How to Cite:
Patel, J., Thakkar, S., Anjali, A., Mehta, M., & Chauhan, D. (2022). A comparative study of different doses of intrathecal nalbuphine as an adjuvant to bupivacaine in subarachnoid block in cesarean section. *International Journal of Health Sciences*, *6*(S2), 3315–3328. https://doi.org/10.53730/ijhs.v6nS2.5820

A comparative study of different doses of intrathecal nalbuphine as an adjuvant to bupivacaine in subarachnoid block in cesarean section

Jatin Patel
Professor, Department of Anaesthesiology, Shrimati Bhikhiben Kanjibhai Shah Medical Institute &Research Centre, Sumandeep Vidyapeeth (An Institute Deemed to be university), Piparia, Vadodara, Gujarat, India

Sujay Thakkar
Assistant Professor, Department of Anaesthesiology, Shrimati Bhikhiben Kanjibhai Shah Medical Institute &Research Centre, Sumandeep Vidyapeeth (An Institute Deemed to be university), Piparia, Vadodara, Gujarat, India

A. Anjali
Senior Resident, Department of Anaesthesiology, Shrimati Bhikhiben Kanjibhai Shah Medical Institute &Research Centre, Sumandeep Vidyapeeth (An Institute Deemed to be university), Piparia, Vadodara, Gujarat, India

Mehul Mehta
3rd Year Resident, Department of Anaesthesiology, Shrimati Bhikhiben Kanjibhai Shah Medical Institute &Research Centre, Sumandeep Vidyapeeth (An Institute Deemed to be university), Piparia, Vadodara, Gujarat, India
Email: mehulmehta359@gmail.com

Dinesh Chauhan
Professor & HOD, Department of Anaesthesiology, Shrimati Bhikhiben Kanjibhai Shah Medical Institute &Research Centre, Sumandeep Vidyapeeth (An Institute Deemed to be university), Piparia, Vadodara, Gujarat, India

***Abstract*---**Background: Spinal anesthesia is preferred over general anesthesia by most of the anesthetists in cesarean section as it provides post-operative analgesia. Materials and methods: The parturient were randomly divided two groups of 30 each. Inj. Bupivacaine 2ml with Inj. Nalbuphine 0.75 mg (GROUP A) and 1 mg (GROUP B) diluted till 0.5 ml, making a total volume of 2.5 ml. The onset and duration of sensory and motor blockade, time of absolute

International Journal of Health Sciences ISSN 2550-6978 E-ISSN 2550-696X © 2022.
***Corresponding author**: Mehta, M.; Email: mehulmehta359@gmail.com*
Manuscript submitted: 27 Feb 2022, Manuscript revised: 18 March 2022, Accepted for publication: 05 April 2022

and effective analgesia, number of rescue analgesia required in 24 hours, hemodynamic stability and side-effects were noted. Results: Onset time of motor block was significantly prolonged in group A (3.93±0.59) as compared to group B (3.29±0.46). Duration of absolute analgesia (185.74±4.17) and effective analgesia in Group B (197.25±5.58) is higher as compared to group A, thus number of rescue analgesia required in 24hrs is more in Group A (2.03±0.72) as compared to group B (0.77±0.57)Conclusion: 1mg Intrathecal Nalbuphine as an adjuvant to 0.5% hyperbaric Bupivacaine is more efficient in prolonging postoperative analgesia compared to 0.75 mg dose.

***Keywords*---**analgesia, bupivacaine, cesarean, intra-thecal, nalbuphine.

Introduction

Most of the anesthetists prefer spinal (regional) anesthesia over general anesthesia (GA) for cesarean section (CS) delivery, because it avoids risk of aspiration which may occur with general anaesthesia, also the risk of neonatal depressant effect of GA can be avoided and additionally provides postoperative analgesia also it is safe, simple to perform, bondage between mother and the newborn and also early breastfeeding, early ambulation of the mother and hence decrease in the incidence of Deep Vein Thrombosis (DVT). But, it also has disadvantages because it only provides a relatively and fixed shorter duration of anesthesia, causes sympathetic blockade which can lead to hypotension and bradycardia, less control on the block level, insufficient visceral pain relief and possibility of occurrence of side-effects like nausea and vomiting mainly manipulating the uterus and closure of the peritoneal cavity. [1]

Bupivacaine, the most widely used local anesthetic drug for subarachnoid block, has slower onset of action, high potency and relatively shorter duration of post-operative analgesic effect. Dose of intra-thecal hyperbaric Bupivacaine varies form 12-15mg. Handling of the peritoneum during cesarean section may lead to intra-operative visceral pain. However, increasing the dose of hyperbaric Bupivacaine leads to reduction of the incidence of intra-operative visceral pain but on the other hand there is a greater risk of higher blockade and its subsequent adverse effects. [2]

To avoid these adverse effects and improving the quality and duration of sensory blockade and prolonging postoperative analgesia, various adjuvant have been used along with local anesthetics. The commonly used adjuvant are Opiates like Fentanyl and Nalbuphine, α-2 receptor agonists like clonidine and dexmedetomidine, NMDA receptor blocker such as Ketamine & GABA receptor modulator such as Midazolam. [3,4]

