

## Comparison of intrathecal levobupivacaine and levobupivacaine with fentanyl in caesarean section - a randomised trial

Selvakumar Rajasekaran<sup>1,\*</sup>, Suresh Murugaiah<sup>2</sup>, Asha Anandan<sup>3</sup>, Ayshvarya Ramalingam<sup>4</sup>

<sup>1</sup>Professor & HOD, <sup>2</sup>Associate Professor, <sup>3</sup>Assistant Professor, <sup>4</sup>Senior Resident, Dept. of Anaesthesia, KAPV Govt. Medical College, Trichy

**\*Corresponding Author:**

Email: drselvakumar@rediffmail.com

### Abstract

**Introduction:** Levobupivacaine is less cardio toxic and has a longer duration of analgesia compared to bupivacaine. There are limited studies comparing the effects of addition of fentanyl with levobupivacaine. To compare the characteristics of sensory and motor blockade, associated haemodynamic changes and side effects following intrathecal levobupivacaine and levobupivacaine with fentanyl in patients undergoing elective caesarean section.

**Materials and Method:** A prospective, double blind, randomised control study. 80 patients belonging to age group 18 to 35 years, ASA I & II posted for elective LSCS in a tertiary care centre were randomly allocated into two groups, Group L (n=40) received injection levobupivacaine 0.5%, Group LF (n=40) received 0.5% levobupivacaine with 15 mcg fentanyl. Intra-operative and post-operative haemodynamic parameters, sensory and motor block characteristics along with incidence of side effects in the two groups were noted. The observed data's were analysed by SPSS version 21.0 software

**Result:** The haemodynamic parameters were comparable in both the groups. The mean onset time of sensory block in group L was 4.38±.490 mins and 2.28±.452 mins in group LF. Effective analgesia period is longer in group LF with a mean value of 179.90±6.953 mins, when compared to 132.70±8.058 mins in Group L. The mean onset time for motor block was 5.75±0.840 mins in group L while in group LF it was 2.70±0.464. Complete reversal of motor blockade occurred in 152.75 minutes in group L while it took 116.33 minutes in group LF. APGAR scores were comparable in both the groups. The incidence of nausea and vomiting was found to be 20% in Group LF and only 7.5% in Group L. 15% of patients among group LF complained of pruritus while there was no incidence of pruritus among patients in group L

**Conclusion:** Addition of intrathecal fentanyl 15µg to 10 mg of 0.5% levobupivacaine in caesarean section shortens the onset of sensory and motor block, prolongs the duration of postoperative analgesia with rapid motor recovery with increased incidence of pruritus, nausea and vomiting.

**Keywords:** Levobupivacaine, Fentanyl, Spinal anaesthesia, Caesarean section

**Received:** 8<sup>th</sup> January, 2017

**Accepted:** 4<sup>th</sup> February, 2017

### Introduction

Spinal anaesthesia is the most commonly performed anaesthetic technique for caesarean section.<sup>(1)</sup> Levobupivacaine, an enantiomer of bupivacaine, being less cardiotoxic has a better safety profile over conventionally used bupivacaine.<sup>(2)</sup> Studies on use of intrathecal levobupivacaine have suggested extended duration of analgesia.<sup>(3)</sup>

Spinal adjuvants have been demonstrated to improve the quality of spinal anaesthesia. Fentanyl has been proven to be a safe drug when administered intrathecally for caesarean section by several studies.<sup>(4)</sup> It has been shown to prolong the period of post-operative analgesia when administered with bupivacaine intrathecally for caesarean section.<sup>(5)</sup> This study aims to find out the impact of addition of fentanyl to levobupivacaine in subarachnoid block for LSCS.

### Materials and Method

This prospectively designed randomised controlled study was done after getting approval from Institutional

ethical committee. Period of study was from August 2015 to April 2016. 80 patients were included in the study, were randomly divided into two groups of 40 each. Sample size was calculated by using PSS software, assuming 80% power of study and p<0.05 as level of statistical significance.

Patients of age 18 to 35 years, ASA physical status 1 or 2, singleton pregnancy, term gestational age, scheduled to undergo elective caesarean section under spinal anaesthesia were included in the study. Patient's refusal, patients with body weight > 80kg, height <150cm, any history of allergy to drugs, maternal factors like coagulopathy, spinal disorders, uterine anomaly, IUGR (intrauterine growth retardation), intrauterine anomaly, Premature rupture of membranes were excluded from the study.

