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Original Research Article

Comparison of Bolus Dose versus Fractional Dose of Hyperbaric Bupivacaine in Spinal Anaesthesia among Adult Patients Undergoing Vaginal Hysterectomy: A Prospective Observational Study

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Abstract:

Background: Spinal anaesthesia is gold standard technique for lower abdominal gynecological surgeries. We conducted a study to compare bolus dose versus fractional dose of hyperbaric bupivacaine in spinal anaesthesia among adult patients undergoing vaginal hysterectomy.

Methodology: This prospective, observational study was done on total 60 patients of American society of Anaesthesiologists physical status I, II & III, posted for vaginal hysterectomy under spinal anaesthesia. Patients were divided into two groups as Group B (Inj. Bupivacaine (0.05%) 3.75 cc as a bolus dose) and Group F (Inj. Bupivacaine (0.05%) 3.75 cc in two fractions, 1st 2/3rd dose 2.5 cc and after time gap of 60 seconds remaining 1/3rd dose 1.25 cc). Intraoperatively pulse rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, Spo2, Sensory and motor effect was checked every 2 minutes for first 20 minutes, thereafter every 10 minutes till 30 minutes & then every 30 minutes for rest of the study period.

Results: The mean duration of sensory and motor block was significantly longer in fractional group as compared to bolus group. Duration of analgesia was longer in fractional group (335.17 ± 32.07 min) as compared to bolus group (296.67 ± 47.28 min, $p<0.001$). Total 10 patients (out of 30) in bolus group and only 2 patients (out of 30) in fractional group required ephedrine for hypotension ($p<0.05$).

Conclusion: Fractional dosage of spinal anaesthesia can be used as an acceptable and safe alternative to a conventional bolus method in lower abdominal and lower limb surgeries.

Keywords: Spinal Anesthesia, Bupivacaine, Hypotension.

Introduction

Gynaecological surgery is a dynamic area of medicine that always evolves for the benefit of women's health by eradicating or reducing the symptoms of gynaecological disease. For that we need minimally invasive technique that provides good intraoperative and postoperative effective analgesia. Vaginal hysterectomy is the commonly done surgery for fibroids, endometriosis, uterine prolapse,

dysfunctional uterine bleeding and cancer of uterus, cervix or ovaries. Vaginal hysterectomy having following advantages over abdominal hysterectomy: no abdominal scar, fewer complications, require a shorter hospital stay and allows a faster recovery. [1,2]

Spinal anaesthesia is commonly used safe and simple technique for gynaecological hysterectomies. Rapid onset, surety of effect, decreased blood loss, protection against thromboembolic complications and full preservation of mental status are the main advantages of spinal anaesthesia over general anaesthesia. Spinal anaesthesia is considered gold standard technique for vaginal hysterectomy. Spinal anaesthesia is quicker, easier, provides dense block and more cost effective in comparison to epidural anaesthesia, so more preferred. Hyperbaric bupivacaine is most commonly used due to its long duration of action. Dose of hyperbaric bupivacaine depends on weight and height of patient for its density and duration of spinal block. Achieving the necessary sensory level for surgery corresponds inversely with weight and incrementally with height. Spinal anaesthesia causes sympathetic block which may lead to hypotension. Rapidly developing sympathetic block before the adaptation of cardiovascular system is the main cause for this hypotension. [3,4,5]

Various measures like low dose bupivacaine, preloading or coloading with colloids or crystalloids, prophylactic use of vasopressors etc are used to prevent hypotension. The addition of adjuvants to spinal anaesthesia prolongs the duration and intensity of sensory, motor and analgesic effects, but addition of adjuvants brought their own side effects. Spinal anaesthesia related hypotension can be prevented by modifying the technique of administering hyperbaric drug. Fractionating the dose of drug is one such technique in which 2/3rd dose is administered initially & 1/3rd dose is administered after time gap varying from 30 seconds to 90 seconds. This in turn help the cardiovascular system to buy time to adapt the developing sympathetic block, it also provides better hemodynamic stability without compromising the quality of block. Many studies are done regarding fractionated dose of spinal anaesthesia in lower segmental caesarean section & lower limb surgeries, but no any study was done in vaginal hysterectomy patients. So we want to evaluate the effectiveness of bolus versus fractionated dose of hyperbaric bupivacaine in spinal anaesthesia in adult female patients posted for vaginal hysterectomy. [6,7]

Material and Methods

The present prospective observational study was conducted at a tertiary care centre, after obtaining approval from institutional research and ethical committee from July 2021 to July 2022. The study included 60 adult patients of ASA physical status I, II & III between age group 18-60 years and BMI 18.5-22.5 posted for vaginal hysterectomy under spinal anaesthesia, who gave informed consent.