Intrathecal Opioids are highly synergistic with the local anesthetics, and hence they intensify the sensory blockade without increasing sympathetic blockade and provide excellent post-operative analgesia. [5] Nalbuphine, a synthetic Opioid , is a

ķ--receptor agonist and µ -- receptor antagonist. Adding Nalbuphine to local anesthetic agents increases the efficacy and the duration of post-operative analgesia. Nalbuphine as a sole analgesic agent provides satisfactory cover of mild to moderate types of pain with a low incidence of side effects. The binding of Nalbuphine to µ - receptors will only competitively displace other µ - agonists like morphine and fentanyl form µ - receptors without Nalbuphine itself displaying any agonistic properties. However, when it binds with ķ- receptors it displays agonist properties at µ -receptors. ķ-receptors are widely spread throughout the brain and spinal cord and are involved in nociceptive properties. Nalbuphine binds to ķ- opioid receptors here and produces analgesia. This pattern of binding and the effects defines the property of Nalbuphine as a mixed agonist-antagonist along with decrease in the common µ-agonistic side effects (itching, nausea/vomiting, urinary retention, constipation, respiratory depression and prolonged sedation). [6]

Materials and Methods

After the ethical committee's approval (letter no. SVIEC/ON/MEDI/BNPG18/D19233), an observational study was carried out in the department of Anesthesiology of Dhiraj Hospital. 60 patients aged between 18 to 35 years old belonging to American Society of Anesthesiologists (ASA) grade I or II undergoing ELECTIVE LOWER SEGMENT CESAREAN SECTION (LSCS) were taken for the study.

Inclusion Criteria

- ASA I & ASA II patients undergoing spinal anaesthesia.
- Patients in the age range 18- 35 years.
- No known history of allergy, sensitivity or other form of reaction to local anesthetics of the amide type.
- Patient willing to sign informed consent.

Exclusion Criteria

- Patient refusal.
- Allergy to any drugs.
- History of seizure disorder.
- Known allergy to trial drug.
- Patients with neurological disorders and neuropathies or receiving medications known to influence neuromuscular junction.
- ASA III, IV, V Patients.
- Parturient with prior pre existing Co-morbidities (Heart diseases, Respiratory disease, Kidney diseases, known fetal abnormalities)
- Any intake of drug that influence hemodynamic factors
- Failed spinal anesthesia converted to general anesthesia
- Any contraindication to Spinal Anaesthesia (local site infection, spine deformity, clotting abnormalities)