Group L (n=40) received 2.3ml of injectate consisting of 2ml of 0.5% Levobupivacaine combined with 0.3 ml of normal saline.<sup>(6,7,8)</sup> Group LF (n=40) received 2.3ml of injectate consisting of 2ml of 0.5% Levobupivacaine combined with 0.3ml (15mcg) of fentanyl.<sup>(9)</sup>

Groups	Volume	Specific gravity	Drugs
Group L	2.3ml	1.015	Levobupivacaine 10mg + 0.3ml NS
Group LF	2.3ml	1.015	Levobupivacaine 10mg + 0.3ml fentanyl

The study drug solution was prepared by the consultant who was not involved in the study. Both anaesthetist and patients were blinded to the study drug.

All patients subjected to the study fasted overnight, received anti-aspiration prophylaxis with oral ranitidine 150mg and metoclopramide 10mg night before surgery. In the preoperative room, intravenous access secured. Preloading was done with 15ml/kg of lactated ringer's solution for 15minutes. After arrival in the operating room, patient was connected to monitors like ECG, NIBP, SpO<sub>2</sub>. Baseline pulse rate, blood pressure, SpO<sub>2</sub> of the patient were noted.

Under sterile aseptic precaution, in the right lateral position, using either 25G or 26G Quincke's needle, by midline approach spinal anaesthesia was performed at L3-L4 intervertebral space. After completion of spinal injection, patient was turned to supine posture, a wedge was placed underneath the right buttock, and oxygen administered through facemask at 4-6L/min.

Zero time was the time of induction of spinal anaesthesia. Sensory block was assessed by pinprick using a small needle at mid axillary line every minute until it reached its maximum level. When the sensory block reached T6, surgery was allowed to proceed. Onset of sensory block was considered when the level of blockade reached T8. Motor block was assessed by modified bromage scale (Table 1). Onset of motor block was considered when Bromage grade 3 was reached. Maximum sensory block height reached, two segment regression time, time taken to regress to T12 dermatome, time taken for complete motor recovery (Bromage scale-0) were recorded.

**Table 1: Modified Bromage scale**

Bromage scale-0	no paralysis, able to flex hip/knees/ankle
Bromage scale- 1	able to move knees, unable to raise extended legs
Bromage scale- 2	able to flex ankles, unable to flex knees
Bromage scale- 3	unable to move any part of lower limb

Maternal pulse rate and blood pressure were recorded every 1 minute until baby delivery, every 5 minutes until the end of surgery, every 15minutes until the period of observation for sensory and motor block endpoints. In our study, hypotension was defined as decrease in systolic blood pressure to less than 90mmHg or 30% fall from baseline value and treated with IV ephedrine 6mg bolus. Maternal bradycardia was defined as pulse rate below 60/ minute, treated with inj. Atropine 0.3-0.6mg IV. Complications like nausea and vomiting, pruritus, respiratory depression were noted in both intraoperative and postoperative period. Respiratory depression was defined as respiratory rate of less than 10/minute.<sup>(10)</sup> Both mother and neonate were observed for 24 hours after the initiation of spinal anaesthesia for the complications mentioned above.

Effective analgesia is defined as the time period between induction of spinal anaesthesia and the first request for analgesia. Postoperative pain was assessed by visual analogue score using word scale (Table 2). The rescue analgesia used was injection Tramadol 100mg i.m. The study was concluded with administration of the first dose of rescue analgesic.

Neonatal assessment was done using APGAR scoring (Table 3) at 1st and 5th minute of delivery.

**Table 2: Visual analogue score**

Score 0	No pain
Score 1-2	Least pain
Score 3-4	Mild pain
Score 5-6	Moderate pain
Score 7-8	Severe pain
Score 9-10	Excruciating pain

**Table 3: APGAR score**

Apgar sign	0	1	2
Appearance (skin colour)	Cyanosis over entire body	Pink colour over body, hands and feet are bluish	Normal colour over the entire body (pink)
Heart rate(pulse)	Absent-no heart beat	<100 beats /min	>100 beats/min
Grimace(reflex irritability)	Absent –no response to stimulation	Only facial movements at stimulation	Pulls away, sneezes, coughs at stimulation

Activity (muscle tone)	Absent movements. Floppy tone.	Arms and leg flexed with little movements. Low tone.	Active flexor tone, spontaneous movements.
Respiration (rate and effort)	Absent-no breathing effort.	Slow, irregular breathing, weak cry.	Regular breathing, strong cry.

