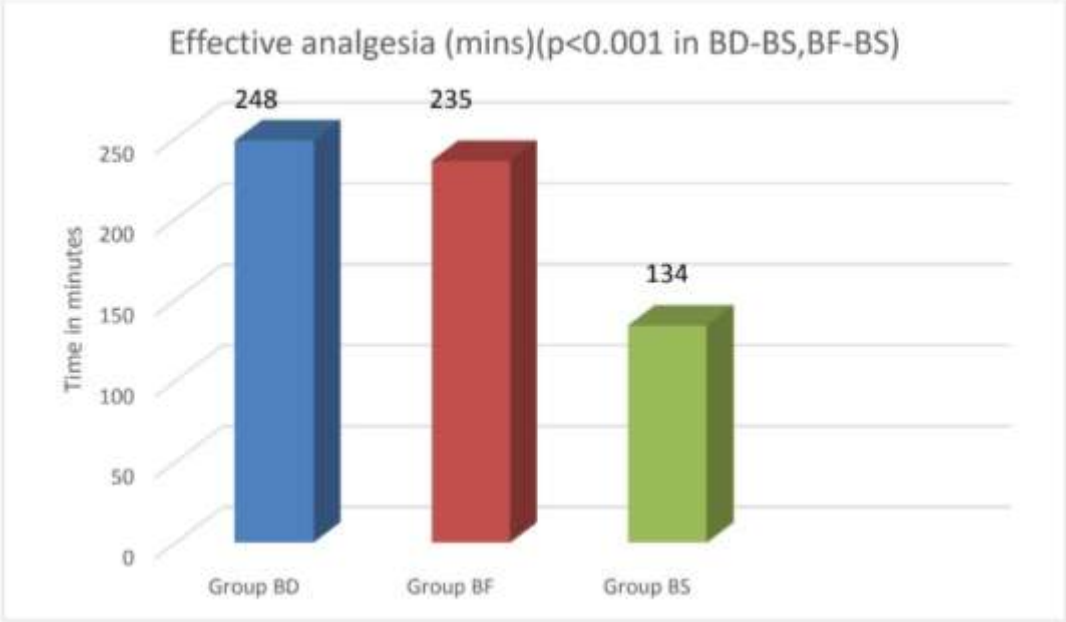

Image 4:- Comparison of effective analgesia in minutes (minutes).

Conclusion:-

Addition of Dexmedetomidine and Fentanyl to low dose Bupivacaine in unilateral spinal anaesthesia increases the duration of the motor, sensory block and post-operative analgesia without significant complications.

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