Inclusion Criteria

a) Patients posted for gynaecological hysterectomy under spinal anaesthesia
b) Female patients between the age group of 18-60 years
c) Patients having BMI *18.5 – 22.5*
d) Patients belonging to ASA grade I, II or III
e) Patients giving valid informed consent

Exclusion Criteria

a) Contraindication to spinal anaesthesia (Coagulopathy, localized infection and neurological diseases)

A detailed preanaesthetic checkup was done one day before surgery. The procedure to be performed was explained to patient and her relatives. On the day of operation informed consent of patient and her relative were taken. All patients were kept nil by mouth for at least 6 hours. In

the pre-operative room patient's baseline pulse rate, blood pressure was recorded and 20 G intravenous cannula was secured and patients was preloaded with 10ml/kg of ringer lactate. Patient was pre medicated with inj. Midazolam 0.02mg/kg intravenously. After taking patient on operation table, non-invasive blood pressure cuff, pulse oximeter (Spo2) and ECG leads was attached. Patients were placed in the sitting position and a 25G Quincke's spinal needle was inserted with bevelled end facing laterally, in L3-L4 intervertebral space for spinal anaesthesia. All the patients under spinal anaesthesia received inj. Bupivacaine (0.5%) heavy. Study patients were divided into following two groups:

- Group B: Patients received Inj. Bupivacaine (0.5%) 3.75 cc as a bolus dose.
- Group F: Patients received Inj. Bupivacaine (0.5%) 3.75 cc in two fractions, 1st 2/3rd dose 2.5 cc and after time gap of 60 seconds remaining 1/3rd dose 1.25 cc.

Intraoperatively pulse rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure (by non-invasive blood pressure) & Spo2 were monitored every 2 minutes for first 20 minutes, thereafter every 10 minutes till 30 minutes & then every 30 minutes for rest of the study period. The sensory blockade was assessed by pin prick method [8] and motor block was assessed by Modified Bromage Scale [9]. Sensory and motor effects were checked every 2 minutes for first 20 minutes, thereafter every 10 minutes till 30 minutes & then every 30 minutes for rest of the study period. Duration of sensory and motor block as well as dutation of analgesia was reported.

Post operatively patients were monitored in recovery room every 30 minutes interval up to 2 hours, after that every 1 hourly till complete regression of motor and sensory effect and pain. Pain was assessed postoperatively using Visual Analogue Scale (VAS), with VAS 0 = no pain and VAS 10 = extreme pain. Duration of analgesia is calculated by time giving spinal anaesthesia to first demand of analgesic by patient. Injection diclofenac sodium 75 mg intravenously was given when VAS score was ≥4. All patients were observed for the following side effects:

- Hypotension (systolic blood pressure <20% of baseline value or systolic BP < 80 mmHg): Treated with i.v. fluids/ Inj. Ephedrine 6 mg i.v. bolus.
- Bradycardia (pulse rate <60/ min): Treated with Inj. Atropine 0.6 mg i.v.
- Nausea & vomiting: Treated with Inj. Ondansetron 4 mg i.v.

Data thus collected was subjected to statistical analysis and results were drawn.

Results

The mean age of patients in Group B was 44.97 ± 7.67 years and in Group F was 43.96 ± 8.77 years. The mean BMI of patients in Group B was 20.87 ± 0.83 kg/m2 and in Group F was 20.77 ± 1.03 kg/m2. Both the groups were comparable in term of age and BMI of the patients. ($p>0.05$) (Table 1)

Table 1: Demographic profile of study patients

Parameter	Group B	Group F	p-value	Significance
Mean age(years)	44.97 ± 7.67	43.96 ± 8.77	0.6367	Nonsignificant
Mean BMI (kg/m2)	20.87 ± 0.83	20.77 ± 1.03	0.6804	Nonsignificant

In the present study, mean duration of sensory block in Group B was 237.5 ± 29.44 min and Group F 257 ± 24.19 min, which was statistically significant ($p<0.05$). Similarly the mean duration of motor block in Group B was 260.83 ± 31.38 min and Group F 279.67 ± 27.69 min, which was statistically significant ($p<0.05$). This suggested that the duration of sensory and motor block was longer in Group F compared to Group B. (Table 2)