The observed data's were analyzed by SPSS version 21.0 software. The collected data were tabulated and expressed as mean, standard deviation, numbers and percentages. Continuous variables were compared with one way ANOVA. The comparison was done using chi-Square or Benfornoni test as appropriate value reported at the 95% confidence interval. P value <0.05 was considered as statistically significant.

## Results

Eighty patients were enrolled in the study during the period august 2015-april 2016. Demographic variables like age, weight, height and ASA status are comparable in both groups as seen in **Table 4**.

In comparing the haemodynamic changes between the two groups, both intraoperative and postoperative pulse rate, and mean arterial pressure are comparable and the difference is not statistically significant.

In comparing the spinal block characteristics, the results obtained are shown in **Table 5**. We observed a shorter onset time for sensory blockade in group LF. The mean onset time of sensory block in group L was 4.38±0.490 mins and 2.28±0.452 mins in group LF. The time taken for two segment regression of sensory

blockade is 78.55±13.399 minutes in group L and it is 95.60±6.559 minutes in group LF. In group L, majority of patients developed maximum sensory block height of T6, while in group LF majority of patients developed maximum sensory block height of T4 which is statistically significant.

Effective analgesia period is longer in group LF with a mean value of 179.90±6.953 mins, when compared to 132.70±8.058 mins in Group L as shown in **Table 6**.

In group L the mean onset time for motor block for grade 3 Bromage was 5.75±0.840 minutes while group LF it was 2.70±0.464, which is statistically significant (**Table 7**). Complete reversal of motor blockade occurred in 152.75 minutes in group L while it took only 116.33 minutes in group LF.

As seen in **Table 8**, neonatal assessment in the form of Apgar scoring done in both group L and LF were comparable with a score of more than 8. **Table 9** shows the incidence of side-effects, where the incidence of nausea and vomiting was found to be 20% in Group LF, higher than that in Group L with an incidence of 7.5%, though not statistically significant. 15% of patients among group LF complained of pruritus while there was no incidence of pruritus among patients in group L.

**Table 4: Demographic Distribution**

Demographic data	Mean	S.D	Statistical inference
<b>Age (years)</b>			
Group L (n=40)	24.95	2.124	P=1.000 Not Significant
Group LF (n=40)	24.95	2.025	
<b>Weight(kg)</b>			
Group L (n=40)	64.18	5.638	P=0.411 Not Significant
Group LF (n=40)	65.08	3.964	
<b>Height (cm)</b>			
Group L (n=40)	155.88	2.662	P=0.832 Not Significant
Group LF (n=40)	156.00	2.602	
<b>ASA Status</b>			
	<b>ASA I</b>	<b>ASA II</b>	
Group L	23	17	P= 0.653 Not Significant
Group LF	21	19	

**Table 5: Characteristics of Sensory blockade**

Sensory block	Mean	SD	Statistical inference
<b>Onset time (in minutes)</b>			
Group L (n=40)	4.38	0.49	P = .000 Significant
Group LF (n=40)	2.28	0.45	
<b>2 segment regression (in minutes)</b>			
Group L (n=40)	78.55	13.399	P = .000 Significant
Group LF (n=40)	95.60	6.559	
<b>Regression to T12 (in minutes)</b>			

Group L (n=40)	129.23	11.617	P= .000
Group LF (n=40)	176.50	11.052	Significant

**Table 6: Duration of effective analgesia**

Time for Rescue Analgesia (in minutes)	Mean	SD	P value
Group L (n=40)	132.70	8.058	.000
Group LF (n=40)	179.90	6.953	Significant

**Table 7: Motor onset and recovery time**

Motor Onset (minutes)	Mean	SD	Statistical inference
Group L (n=40)	5.75	.840	P = .000 Significant
Group LF (n=40)	2.70	.464	
Motor Recovery (minutes)	Mean	SD	Statistical inference
Group L (n=40)	152.75	9.407	P = .000 Significant
Group LF (n=40)	116.33	4.543	

**Table 8: APGAR at 1 Minute and 5 Minute**

APGAR (1minute)	mean	SD	
Group L (n=40)	8.18	.385	P= 0.336
Group LF (n=40)	8.10	.304	Not Significant
APGAR (5minutes)			
Group L (n=40)	8.35	.483	P = 0.638
Group LF (n=40)	8.30	.464	Not Significant

