Section: Anaesthesiology

Original Research Article

A RANDOMISED CONTROLLED STUDY ON THE EFFICACY OF PREMIXED VS SEQUENTIAL ADMINISTRATION OF FENTANYL AND BUCIVACAINE IN SUBRACHNOID BLOCK FOR LOWER LIMB TIBULAR SURGERY.

Received : 10/05/2024
Received in revised form : 01/07/2024
Accepted : 15/07/2024

Keywords:
Fentanyl, Bucivacaine, Subrachnoid Block.

Corresponding Author:
Dr. Sagar Bavisetti,
Email: sagarbavisetti@yahoo.com

DOI: 10.47009/jamp.2024.6.4.23

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (4); 109-113

Sagar Bavisetti[1], Apeksha Patwa[2], Parvathy D[3], Dixita Vaghela[4], Sudarshan Yadav B V[5], Sapna Yadav[6]

[1]Junior Consultant, Department of Anaesthesiology, AIG Hospital, Hyderabad, India.
[2]Associate Professor, Department of Anaesthesiology, Government Medical College Baroda, India.
[3]Senior Resident, Department of Anaesthesiology, Sree Chitra Tirunal Institute of Medical Sciences, India.
[4]Senior Resident, Department of Anaesthesiology, Government Medical College Baroda, India.
[5]Senior Resident, Department of Anaesthesiology, ESIC model hospital, Peenya, India.
[6]Consultant, Department of Anaesthesiology, Hinduja hospital, Mumbai, India.

Abstract

Background: A randomised controlled trial was conducted to evaluate the effectiveness of premixed vs sequential administration of bupivacaine and fentanyl in subarachnoid block for lower limb tibial operations. The most typical usage of opioids is as adjuvants in subarachnoid blocks. The different block properties are influenced by the medicine and how it is administered. A comparison is made between sequential dosing in two separate syringes and intrathecal injection of premixed bupivacaine and fentanyl. **Materials and Methods:** A total of 100 patients were divided into two groups of 50 each at random: 0.5 ml (25 microgram) of fentanyl and premixed 0.5% heavy bupivacaine 2.5 ml (12.5 mg) were given to Group M (Mixed) in a single 5.0 ml syringe. Group S (Sequential) got 0.5 ml (25 microgram) of fentanyl in a 2.0 ml syringe and then 0.5% heavy bupivacaine 2.5 ml (12.5 mg) in a 5.0 ml syringe. In every instance that was handled, double blinding was guaranteed. Hemodynamic parameters were monitored, along with the beginning and length of sensory and motor blockage. Software called MedCalc was used to analyse the data. **Results:** Group S experienced a lower mean time for the onset of sensory and motor block ($P<0.001$). Group S experienced a longer sensory and motor block duration ($P<0.001$). Compared to group S, patients in group M had higher rates of hypotension ($P<0.05$). Group S had a longer total duration of effective analgesia ($P<0.001$) and required less rescue analgesia in a 24-hour period ($P<0.01$). **Conclusion:** Injecting fentanyl first, then hyperbaric bupivacaine, results in greater hemodynamic stability, a longer-lasting sensory and motor block, and a decreased requirement for rescue analgesia during a 24-hour period.

INTRODUCTION

The history of medical science has always been significantly impacted by anaesthesia and its advancements. The term "pain" comes from the Latin "Poena," which means anguish. Merokey describes it as a "disgusting sensory and emotional experience connected to actual or potential tissue damage." One of the most often used anaesthetic techniques for lower limb and lower abdomen procedures is spinal anaesthesia, which was administered for the first time by August Bier in 1898. This is because it has well-known benefits like —

1. Maintenance of awareness
2. Easy to understand and execute
3. Sufficient anaesthesia for surgery
4. Very little alteration to blood biochemistry
5. Reduced haemorrhaging
6. Preventing general anesthesia-related problems

While there are benefits to spinal anaesthesia, there are also drawbacks, including bradycardia, hypotension, nausea, vomiting, and shivering. A local anaesthetic agent plus a neuraxial adjuvant can be used to lower the dosage of the local anaesthetic medicine, which will lessen the adverse effects of traditional spinal anaesthesia. The selection of the

ISSN (O): 2687-5365; ISSN (P): 2753-6556

local anaesthetic (LA) used in SAB is determined by on the drug's pharmacologic characteristics. Bupivacaine, levobupivacaine, and lignocaine hydrochloride are examples of commonly used local anaesthetics. The reason hyperbaric bupivacaine is most frequently used is because it provides a more predictable block and acts for a longer period of time than other local anaesthetics.