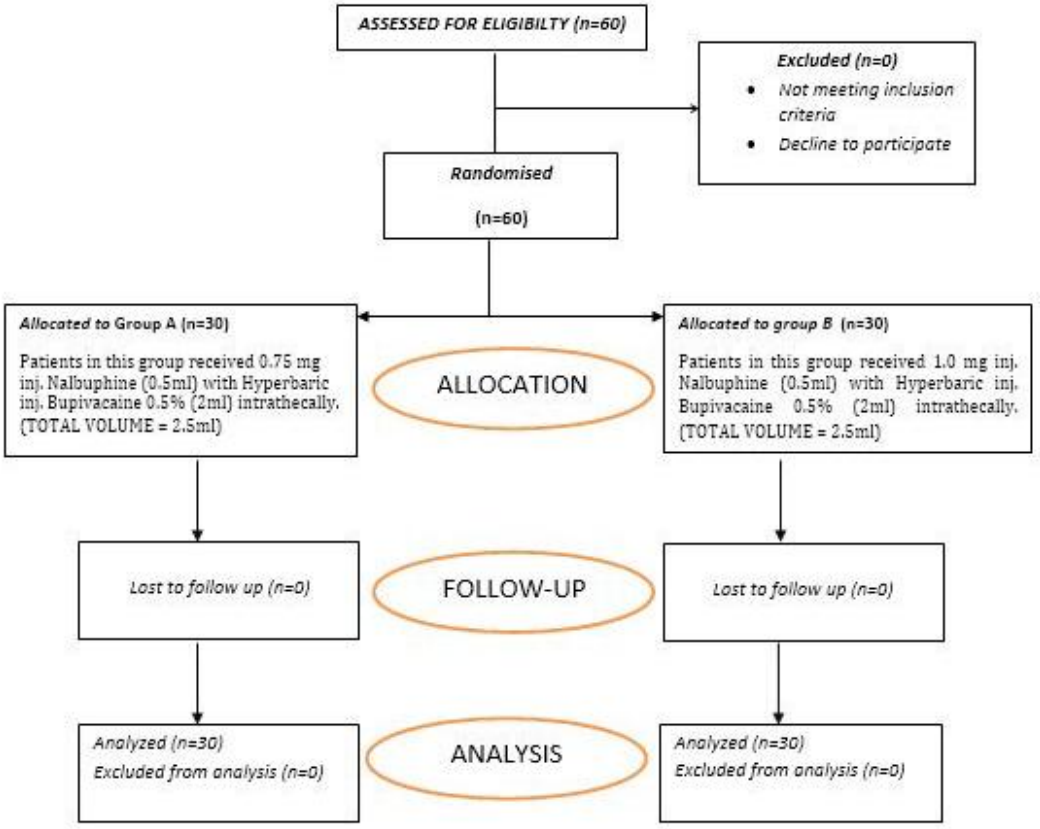
Procedure

Patient's written and informed consent was taken. An 18G IV cannula was secured. Each patient received inj. Glycopyrrolate 0.004 mg/kg, inj. Ondansetron 0.08 mg/kg, inj. Ranitidine 1mg/kg IV preoperatively as pre-medications. In the operating room multi-para monitor attached and Baseline parameters like Systolic Blood Pressure, Diastolic Blood Pressure, Pulse rate and Oxygen saturation were recorded before spinal anaesthesia.

Each patient was preloaded with 15 ml/kg of ringer lactate i.v. solution. With the patient in the sitting position according to convenience, under all aseptic and antiseptic precautions lumbar puncture was performed at the L2-3 lumbar space with 2.5 ml of total volume bupivacaine (0.5% Heavy) and inj. Nalbuphine (dose according to the group alloted) via a 23-guage Quincke spinal needle.

Patients were assigned to receive one of two doses of inj. Nalbuphine with inj. Bupivacaine 0.5% (H) intrathecally according to the group allotted (Figure I) as follows:

- Group A: Patients in this group received 0.75 mg inj. Nalbuphine (0.5ml) with Hyperbaric inj. Bupivacaine 0.5% (2ml) intrathecally. (TOTAL VOLUME = 2.5ml)
- Group B: Patients in this group received 1.0 mg inj. Nalbuphine (0.5ml) with Hyperbaric inj. Bupivacaine 0.5% (2ml) intrathecally. (TOTAL VOLUME = 2.5ml)



Immediately after completing the intra-thecal injection, patients were positioned supine. From this moment, the level of the sensory block will be evaluated by Pinprick method and Motor block will be evaluated by Bromage scale every 5 minutes till maximum levels of both sensory and motor blocks are achieved.

Assessment of Sensory Blockade

The level of sensory block was determined by using pin prick test. To assess the height of the block; sensory block was assessed at 5 min post-injection and at 5-min intervals thereafter until two consecutive levels of sensory block will be identical (i.e. fixation of the level), after which assessment will be done every 30 minutes. If the sensory block will be above or equal to $T_{12,}$ surgeon will allow to start the surgery. Data was collected regarding the onset of sensory block (Time taken from intra-thecal injection to loss of pinprick sensation at $L_{1).}$

Assessment of Motor Blockade

Assess by Bromage scale, time of onset (Time taken from intra-thecal injection to grade 3 motor block) and duration of motor block (Time taken from intra-thecal injection to return to grade 0 motor block) was recorded.

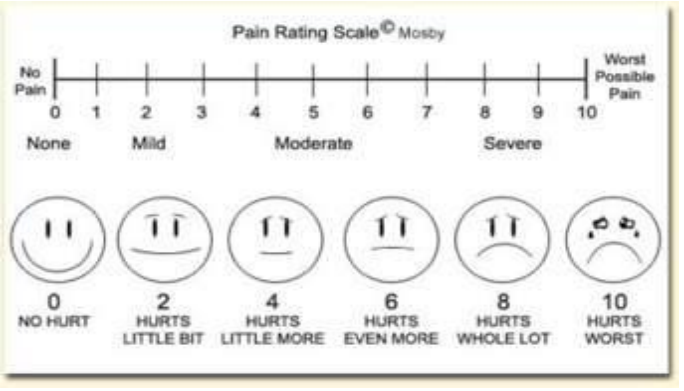
Bromage scale

Bromage 0: The patient is able to move hip, knee and ankle.
Bromage 1: The patient is unable to move the hip, but is able to move knee and ankle.
Bromage 2: The patient is unable to move the hip and knee, but is able to move ankle.
Bromage 3: The patient is unable to move the hip, knee and ankle.

Total duration of absolute analgesia (intra-thecal injection to vas score 1) and total duration of effective analgesia (intra-thecal injection to vas score 4) were also recorded.

Number of rescue analgesia required in 24hours was also noted

Figure II: Vas Score (Visual Analogue Score)



Side effects will be noted and treated. Bradycardia will be defined as pulse rate < 60/min and will be treated with IV atropine sulfate 0.6mg. Hypotension will be defined as systolic BP≥20% from the baseline level and will be treated with I V mephentermine 6mg.