**Table 9: Incidence of adverse effects**

Adverse effects	Group L n=40	Percentage	Group LF n=40	Percentage	Statistical inference
Nausea and Vomiting	3	7.50%	8	20.00%	P=0.105 Not significant
Pruritis	0	0	6	15.00%	P=0.011 Significant

## Discussion

Adequate pain relief following caesarean section promotes emotional bonding with the child, adequate breast feeding, reducing the risk of developing deep vein thrombosis and pulmonary thromboembolism.<sup>(11)</sup> Spinal adjuvants increases the duration of postoperative analgesia, reduces intraoperative side effects of local anaesthetics, lessens the duration of motor block promoting early ambulation.<sup>(5)</sup> Fentanyl, a synthetic opioid agonist, by acting on mu opioid receptors provides dense spinal blockade and local anaesthetic sparing effect. It can be used intrathecally in the range of 5 – 25 mcg.<sup>(12)</sup>

In our study, the addition of 15 mcg of fentanyl to levobupivacaine improves the onset and duration of sensory blockade.

In a study by **Joginder Pal et al**, where 100 patients posted for infraumbilical surgeries were divided into two groups, Group L and Group LF of 50 each. Group L received 2ml of 0.5% isobaric levobupivacaine and LF received it in addition to 25mcg of fentanyl.<sup>(13)</sup> The onset of sensory block (4.8+1.50 mins) was rapid in Group LF compared to Group L (7.6+ 1.46mins). The onset time for sensory blockade was 2.28±0.45 in group LF and 4.38±0.49 for Group L, in our study. The results are consistent with their study showing *faster onset of sensory blockade with addition of fentanyl*. The difference in onset times between the two studies in Group L and Group LF is probably because of the exclusion of pregnant patients in their study.

The effective analgesia period is longer in group LF with a mean value of 179.90±6.953 minutes, whereas it

is only  $132.70 \pm 8.058$  minutes in group L. Thus our study shows that **addition of fentanyl increases the duration of sensory blockade**. It is consistent with the results of the study by Joginder Pal, who observed a prolonged duration of analgesia in group LF ( $265.16 \pm 26.18$  min) in comparison to  $168.16 \pm 11.08$  min in group L.

The longer duration of analgesia ( $265.16 \pm 26.18$  min) in Group LF, observed in their study in comparison to  $179.90 \pm 6.953$  mins of analgesia observed in group LF in our study, is probably due to higher dose of fentanyl (25mcg) used in their study.

**Turkmen et al** compared the anaesthetic effects 7.5 mg of 0.5% bupivacaine and levobupivacaine, each combined with  $15 \mu\text{g}$  fentanyl in spinal anaesthesia for caesarean section.<sup>(14)</sup> The duration of analgesia was 118 minutes in levobupivacaine with fentanyl group. With a similar dose of fentanyl, in our study, a dose of 10mg of levobupivacaine provided analgesia for a period of  $179.90 \pm 6.953$  minutes. **Increasing the dose of levobupivacaine had increased the duration of postoperative analgesia.**

**Gulen guler et al** compared the block characters, side effects, hemodynamic changes in 60 pregnant women divided into two groups posted for elective caesarian section.<sup>(15)</sup> Group LF were given 10mg of 0.5% isobaric levobupivacaine with 15 mcg fentanyl and group BF received 10mg of 0.5% hyperbaric bupivacaine combined with  $15 \mu\text{g}$  fentanyl. In group LF, Sensory onset was  $2 \pm 0.37$  minutes, similar to that obtained in our study, which was  $2.28 \pm 0.452$  mins. The 2 segment regression time was  $71.43 \pm 12.96$  minutes in their study and  $95.60 \pm 6.559$  mins in our study. The time to regression to T12 was 150mins in their study and 176.50mins in ours. The onset time for motor block was  $4.1 \pm 0.88$  minutes in group LF, in their study and  $2.70 \pm 0.464$  minutes in our study. The regression time for motor blockade was  $99 \pm 9.13$  min similar to our study,  $116.33 \pm 4.543$  mins. Results of our study is comparable with the above study except for the faster onset of motor blockade in our study which may be due to widespread of local anaesthetic leading to lower density of local anaesthetic molecules per segment.