Table 2: Comparison of mean duration of Sensory and Motor Block between the groups

Parameter	Group B	Group F	p-value	Significance
Mean duration of sensory block(min)	237.5 ± 29.44	257 ± 24.19	0.0069	Significant
Mean duration of motor block(min)	260.83 ± 31.38	279.67 ± 27.69	0.0167	Significant

The total duration of analgesia in the present study was significantly longer in Group F as compared to Group B. Total duration of analgesia in Group B was 296.67 ± 47.28 min and in Group F was 335.17 ± 32.07 min ($p<0.001$). (Table 3)

Table 3: Comparison of Total duration of analgesia between the groups

Parameter	Group B	Group F	p-value	Significance
Total duration of analgesia(min)	296.67 ± 47.28	335.17 ± 32.07	0.0005	Highly significant

In the bolus group, intragroup comparison of mean pulse rate with the baseline data showed that the mean pulse rate was comparable at all time interval except at 8 minute, when it showed significant change ($p<0.05$). In the fractional group, intragroup comparison of mean pulse rate with the baseline data revealed that mean pulse rate was comparable at all time intervals except at 30 min, 60 min & 150 min, when it showed significant decrease in pulse rate ($p<0.05$). In intergroup comparison, we observed that pulse rate at 16 minute & 180 minutes in Group B was high which was statistically significant than Group F. (Table 4)

Table 4: Changes in Mean Pulse Rate in both the groups

Mean Arterial Pressure	Bolus group	p-value (Bolus intragroup)	Fractional group	p-value (Fractional intragroup)	p-value (intergroup)
0 minute	93.4 ± 7.15		92.9 ± 7.08		0.7865
2 minutes	87.87± 6.38	0.0881	91.9 ± 7.08	**0.0325**	**0.0241**
4 minutes	83.3 ± 6.84	**0.0195**	90.63 ± 7.72	0.1759	**0.0003**
6 minutes	78.8 ± 6.76	**0.017**	89.53 ± 8.03	0.1749	**0.0001**
8 minutes	76.9 ± 6.72	**0.0166**	88.3 ± 7.69	0.0839	**0.0001**
10 minutes	75.37 ± 5.88	**0.0448**	87.93 ± 8.46	0.1724	**0.0001**
12 minutes	75.27 ± 5.88	**0.0445**	87.5 ± 8.29	0.1403	**0.0001**
14 minutes	74.2 ± 6.42	**0.0208**	88.06 ± 7.76	0.0889	**0.0001**
16 minutes	75.03 ± 5.28	0.0648	88.23 ± 7.56	0.0652	**0.0001**
18 minutes	75.47 ± 5.6	0.0549	87.9 ± 7.29	**0.0267**	**0.0001**
20 minutes	76.1 ± 4.38	0.1011	87.9 ± 6.56	0.066	**0.0001**
30 minutes	76.9 ± 5.31	0.0707	87.4 ± 6.39	0.0795	**0.0001**
60 minutes	77.37 ± 5.2	0.0771	89.23 ± 7.31	**0.0398**	**0.0001**
90 minutes	79.93 ±4.43	0.1108	88.86 ± 7.23	**0.0236**	**0.0001**
120 minutes	81.23 ± 6.29	**0.0449**	90 ± 8.26	0.246	**0.0001**
150 minutes	82 ± 7.69	**0.0301**	87.5 ± 9.62	0.2799	**0.0152**
180 minutes	80.25 ± 0.95	0.2805	82 ± 1.41	0.3054	**0.0001**
210 minutes	81		83		

In Intragroup, we compared baseline mean arterial pressure to the all-time interval mean arterial pressure change in the both groups. In the bolus group, we observed significant fall in blood pressure at 4 min, 6 min, 8 min, 10 min, 12 min, 14 min, 120 min & 150 min ($p<0.05$). In the fractional

group, we observed significant fall in mean arterial pressure at 2min, 18 min, 60 min & 90 min ($p<0.05$). In intergroup comparison, mean arterial pressure was on the higher side in Group F at all time intervals compared to Group B, which was statistically highly significant (<0.001). (Table 5)