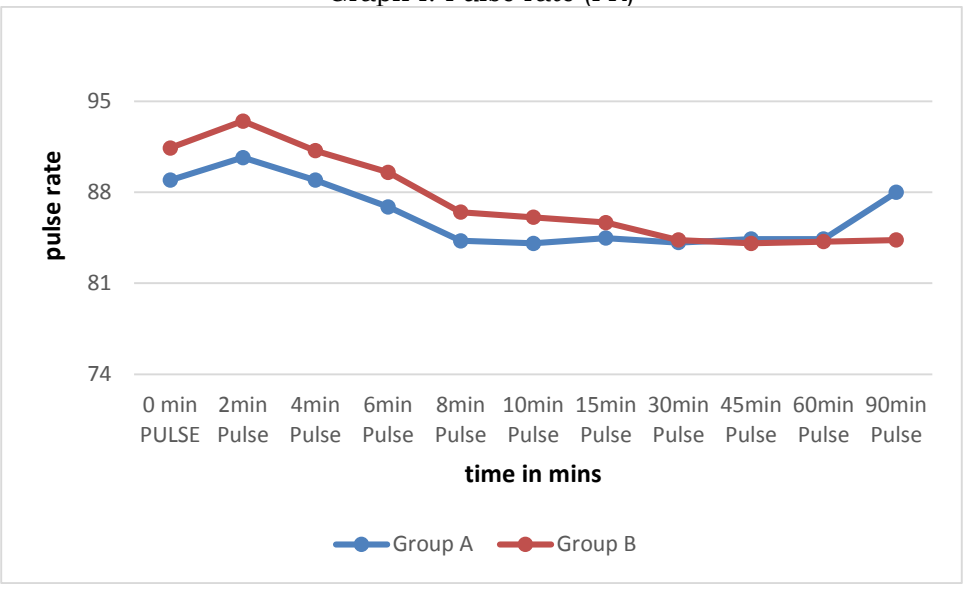
Observations and Result

Table I: Demographic Data and Asa Grading

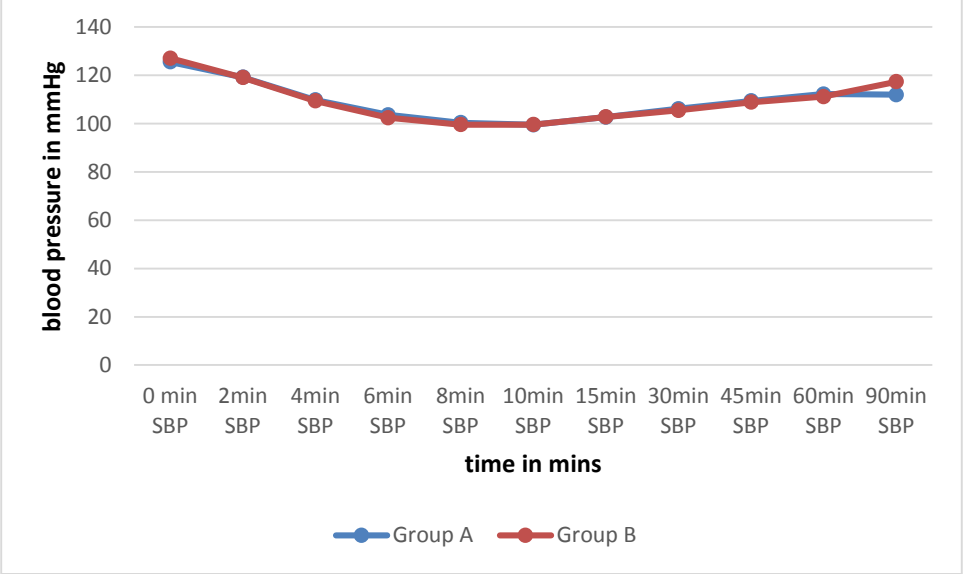
PARAMETER	Group A		Group B		t	P value
	N	Mean ± SD	N	Mean ± SD		
Age(Years)	30	27.07±4.33	30	24.97±4.01	1.948	0.056
Weight(kg)	30	56.5±5.48	30	53.63±9.24	1.462	0.15
ASA I	5		5		0	1
ASA II	25		25			

According to the demographical parameters and ASA grading, both the groups A & B were comparable to each other and was statistically non-significant.

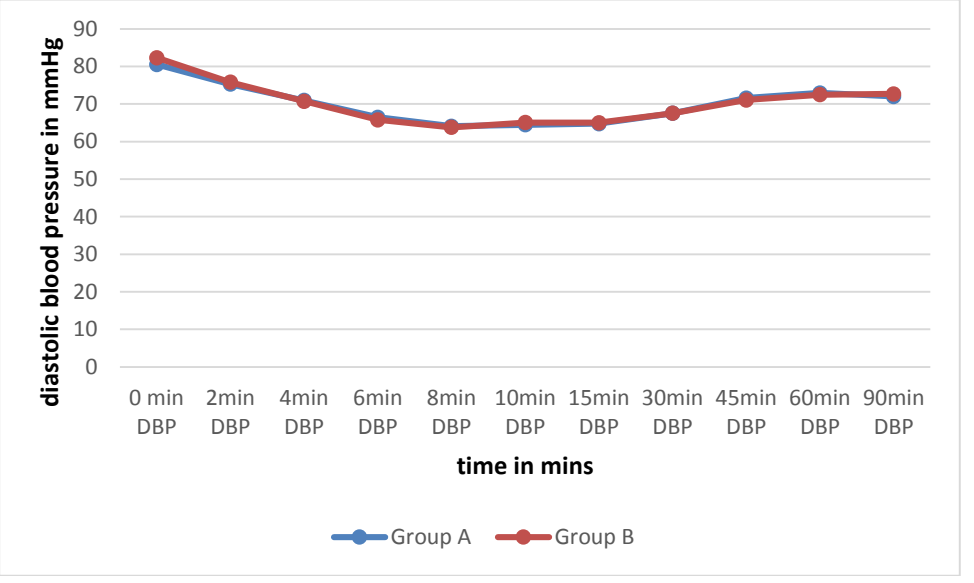
Graph I: Pulse rate (PR)