Adjuvants are applied one more time. Adjuvants are medications that, when taken along with other medications, boost their potency or efficacy. Adjuvants that are neuraxial in nature are used to enhance or extend analgesia while reducing the side effects that might arise from using large amounts of a single local anaesthetic. Neuraxial adjuvants are used not only for dosage sparing but also to improve the quality and duration of neural blockade, as well as to accelerate the start of neural blockade (lower latency). Opioids, vasoconstrictors, agonists of alpha-2 adrenoceptors, cholinergic agonists, N-methyl-d-aspartate (NMDA) antagonists, and agonists of γ-aminobutyric acid (GABA) receptors are examples of neuraxial adjuvants. Hindle A. and others (2008)

Intrathecal opioids are the most often utilised adjuvants among those listed above because they work well in conjunction with local anaesthetics. Various opioids, including as fentanyl, sufentanil, pethidine, and morphine, are used. When compared to other opioids like pethidine and morphine, intrathecal fentanyl is less likely to cause respiratory depression and reduces visceral and somatic pain while also improving the quality of block, lowering pain scores, and reducing the need for analgesics during the postoperative phase. When opioids and hyperbaric bupivacaine are mixed, the density of the hyperbaric solution changes, which impacts the drug's spread in the intrathecal region. In 2010, Atalay C. et al.

MATERIALS AND METHODS

The current study was conducted at the Department of Anaesthesiology at the Govt. Medical College and S.S.G. Hospital, Baroda, between May 2021 and October 2021, with approval from the institute's Ethical Research Committee. One hundred ASA I, II, and III patients, ranging in age from eighteen to sixty years, were planned for lower limb tibial operations. This was a double-blind, randomised clinical trial that was conducted in the following manner.

Inclusion Criteria

1. Age Group – 18 to 60 years of age
2. Either Gender
3. ASA – I/II/III
4. Lower limb Tibial surgeries like Tibia Interlock, Tibia Plating, Tibia external fixator, Tibia Implant Extraction, etc.

Exclusion Criteria

1. Patients with absolute and relative contraindications to spinal anaesthesia (patient refusal, local skin infection, vertebral column abnormalities, bleeding disorders, thyroid disorders, cardiopulmonary disease, neuropathies)
2. Patients with allergy to local anaesthetics
3. Pregnant and lactating females.

RESULTS

The mean age of patients in Group M was 36.94 ± 12.45 years and in Group S was 37.74 ± 12.08 years. There were 37 ASA class I, 10 ASA class II and 3 ASA class III patients in Group M as compared to 33 ASA class I, 9 ASA class II and 8 ASA class III patients in Group S. Mean duration of surgery in Group M was 92.1±39.34 minutes and 96±48.33 minutes in Group S. Thus, this table shows that both groups were comparable with respect to age, gender, ASA grading and mean duration of surgery (p>0.05).. [Table 1]

The baseline mean pulse rate in group M was 85.88 ± 10.65 per minute and 85.5 ± 12.49 per minute in group S. The mean systolic blood pressure was 131.52±14.86 mm Hg in Group M and 129.4 ± 15.2 mm Hg in Group S (Table 6). The mean diastolic blood pressure was 81.72 ± 8.09 mm Hg in Group M and 81.12 ± 7.77 mm Hg in Group S (table 7). Mean oxygen saturation was 98.64±0.56 in Group M and 98.74±0.48 in Group S. From this data it was observed that baseline haemodynamic parameters were comparable in both groups. [Table 2]

The above table shows assessment of sensory block after spinal anaesthesia. The mean time for onset of sensory block at L1 level was 117.38 ± 12.91 seconds in Group M and 101.96 ± 13.79 seconds in Group S. The difference between the mean time is statistically significant between group S when compared to group M. In majority of cases (68%), peak sensory level achieved T12 while 20% of patients achieved T8 and 12% achieved T10 in Group M. In Group S, majority of patients (66%) achieved T12 level, 18% achieved T8 level and 16% achieved T10 level. Time to achieve peak sensory level was 132.14 ± 12.94 seconds in Group M and 118.12 ± 15.36 seconds in Group S. Time taken to achieve peak sensory level was statistically significant in group S when compared with group M. The mean time taken for two segment dermatomal regression was 81.3± 5.01 minutes in Group M and 97.08 ± 5.30 minutes in Group S. The time taken for two segment dermatomal regression was statistically significant in group S when compared with group M. [Table 3]