Table 5: Changes in mean arterial pressure in both the groups

Mean Arterial Pressure	Bolus group	p-value (Bolus intragroup)	Fractional group	p-value (Fractional intragroup)	p-value (intergroup)
0 minute	93.4 ± 7.15		92.9 ± 7.08		0.7865
2 minutes	87.87± 6.38	0.0881	91.9 ± 7.08	**0.0325**	**0.0241**
4 minutes	83.3 ± 6.84	**0.0195**	90.63 ± 7.72	0.1759	**0.0003**
6 minutes	78.8 ± 6.76	**0.017**	89.53 ± 8.03	0.1749	**0.0001**
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10 minutes	75.37 ± 5.88	**0.0448**	87.93 ± 8.46	0.1724	**0.0001**
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16 minutes	75.03 ± 5.28	0.0648	88.23 ± 7.56	0.0652	**0.0001**
18 minutes	75.47 ± 5.6	0.0549	87.9 ± 7.29	**0.0267**	**0.0001**
20 minutes	76.1 ± 4.38	0.1011	87.9 ± 6.56	0.066	**0.0001**
30 minutes	76.9 ± 5.31	0.0707	87.4 ± 6.39	0.0795	**0.0001**
60 minutes	77.37 ± 5.2	0.0771	89.23 ± 7.31	**0.0398**	**0.0001**
90 minutes	79.93 ±4.43	0.1108	88.86 ± 7.23	**0.0236**	**0.0001**
120 minutes	81.23 ± 6.29	**0.0449**	90 ± 8.26	0.246	**0.0001**
150 minutes	82 ± 7.69	**0.0301**	87.5 ± 9.62	0.2799	**0.0152**
180 minutes	80.25 ± 0.95	0.2805	82 ± 1.41	0.3054	**0.0001**
210 minutes	81		83		

In our study, more number of patients suffered from episodes of hypotension in Group B compared to Group F. Total 10 patients in Group B and only 2 patients in Group F required ephedrine for hypotension, which was statistically significant ($p<0.05$). (Table 6)

Table 6: Requirement of Ephedrine in both the groups

Parameter	Group B	Group F	p-value	Significance
Total patients required ephedrine	10	2	**0.0098**	Significant

Discussion

For spinal anesthesia commonly used local anaesthtic is Bupivacaine. Hyperbaric bupivacaine is most commonly used due to its long duration of action. Dose of hyperbaric bupivacaine depends on weight and height of patient for its density and duration of spinal block. Achieving the necessary sensory level for surgery corresponds inversely with weight and incrementally with height. [10] Spinal anaesthesia has limited duration of action. To overcome these limitations, different adjuvants to spinal anaesthesia are used. Dexmedetomidine, buprenorphine, tramadol and clonidine, etc are some of adjuvants that used to extend duration of spinal block and also prolonging duration of postoperative analgesia. But with these adjuvant drugs there are associated side effects to these drugs. [12,13]

Modifying the technique of injection of local anaesthetic drug in spinal anaesthesia can be used to prevent hypotension after spinal anaesthesia and adjuvants related side effects. Various studies have been undertaken to evaluate effect of fractionating the dose of drug given in

spinal anesthesia for lower segment cesarean section and lower limb surgeries. Fractionation of local anaesthetic means some volume of drug given and after fixed time gap another remaining volume of drug given. [1,14] Our study was done to compare Bolus Dose Versus Fractional Dose Of Hyperbaric Bupivacaine In Spinal Anaesthesia Among Adult Patients Undergoing Vaginal Hysterectomy in 60 patients of ASA class I, II & III posted for elective vaginal hysterectomy.

In our study, the mean age, weight, height and body mass index of patients were comparable between the two groups ($p > 0.05$). The total duration of sensory block was defined as time from intrathecal injection of local anaesthetic to L1 segment regression. In our study, mean duration of sensory block was longer in group F (257 ± 24.19 min) as compared to group B (237.5 ± 29.44 min), which was statistically significant($p<0.05$). Badheka JP et al [11] also observed that total duration of sensory block was longer in fractional group (236 ± 42 min) compared to bolus group (161 ± 29min) ($p<0.001$). Similar results were found by Srivastava N et al [12], Derakhshan P et al [13], Hossain MM et al [14], and Sowmya NL et al [15] in their respective studies.

The total duration of motor block was defined as time from intrathecal administration of local anaesthetic to achievement of modified Broamge scale 0. In our study, mean duration of total motor block was longer in group F (279.67 ± 27.69 min) compared to group B (260.83 ± 31.38 min), which was statistically significant ($p<0.05$). These results are in accordance with the results by Badheka JP et al [11], Srivastava N et al [12], Hossain MM et al[14], and Sowmya NL et al [15]. However, our results are in contrast to the results by Derakhshan P et al [13] and Kumar VS et al [16] who observed that total duration of motor block was comparable between bolus and fractional group.