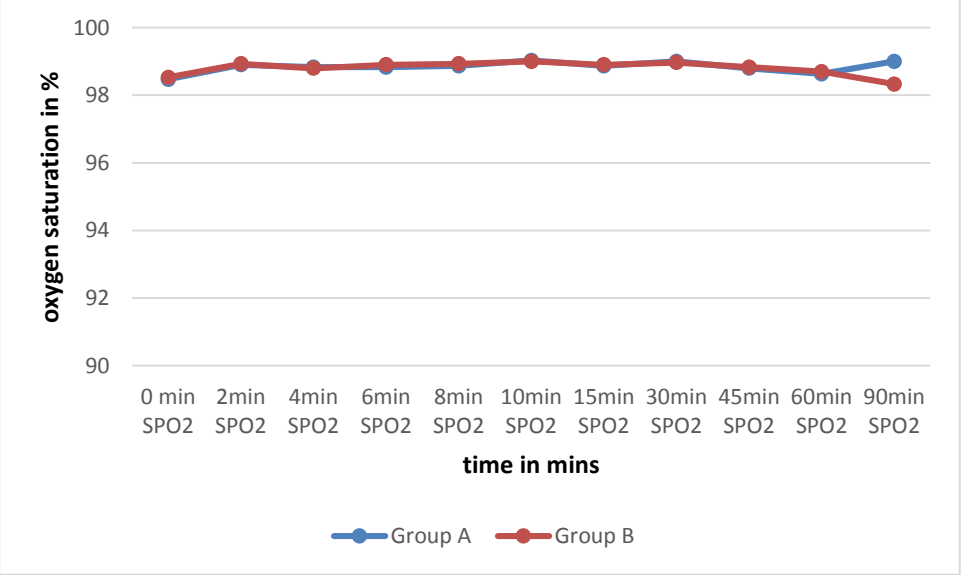
Graph II: Systolic Blood Pressure (SBP)



Graph III: Diastolic Blood Pressure (DBP)

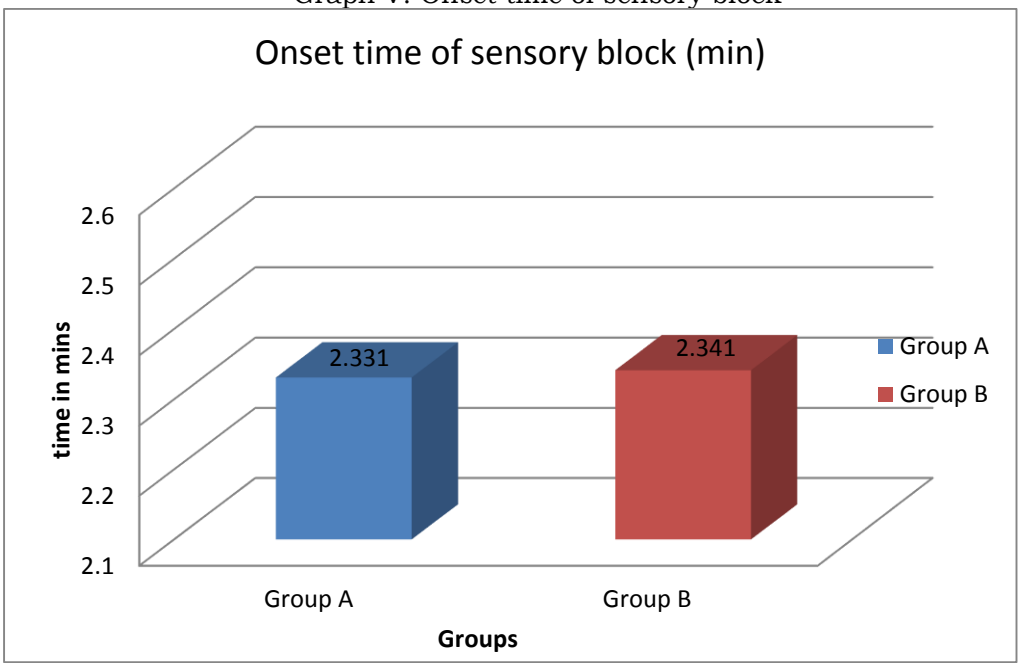


Graph IV: Oxygen Saturation (SpO2)