This table shows characteristics of motor blockade after giving spinal anaesthesia. The mean onset time for motor block was 211.9 ± 23.14 seconds in Group M and 192.5 ± 25.75 seconds in Group S. The difference between the mean times are statistically significant in group S when compared to group M.Time to attain maximum Bromage grade 3 was 7.67 ± 0.88 minutes in Group M and 6.93 ± 1.15 minutes in Group S. Time to attain maximum

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Bromage score was statistically significant in Group S compared with group M. The mean duration of motor block was 174.46 ± 13.57 minutes in Group M and 228.6 ± 22.03 minutes in Group S. The mean duration of motor block was considerably lower in Group M when compared to group S and is also statistically significant. [Table 4]

The table 5 shows the changes in mean pulse rate after giving spinal anaesthesia. There was no statistically significant difference between two groups during intra or postoperative period. On intra and intergroup comparison the difference was statistically not significant (p>0.05). [Table 5]

Table 1: Demographic Data

GROUP	GROUP M	GROUP S	P VALUE
Age in years (Mean ± SD)	36.94 ± 12.45	37.74 ± 12.08	p>0.05
Gender (male:female)	30:20	32:18	
ASA grade (I:II:III)	37:10:03	33:09:08	
Mean duration of surgery (minutes)	92.1±39.34	96±48.33	p>0.05

Table 2: Mean Preoperative Hemodynamic

PARAMETERS	GROUP M	GROUP S	P VALUE
PULSE RATE/MINUTE (MEAN±SD)	85.88 ± 10.65	85.5 ± 12.49	p>0.05
SYSTOLIC BP(mm hg) (MEAN±SD)	131.52±14.86	129.4±15.2	p>0.05
DIASTOLIC BP(mm hg) (MEAN±SD)	81.72 ± 8.09	81.12 ± 7.77	p>0.05
SpO2% (MEAN±SD)	98.64±0.56	98.74±0.48	p>0.05

Table 3: Assessment of Sensory Block

SR.NO	PARAMETER	GROUP M (Mean±SD)	GROUP S (Mean±SD)	P VALUE
1	Onset of sensory block at L1 (Secs)	117.38 ± 2.91	101.96 ± 13.79	P<0.001
2	Highest sensory level achieved			
	T8 level	10(20%)	9(18%)	
	T10 level	6(12%)	8(16%)	
	T12 level	34(68%)	33(66%)	
3	Time to achieve highest sensory level (Secs)	132.14 ± 12.94	118.12 ± 15.36	P<0.001
4	Time of two segment regression from highest level of block (mins)	81.3 ± 5.01	97.08 ± 5.30	P<0.001

Table 4: Assessment of Motor Block

SR NO	PARAMETER	GROUP M (Mean±SD)	GROUP S (Mean±SD)	P VALUE
1	Onset of motor blockade(seconds)	211.9 ± 23.14	192.5 ± 25.75	P<0.001
2	Time to attain maximum motor block (minutes)	7.67 ± 0.88	6.93 ± 1.15	P<0.001
3	Duration of motor block (minutes)	174.46 ± 13.57	228.6 ± 22.03	P<0.001

Table 5: Changes in Mean Pulse Rate

TIME	GROUP M		GROUP S		P value (Inter group)
	PULSE/ MINUTE (Mean +SD)	Intra group p value	PULSE/ MINUTE (Mean +SD)	Intra group p value	
PRE – OPERATIVE	85.88 ± 10.65		85.50 ± 12.49		p>0.05
1 MIN	87.28 ± 11.87	p>0.05	87.88 ± 12.60	p>0.05	p>0.05
3MIN	86.44 ± 12.95	p>0.05	87.28 ± 13.67	p>0.05	p>0.05
5 MIN	86.92 ± 11.63	p>0.05	88.28 ± 12.73	p>0.05	p>0.05
10 MIN	85.88 ± 10.88	p>0.05	86.72 ± 11.66	p>0.05	p>0.05
15 MIN	84.04 ± 9.40	p>0.05	85.06 ± 10.69	p>0.05	p>0.05
30 MIN	84.88 ± 9.45	P>0.05	85.98 ± 9.89	P>0.05	P>0.05