Caesarean section done under spinal anaesthesia requires a sensory block height of T5. Group L in our study showed a maximum sensory block level of T6 whereas a higher level of sensory block (T4) was achieved with LF group. Thus, **addition of fentanyl has led to higher level of sensory blockade compared to plain levobupivacaine.**

**Subasi et al** compared block characteristics and hemodynamic variables in 80 patients subjected to caesarean section under spinal anaesthesia, of 40 each.<sup>(16)</sup> Group BF received 7.5mg hyperbaric bupivacaine and group LF received 7.5mg levobupivacaine, both combined with  $25 \mu\text{g}$  fentanyl. Group LF in their study showed a block height of T2 – T4, consistent with the maximum block height of T4 observed in patients receiving levobupivacaine with fentanyl in our study.

In group L the mean onset time for motor block for grade 3 Bromage was  $5.75 \pm 0.840$  minutes while group LF showed earlier onset of motor blockade ( $2.70 \pm 0.464$  mins). Complete reversal of motor blockade occurred in 116.33 minutes in group LF while it took 152.75 minutes in group L. Hence our study shows **addition of fentanyl to levobupivacaine causes early onset and recovery of motor blockade.**

The maximum level of blockade is T4 in group LF, whereas it is only T6 in group L. This may lead to low concentration of levobupivacaine per segment in group LF than compared to group L and hence low density of motor block. Therefore during reversal, this could have attributed to rapid regression of motor block in group LF and hence rapid recovery of motor blockade.

**Prabha et al** compared the hemodynamic effects, sensory and motor block characteristics by administering 8.75mg of 0.5% bupivacaine and fentanyl  $12.5 \mu\text{g}$  intrathecally to group B and 8.75mg of 0.5% levobupivacaine with  $12.5 \mu\text{g}$  fentanyl to group L in 40 patients of 20 each for caesarian section.<sup>(17)</sup> Stable hemodynamics, prolonged sensory blockade are the features observed by the above study in Levobupivacaine + fentanyl group. Hence it is recommended by them for spinal anaesthesia in caesarean section. Time for complete motor recovery in Levobupivacaine + fentanyl group is observed to be  $109.50 \pm 16.37$  minutes. We have observed time for complete motor reversal as  $116.33 \pm 4.543$  minutes, which may be due to the higher dose of 10mg of 0.5% levobupivacaine with  $15 \mu\text{g}$  fentanyl used in our study.

In our study, the neonatal assessment with APGAR at 1<sup>st</sup> and 5<sup>th</sup> minute showed scores more than 8 in both the groups, showing that **addition of fentanyl to levobupivacaine did not cause any significant neonatal depression.**<sup>(18)</sup>

In our study, the incidence of nausea and vomiting was found to be higher in group LF with 20% having nausea and vomiting. Only 7.5% in group L had nausea and vomiting. This may be due to the effects of systemic absorption of fentanyl, which is known to cause nausea and vomiting.<sup>(19)</sup> So, addition of fentanyl to levobupivacaine increased the incidence of nausea and vomiting.

15% of patients among group LF complained of pruritus while there was no incidence of pruritus among patients in group L. Fentanyl, a synthetic opioid is known to produce side effects like pruritus.<sup>(19)</sup> So **adding fentanyl to levobupivacaine has caused incidence of pruritus** in group LF. This result is consistent with the results obtained in the study by **Joginder Pal et al**, who documented 8% incidence of pruritus in LF group.<sup>(11)</sup>

### Limitations of the study

The study was concluded with administration of the first dose of rescue analgesic in the post-operative period, hence the total opioid consumption in the post-operative period could not be studied in both the groups.

## Conclusion

Addition of intrathecal fentanyl 15µg to 10 mg of 0.5% levobupivacaine in caesarean section shortens the onset of sensory and motor block, prolongs the duration of postoperative analgesia with rapid motor recovery. Incidence of pruritus, nausea and vomiting were relatively high in levobupivacaine with fentanyl group, though not warranting any specific treatment. Apgar scoring of neonates were comparable in both groups and no adverse effects were noted among neonates in both groups.