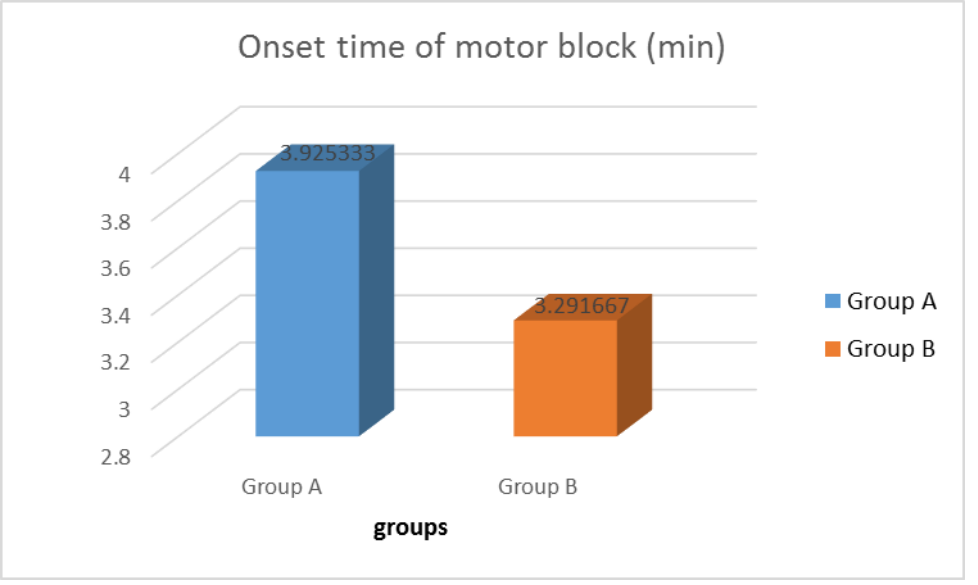


Hemodynamic parameters (pulse rate, systolic and diastolic blood pressure and oxygen saturation) were comparable for both the groups.