Table 6: Changes in Systolic Blood Pressure

TIME	GROUP M		GROUP S		P value (Inter group)
	mmHg (Mean +SD)	Intra group p value	mmHg (Mean +SD)	Intra group p value	
PRE – OPERATIVE	131.52 ± 14.86		129.4 ± 15.28		p>0.05
1 MIN	132 ± 13.32	p>0.05	131.04 ± 13.35	p>0.05	p>0.05
3MIN	126.32 ± 12.69	p>0.05	129.48 ± 13.19	p>0.05	p>0.05
5 MIN	123.04 ± 12.13	p>0.05	128.56 ± 13.90	p>0.05	P<0.05
10 MIN	119.80 ± 11.81	p>0.05	124.76 ± 13.17	p>0.05	P<0.05
15 MIN	117.48 ± 11.00	p>0.05	124.16 ± 12.58	p>0.05	P<0.05
30 MIN	117.04 ± 11.81	p>0.05	122.24 ± 1.29	p>0.05	P<0.05

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Table 7: Changes in Diastolic Blood Pressure

TIME	GROUP M		GROUP S		P value (Inter group)
	mmHg (Mean +SD)	Intra group p value	mmHg (Mean +SD)	Intra group p value	
PRE – OPERATIVE	81.72 ± 8.09		81.12 ± 7.77		p>0.05
1 MIN	81.68 ± 7.64	p>0.05	82.28 ± 7.40	p>0.05	p>0.05
3MIN	77.24 ± 7.51	p>0.05	80.60 ± 6.88	p>0.05	p>0.05
5 MIN	75.12 ± 7.19	p>0.05	79.60 ± 6.90	p>0.05	P<0.05
10 MIN	73.24 ± 7.03	p>0.05	77.68 ± 7.12	p>0.05	P<0.05
15 MIN	71.88 ± 7.43	p>0.05	76.92 ± 6.49	p>0.05	P<0.05
30 MIN	71.32 ± 6.52	p>0.05	75.72 ± 6.85	p>0.05	P<0.05

DISCUSSION

Since a long time ago, central neuraxial blockade in the form of subarachnoid blocks has been effectively used all over the world. For procedures on the lower abdomen and lower limbs, spinal anaesthesia is the preferred anaesthetic method. Although spinal anaesthesia provides many benefits, it also has drawbacks, including hypotension, bradycardia, nausea, vomiting, and shivering. These adverse effects can be minimised by lowering the dosage of the local anaesthetic and by using other administration methods, such as sequential approach. Bupivacaine is one of the most often utilised local anaesthetics in spinal anaesthesia for tibial procedures on the lower leg. A very brief post-operative analgesia is a drawback of utilising Bupivacaine alone for spinal anaesthesia. The effects of a local anaesthetic are enhanced and prolonged with the application of neuraxial adjuvants. Of the several adjuvants, the most often used opioid is fentanyl. It is a very strong lipophilic opioid that attaches to spinal cord dorsal horn receptors quickly because of its high lipid solubility. By strengthening sensory and motor blockage and extending the duration of action without causing hemodynamic instability, it enhances the quality of spinal anaesthesia. The sequential strategy of intrathecal block administration enhances the quality of both motor and sensory features. When opioids and hyperbaric bupivacaine are mixed, the density of the hyperbaric solution changes, which impacts the drug's spread in the intrathecal region. Normal human CSF has a mean specific gravity of 1.00059. The specific gravity of a solution is determined by dividing its density by the water. The solution is referred to as "isobaric" if this ratio is 1; "hyperbaric" if it is larger than 1; and "hypobaric" if it is less than 1. Whereas a hypobaric solution gravitates towards the highest position of the spinal cord, a hyperbaric solution tends to gravitate towards the lowest place. Injection Fentanyl has a baricity of 1.000 whereas Injection Hyperbaric Bupivacaine has a baricity of 1.032. Baricity of the fluid after fentanyl is added to the same heavy-duty Bupivacaine syringe is 1.026. (Densitometer, Govt. Food and Drugs Lab, Vadodara)