Duration of analgesia was defined as time from achieve T10 sensory level to 1st requirement of analgesia by patient (when VAS ≥ 4), We used Diclofenac sodium 75 mg IM/IV as a rescue analgesic. In our study, mean duration of analgesia was longer in group F (335.17 ± 32.07 min) compared to group B (296.67 ± 47.28 min), which was statistically highly significant($p<0.001$). Badheka JP et al [11], in their study observed that total duration analgesia was longer in fractional group (273 ± 20 min) compared to bolus group (231 ± 32 min) ($p<0.001$). Similar results were found in the studies done by Srivastava N et al[12], Hossain MM et al[14], Sowmya NL et al [15] and Kumar VS et al [16].

In the bolus group, we observed that mean pulse rate was comparable at all time interval except only at 8 minute it shows significant rise ($p<0.05$). which is suggestive reflex tachycardia in response to fall in blood pressure. In the fractional group, we observed that mean pulse rate was comparable at all time interval except at 30 min, 60 min & 150 min it shows significant decrease in pulse rate ($p<0.05$). In intergroup comparison, we observed that pulse rate remained stable throughout the surgery, only at 16 minute & 180 minutes in Group B pulse rate was statistically significant than Group F($p<0.05$). At 16 minutes higher pulse rate is suggestive of reflex tachycardia in response to hypotension by sympathetic blockade in Group B. In both groups, changes in pulse rate was within 20% of baseline pulse rate in all patients, so that was clinically insignificant & no treatment required. Sowmya NL et al [15] and Kumar VS et al [16] have observed that mean pulse rate was comparable between bolus and fractional group throughout study period ($p>0.05$). Derakhshan P et al [13] observed that mean pulse rate was higher in bolus group compared to fractional group($p<0.05$).

In the bolus group, we observed significant fall in mean arterial blood pressure at 2 min, 4 min, 6 min, 8 min, 10 min, 12 min, 14 min, 120 min & 150 min ($p<0.05$). In the fractional group, we observed significant fall in mean arterial pressure at 2min, 18 min, 60 min & 90 min ($p<0.05$). In intergroup, we observed mean arterial pressure was on the higher side in Group F at all time intervals compared to Group B, which was statistically highly significant (<0.001). Main reason for hypotension after spinal anaesthesia is rapidly developing sympathetic block before the adaptation of cardiovascular system. When we inject drug as bolus, rapidly developing sympathetic block lead to hypotension. In that case, spread of local anaesthetic is fast, not giving time to cardiovascular system for adaptation. When we inject drug as fractional technique, hyperbaric drug tries to settle more in lower level, that gives time to cardiovascular system for adaptation to sympathetic block. Hossain MM et al [14] and Nugroho AM et al [17] have observed that mean arterial pressure was comparable between bolus and fractional group throughout the study period ($p>0.05$).

We used Ephedrine for the treatment of hypotension. In bolus group, majority of patients achieved T6 sensory level, whereas in fractional group, majority of patients achieved T8 sensory level. So, more chances of hypotension in bolus group due to higher level of sympathetic block. More number of patients suffered from episode of hypotension in Group B compared to Group F. Total 10 patients (out of 30) in Group B and only 2 patients (out of 30) Group F required ephedrine for hypotension, which was statistically significant ($p<0.05$). Srivastava N et al [12] observed that 10 patients (out of 30) in bolus group and only 5 patients (out of 30) in fractional group required vasopressor($p<0.05$). Similar observations were made by Badheka JP et al[11], Hossain MM et al[14], Sowmya NL et al [15] and Kumar VS et al [16]. However, Derakhshan P et al [13] and Nugroho AM et al [17] observed that total ephedrine dose given was not significantly different between the two groups ($p>0.05$). There were no any postoperative complications like nausea, tachyardia, bradycardia, hypotension or hypoxia.

Conclusion

In patients undergoing vaginal hysterectomy, fractional dosage of spinal anaesthesia offers greater haemodynamic stability and a longer duration of analgesia than a bolus dose with comparable quality of sensory and motor block.