Graph V: Onset time of sensory block

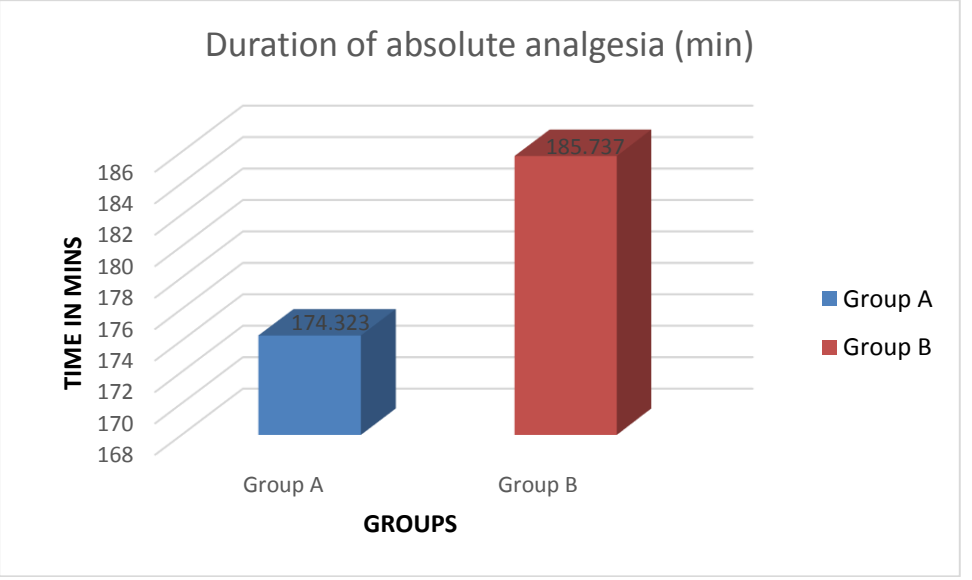


Graph VI: onset time of Motor block

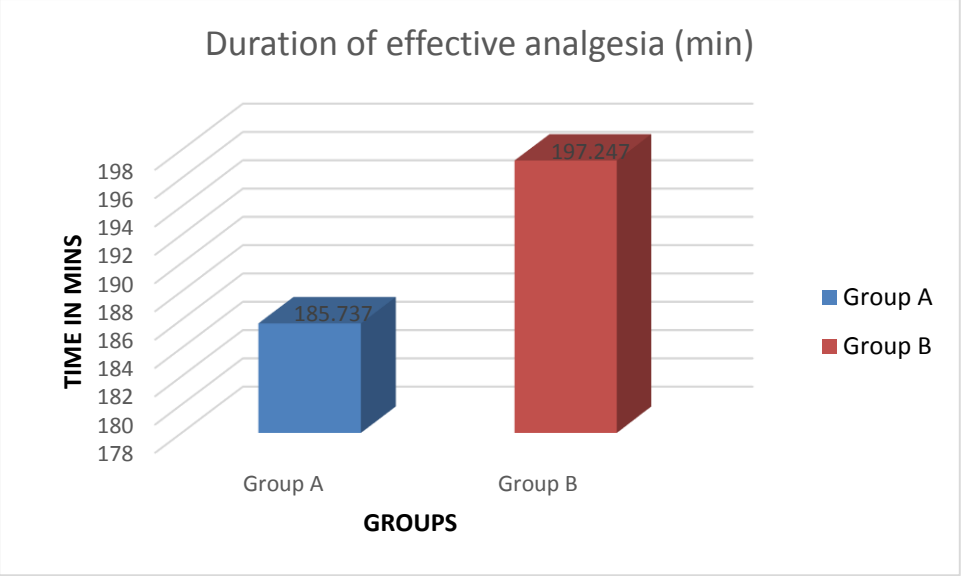


Early Onset time of sensory block (p=0.928) was seen in group A (2.33mins) as compared to group B (2.34mins) but statistically non-significant, however, onset time of motor block (p=<0.001) significantly prolonged in group A (3.92mins) than Group B (3.29mins).

Graph VII: Duration of Absolute Analgesia

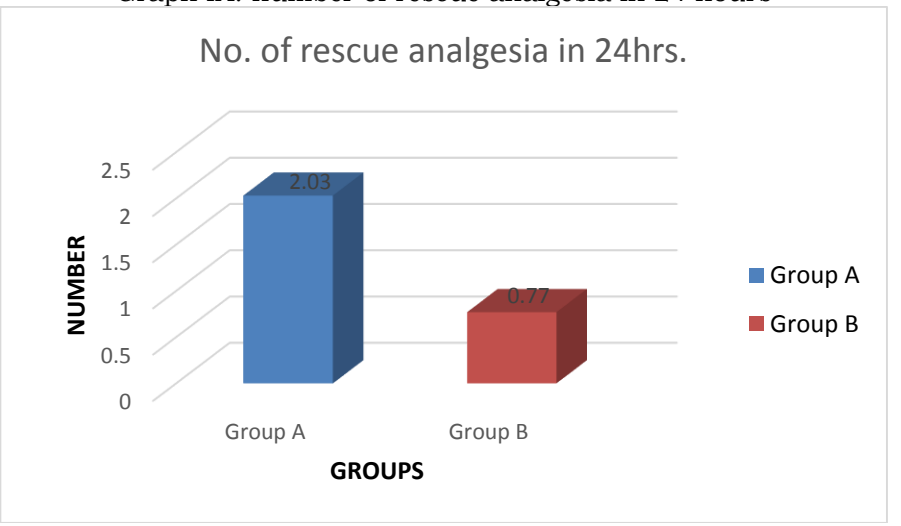


Graph VIII: Duration of effective analgesia



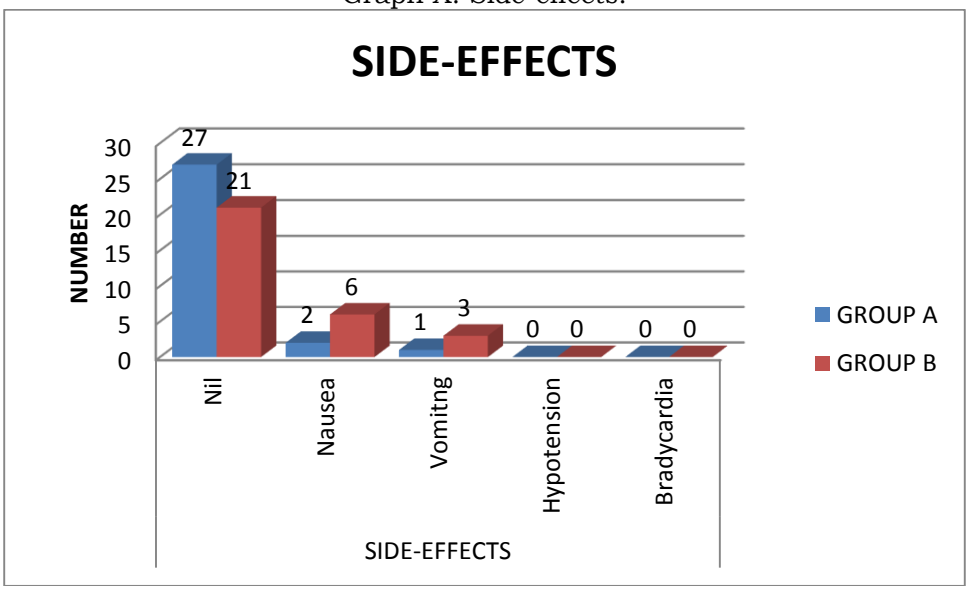
The duration of absolute analgesia (p=<0.001) prolonged in group B (185mins) as compared to group A (174mins) and was statistically significant. The duration of effective analgesia (p=<0.001) also prolonged in group B (197mins) as compared to group A (185mins) and was statistically significant

Graph IX: number of rescue analgesia in 24 hours



The number of rescue analgesia required in 24hours (p=<0.001) was more in group A as compared to group B and was statistically significant.