## References

- Cousins M, Bridenbaugh P. Cousins and Bridenbaugh's neural blockade in clinical anesthesia and pain medicine. Philadelphia: Lippincott Williams & Wilkins; 2009. P. 549-50.
- Foster RH, Markham A. Levobupivacaine: a review of its pharmacology and use as a local anaesthetic. *Drugs*. 2000 Mar;59(3):551-79.
- D'Souza, A. D., Saldanha, N. M., Monteiro, A. D. & H, H. (2014) Comparison of Intrathecal Hyperbaric 0.5% Bupivacaine, Isobaric 0.5% Levobupivacaine and Isobaric 0.75% Ropivacaine for Lower Abdominal Surgeries. *International Journal of Health Sciences and Research (IJHSR)*, 4 (1), 22-29.
- Shahriari A, Khooshideh M. Intrathecal fentanyl added to lidocaine for Cesarean delivery under spinal anesthesia--a randomised clinical trial. *Middle East J Anaesthesiol*. 2007 Jun;19(2):397-406.
- B.N. Biswas, Rudra A, Bose BK, Nath S, Chakrabarty S, Bhattacharjee S. Intrathecal fentanyl with hyperbaric bupivacaine improves analgesia during cesarean delivery and in early postoperative period. *Indian J Anaesth* 2002; 46(6):469-472.
- Chakraborty S, Chakrabarti J, Bhattacharya D. Intrathecal tramadol added to bupivacaine as spinal anesthetic increases analgesic effect of the spinal blockade after major gynecological surgeries. *Indian Journal of Pharmacology*. 2008;40(4):180-182.
- Nayagam HA, Singh N R, Singh H S. A prospective randomised double blind study of intrathecal fentanyl and dexmedetomidine added to low dose bupivacaine for spinal anesthesia for lower abdominal surgeries. *Indian J Anaesth* 2014;58:430-5.
- Kim SY, Cho JE, Hong JY, Koo BN, Kim JM, Kil HK. Comparison of intrathecal fentanyl and sufentanil in low-dose dilute bupivacaine spinal anaesthesia for transurethral prostatectomy. *Br J Anaesth*. 2009 Nov;103(5):750-4.
- Y. Y. Lee, K. Muchhal, C. K. Chan, A. S. P. Cheung, Levobupivacaine and fentanyl for spinal anaesthesia: a randomized trial, *European Journal of Anaesthesiology* 2005;22:899-903.
- Gonzalez Cardenas Neonatal Respiratory Depression and Intrathecal Fentanyl. *Rev Colombian journal of Anesthesiology*. 2012;40(2):100-105.
- Minal Harde, Varsha Suryavanshi, Anjana Sahu, Sachin K Wagh. Comparative study of ropivacaine and bupivacaine in bilateral ilioinguinal and iliohypogastric nerve block for post caesarean section analgesia. *International Journal of Contemporary Medical Research* 2016;3(4):1167-1171.
- Alan C. Santos, MD, Brenda A. Bucklin, MD. Local Anesthetics and Opioids. David H. Chestnut editor. *Obstetric Anesthesia: Principles and Practice*. 4th edn. Philadelphia: Mosby Elsevier. 2009. P.270-71.
- Attri JP, Kaur G, Kaur S, Kaur R, Mohan B, Kashyap K. Comparison of levobupivacaine and levobupivacaine with fentanyl in infraumbilical surgeries under spinal anaesthesia. *Anesthesia, Essays and Researches*. 2015;9(2):178-184.
- Turkmen A, Moralar DG, Ali A, Altan A. Comparison of the anesthetic effects of intrathecal levobupivacaine + fentanyl and bupivacaine + fentanyl during caesarean section. *Middle East Journal of Anesthesiology*. 2012 Feb;21(4):577-82.
- Gulen Guler, Gokhan Cakir, Ayşe Ulgey, Fatih Ugur, Cihangir Bicer, Isın Gunes, Adem Boyaci. A Comparison of Spinal Anesthesia with Levobupivacaine and Hyperbaric Bupivacaine for Cesarean Sections: A Randomized Trial. *Open Journal of Anesthesiology*, 2012, 2, 84-89.
- Subaşı D, Ekinci O, Kuplay Y, Müftüoğlu T, Terzioğlu B. Comparison of intrathecal hyperbaric bupivacaine and levobupivacaine with fentanyl for caesarean section. *Göztepe Tıp Derg*. 2012;27:22-9.
- Prabha. P. Comparative study of Intrathecal Bupivacaine and Levobupivacaine with Fentanyl for caesarean section. *Scholars Journal of Applied Medical Sciences (SJAMS)* 2014,2(4B):1255-1259.
- Goyal A, Shankaranarayan P, Ganapathi P. A randomized clinical study comparing spinal anesthesia with isobaric levobupivacaine with fentanyl and hyperbaric bupivacaine with fentanyl in elective cesarean sections. *Anesthesia, Essays and Researches*. 2015;9(1):57-62.
- Gupta R, Verma R, Bogra J, Kohli M, Raman R and Kushwaha JK. A Comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to Bupivacaine. *J Anaesthesiol Clin Pharmacol*. 2011;27:339-43.