Hyperbaric Bupivacaine – **1.032**


Fentanyl – **1.000**


Fentanyl + Injection hyperbaric Bupivacaine (premixed) – **1.026**

When fentanyl and bupivacaine are combined, the potency of the fentanyl is diluted and less receptor occupancy is observed, producing less effect; however, when fentanyl is administered separately, it mixes freely with the CSF and has more cephalad spread because the baricity of both fluids is similar and the difference between their baricity is less than 0.0006. As a result, the sensory block characteristics, such as onset, time to reach the highest sensory level, and two segment regression, are significantly improved in the sequential group. Intrathecal fentanyl's antinociceptive action involves both spinal and supraspinal opioid receptors. When injectable fentanyl is combined with injectable hyperbaric bupivacaine, the drug's characteristics change; it binds to spinal cord receptors and has less supraspinal binding, which lessens its analgesic effect.

Because the premixed solution is less viscous and spreads more readily in subarachnoid space while the hyperbaric drug, which is more viscous, when administered in intrathecal space is less influenced by gravity, the hemodynamic profile of the patients in the sequential group was significantly better. Bupivacaine is injected individually in sequential group, and its gravity-dependent distribution postpones the onset of sympathetic inhibition, providing more time for compensatory mechanisms to avert hypotension. According to studies by Malhotra et al. (2020), Anita K. et al. (2020), Takkillapati et al. (2020), and Noopur et al. (2016), there is more hemodynamic stability in the sequential group.

CONCLUSION

After conducting research, we have determined that patients having lower limb tibial operations will benefit from the sequential administration of injectable fentanyl at a dosage of 25ug (0.5ml) and injectable bupivacaine 0.5% (2.5ml). Sensory block onset was quicker. The time it took to reach the highest degree of sensory perception was shortened. Increase in the two segment regression time of the sensory block. The motor block had a quicker onset. A shorter time was required to obtain a higher

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Bromage score. Extends the time that a motor block effect lasts. Hypotension was shown to occur less frequently. Extends the duration of postoperatively effective analgesia. Cuts down on the need for post-operative rescue analgesia. Critical measures such as respiration rate, oxygen saturation, and pulse rate did not significantly vary in either group. No major problems were seen. We therefore draw the conclusion that administering fentanyl (25 ug) first and then bupivacaine (12.5 mg) in a sequential manner results in a quicker onset and longer duration of sensory and motor blockade. It also extends the duration of postoperative analgesia while maintaining hemodynamic stability and producing no appreciable side effects.