References

1. Sonavia VJ, Singh KK. A comparative study of intrathecal 0.5% isobaric levobupivacaine with 0.5% hyperbaric bupivacaine for vaginal hysterectomy. Int J Med Sci Public Health 2017; 6(11):1558-1561.
2. Basnet U. A Comparative Study of Intrathecal Hyperbaric Bupivacaine with or without Morphinr For Post-Operative Analgesia In Hysterectomy. NJOG 2018; 24(!):20-3.
3. Bernards CM Epidural and spinal anaesthesia. 6th ed. Chapter 37. In: Clinical Anaesthesia, Barash PG, Cullin BF, Stoelting RK, eds. Philadelphia: Lippincott Williams & Wilkins; 2009. pp. 928-37.
4. Arun R and Girish Kumar J. Comparison of Hyperbaric and Isobaric Solution of Bupivacaine in Spinal Anaesthesia. Acta Scientific Neurology. 2021;4(8): 60-67.
5. Choudhary AK, Prasad MK, Keshri R, Choudhary S. Effects of IV dexmedetomidine as a pre-medication on clinical profile of bupivacaine spinal anaesthesia in lower abdominal surgeries: a randomized clinical study. Pan Afr Med J. 2022 Jan 26; 41:74.
6. Collin Pinnock, Ted Lin, Tim Smith, Fundamentals of Anaesthesia 2ndedition, Greenwich Medical Media Ltd. 2003:129-130. 47.Collins Vincent

J: Spinal anesthesia- Principles. Principles of Anesthesiology, 3rd edition. Edited by Collins Vincent J. USA, Lea and Febiger. 1993;1464-92.
7. Comparison Of Fractionated Dose Versus Bolus Dose Injection of Heavy Bupivacaine with Fentanyl In Spinal Anaesthesia For Patients Undergoing Elective Caesarean Section: One Year Randomized Clinical Trial, European Journal of Molecular & Clinical Medicine 2022; 9(4):3324-3330.
8. Brown DL. Regional anaesthesia and analgesia. Philadelphia: WB Saunders Company. 1996;1.
9. Bromage PR, Burfoot MF, Crowell DE, Pettigrew RT. Quality of epidural blockade (I) influence of physical factors. Br J Anaesth. 1964;36: 342-52.
10. Lee JA, Atkinson RS, WattMJ Anatomy. Chapter 5 in Sir Robert Macintosh's lumbar puncture and spinal analgesia- Intradural and extradural, Fifth edition, Churchill livingstone, 1985; 118-148.
11. Badheka JP, Oza VP, Vyas A, Baria D, Nehra P, Babu T. Comparison of fractionated dose versus bolus dose injection in spinal anaesthesia for patients undergoing elective caesarean section: A randomised, double-blind study. Indian J Anaesth. 2017 Jan; 61(1):55-60.
12. Srivastava N, Ahluwalia P, Jheetay G S, Singh G, Bolus dose versus fractionated dose injection of hyperbaric bupivacaine in spinal anaesthesia among adult patients undergoing lower limb surgery: A prospective study. Indian J Clin Anaesth. 2020;7(2):238-244.
13. Derakhshan P, FaizSHR, Rahimzadeh P, Salehi R, Khaef G. A Comparison of the Effect of Fractionated and Bolus Dose Injection on Spinal Anesthesia for Lower Limb Surgery: A Randomized Clinical Trial. Anesth Pain Med. 2020 Aug 23;10(5): e1022 28.
14. Hossain M. M., Biswas B., Mohanta P. K., Hassan M. M., Basu P., & Islam F. Comparison between fractionated dose with bolus dose in Spinal Anaesthesia for haemodynamic stability and duration of analgesia in patients undergoing elective Lower Segment Caesarean Section (LSCS). Mediscope, 2020;7(2); 95–102.
15. N. Lakshmi Sowmya, M. V. Rama Rao, Anand Ram, Comparison of Fractionated versus Bolus Dose Injection of Drug in Spinal Anaesthesia for Lower Limb Surgeries, International Journal of Science and Research (IJSR). January 2020; 9(1): 1729-1733.
16. Vanagondi Siva Kumar, Manjula V Ramsali, VankayapatiSaradaDevietal. Fractionated Dose Vs conventional Method of Drug Administrationin Spinal Anesthesia for Pregnant Women Undergoing Cesarean Section: A Comparative Study. Indian J Anesth Analg.2019;6(6Part-II):2206-2211.
17. Nugroho AM, Sugiarto A, Chandra S, Lembahmanah L, Septica RI, Yuneva A. A Comparative Study of Fractionated Versus Single Dose Injection for Spinal Anesthesia During Cesarean Section in Patients with Pregnancy-Induced Hypertension. Anesth Pain Med. 2019 Feb 6;9(1): e85115.