REFERENCES

1. Hindle A. Intrathecal opioids in the management of acute postoperative pain. Continuing Education in Anaesthesia, Critical Care & Pain. 2008; 8: 81-85
2. Atalay C, Aksoy M, Aksoy AN, Dogan N, Kursad H. Combining Intrathecal Bupivacaine and Meperidine during Caesarean Section to Prevent Spinal Anaesthesia induced Hypotension and Other Side-effects. J Int Med Res 2010; 38:1626-36.
3. Brull R, Macfarlane AJR, Chan VWS. Spinal, epidural and caudal anaesthesia. In: Miller RD, Cohen NH, Eriksson LI, Fleisher LA, Wiener-Kronish JP, editors. Miller's Anaesthesia. 8th ed. Canada: Elsevier-Saunders; 2015. p. 1684-720.
4. Malhotra A, Singh U, Singh MR, Sood D, Grewal A, Mahajan A. Efficacy of premixed versus succedent administration of fentanyl and bupivacaine in subarachnoid block for lower limb surgeries: A randomised control trial. Indian J Anaesth 2020; 64:175-9
5. Imbelloni LE, Moreira AD, Gaspar FC, Gouveia MA, Cordeiro JA. Assessment of the densities of local anesthetics and their combination with adjuvants: An experimental study. Rev Bras Anestesiol 2009; 59:154 65.
6. Rashiq S, Finucane TB. Nerve conduction and local anaesthetic action. In: Healy TEJ, Knight PR, editors. Wylie and Churchill Davidson: A Practice of Anaesthesia. 7th ed. Florida: Boca Raton; 2003. p. 267 76.
7. Anita Kanwariya et al., Intrathecal Administration of Fentanyl with Hyperbaric Bupivacaine. Journal of Clinical and Diagnostic Research. 2020 Jun, Vol-14(6): UC06-UC10
8. S. Desai, Y. Lim, C. H. Tan, A. T. H. Sia; A randomised controlled trial of hyperbaric bupivacaine with opioids, injected as either a mixture or sequentially, for spinal anaesthesia for caesarean section; Anaesth Intensive Care 2010; 38: 280-284
9. Soma ganesh raja, Gowri shankar sarate; Comparison of premixed vs sequential administration of fentanyl as an adjuvant to intrathecal hyperbaric bupivacaine in infra umbilical surgeries: a randomized controlled study; Indian Journal of Anaesthesia and Analgesia 2018; 5(5): 843-848
10. Kiruthika B, Cheran K,Suresh V. Comparison of intrathecal fentanyl with bupivacaine administered as a mixture & sequentially in lower abdominal surgeries. AsiaPacJ Res 2017; I: 52 7.
11. Joshi S, Tailor R, Pandya M, Vachhrajani P. Two syringe technique for spinal [17] anaesthesia in cesarean section: A study of a simple way to achieve more satisfactory block, less frequency of hypotension and prolong analgesia. International Journal of Science and Research (IJSR). 2018;7(1):1984-88.
12. Dr Noopur Bansal, DR Sushma D ladi Premixed versus sequential administration of intrathecal fentanyl and bupivacaine in elective cesarean section- a comparative study. Indian journal of applied research volume: 6issue:2 Feb 2016 633-635.
13. Amr Aly Ismail Keera, Ali Mohamed Ali Elnabtity; Two syringe spinal anaesthesia technique for cesarean section: A controlled randomized study of a simple way to achieve more satisfactory block and less hypotension; Anesth Essays Res. 2016 May-Aug; 10(2): 312–318.
14. Kumar and Balaji; Randomized controlled study comparing the efficacy of neuraxial blockade by using intrathecal administration of 0.5% hyperbaric bupivacaine 15mg and fentanyl 25mcg - in a single syringe versus separate syringe techniques in inguinal hernia surgeries; Indian Journal of Clinical Anaesthesia 2020;7(3):394– 398
15. Rania M. Hussien and Amal H. Rabie; Sequential intrathecal injection of fentanyl and hyperbaric bupivacaine at different rates: does it make a difference? A randomized controlled trialKorean J Anesthesiol 2019 April 72(2): 150-155
16. Vincent J. Collins, Principles of general and regional anaesthesia, Third edition, volume 2.
17. Mokaram Dori M, Foruzin F. The Analgesic Efficacy of Intrathecal Bupivacaine and Fentanyl with Added Neostigmine or Magnesium Sulphate. Anesth Pain Med. 2016 Sep 18;6(6): e9651. doi: 10.5812/aapm.9651. PMID: 28975069; PMCID: PMC5560647.
18. Uppal, Vishal FRCA*; Retter, Susanne MD*; Casey, Margaret MD*; Sancheti, Sushil FRCPC*; Matheson, Kara MSc†; McKeen, Dolores M. FRCPC* Efficacy of Intrathecal Fentanyl for Cesarean Delivery: A Systematic Review and Meta-analysis of Randomized Controlled Trials with Trial Sequential Analysis, Anaesthesia & Analgesia: January 2020 – Volume 130 - Issue 1 - p 111-125.
19. Farzi F, Mirmansouri A, Naderi Nabi B, Atrkar Roushan Z, Ghazanfar Tehran S, et al. Comparing the Effect of Adding Fentanyl, Sufentanil,
20. Placebo with Intrathecal Bupivacaine on Duration of Analgesia and Complications of Spinal Anaesthesia in Patients Undergoing Cesarean Section. Anesth Pain Med. 2017;7(5): e12738
21. Jasinski, T.; Migon, D.; Sporysz, K.; Kamysz, W.; Owczuk, R. The Density of Different Local Anesthetic Solutions, Opioid Adjuvants and Their Clinically Used Combinations: An Experimental Study. Pharmaceuticals 2021, 14, 801.
22. Siddik-Sayyid SM, Aouad MT, Jalbout MI, Zalaket MI, Berzina CE, Baraka AS. Intrathecal versus intravenous fentanyl for supplementation of subarachnoid block during cesarean delivery. Anesth Analg. 2002 Jul;95(1):209-13
23. Thornton P, Hanumanthaiah D, O'Leary RA, Iohom G. Effects of fentanyl added to a mixture of intrathecal bupivacaine and morphine for spinal anaesthesia in elective caesearean section. Rom J Anaesth Intensive Care. 2015;22(2):97-102.

ISSN (O): 2687-5365; ISSN (P): 2753-6556