Graph X: Side-effects.



Incidence of side-effects like nausea and vomiting in both the groups were similar and was statistically not significant.

Discussion

Regional anaesthesia is the most commonly used mode of anesthesia for Caesarean sections. Spinal anesthesia is the best and most effective anaesthetic technique because of the simplicity in procedure along with rapidity in onset and

providing excellent muscle relaxation. There are many advantages of Regional anesthesia over general anesthesia which include decrease in stress response because of the surgery, use of multiple drugs, manipulating the airway, decreases incidence of vomiting, reduced risk of aspiration and in providing effective post-op analgesia.

Many adjuvants are used with local anesthetics intra-thecally as to prolong the duration of action of these drugs in spinal anesthesia of which Opioids are highly synergistic with local anesthetics and hence intensify the sensory blockade without increase in the sympathetic blockade, also providing excellent post-operative analgesia. Nalbuphine is a synthetic Opioid which is a μ-receptor antagonist and a ķ- receptor agonist. It provides good intra-operative and post-operative analgesia with minimal respiratory depression and decreasing u-receptor side-effects.

Hence, in this observational study we compared have two doses of 0.75mg and 1mg intra-thecal Nalbuphine. Demographically, in our study both the groups were comparable on the basis of age (p=0.056) and weight (p=0.15) and also ASA physical status (p=1) and the results were insignificant. In our study, onset time for sensory block was earlier in group A but was statistically non-significant (p=0.928). Similar results were observed in following studies. Fareed Ahmed et al[9] in 2016 compared three different doses of Nalbuphine and the results showed that the onset time of sensory block was comparable in all the groups and it was statistically insignificant (p=>0.05).

Jyothi B et al[10] in 2020 compared Nalbuphine in the doses of 0.8mg, 1.6mg and 2.4mg and showed that onset time of sensory block was comparable and statistically non-significant in all these groups (p=0.62). In contrast, the following studies showed different results from our study. Tarangini Das et al[5] in 2017 compared intra-thecal Nalbuphine in three different doses (0.5mg, 0.75mg &1mg) and the results showed statistically significant difference in the onset time of sensory block (p=<0.001). Onset time of motor block was earlier for group B than in group A and this was statistically significant (p=<0.001). Shehla Shakooh et al[8] in 2014 compared Nalbuphine with Bupivacaine alone and the results observed were statistically significant difference in onset time of motor block (p=<0.001).

Fareed Ahmed et al[9] in 2016 showed that there was statistically no significant difference in onset time of motor block when comparing 0.8mg, 1.6mg & 2.4mg Nalbuphine (p=>0.05) which was in contrast to our study. Duration of absolute analgesia & effective analgesia was prolonged in group B as compared to group A and was statistically significant (p=<0.001). Jyothi B et al[10] in 2020 compared 0.8mg, 1.6mg and 2.4mg doses of Nalbuphine intra-thecally with Bupivacaine and concluded that Nalbuphine prolongs duration of analgesia and the result was statistically significant P=<0.001). Shehla Shakooh et al[8] in 2014 compare Nalbuphine with Bupivacaine alone and concluded that addition of Nalbuphine prolongs duration of analgesia and it was statistically significant (p=<0.001). No. of rescue analgesia required in 24hours was significantly more in group A as compared to group B (p=<0.001).

Farahat Ahmed et al[1] in 2019 showed that number of recue analgesia required in 24hours was less in Nalbuphine group as compared to fentanyl intra-thecally with Bupivacaine and was statistically significant (p=<0.005). Tripat Kaur Bindra et al[4] in 2019 showed that number of recue analgesia required in 24hours was less in Nalbuphine group as compared to fentanyl intra-thecally with Bupivacaine and was statistically significant (p=<0.005). Overall side-effects like nausea (13.33%), vomiting (6.66%), hypotension (nil) and bradycardia (nil) were more in group B but was comparable for both groups and was statistically insignificant (p=0.153). Kumkum Gupta et al[3] in 2015 compared Nalbuphine 2mg and 25ug fentanyl with Bupivacaine intra-thecally and concluded that there were no side-effects with Nalbuphine group. Shagufta Naaz et al[11] in 2017 compared Bupivacaine alone versus in combination with fentanyl and Nalbuphine and concluded that Nalbuphine group had minimal side-effects.

Conclusion

From the present study, we conclude that Intra-thecal Nalbuphine 1mg as an adjuvant to 0.5% (H) Bupivacaine is more efficient in prolonging sensory blockade and providing efficient post-operative analgesia when compared to 0.75mg Intra-thecal Nalbuphine with minimal side-effects. Hence, Nalbuphine 1mg is a better adjuvant to sub-arachnoid block.

Conflicts of interest: NIL
External funds: NIL

References

1. Farahat I. Ahmed, Intrathecal nalbuphine versus fentanyl as an adjuvant to bupivacaine in spinal anesthesia for elective cesarean section, Research and Opinion in Anesthesia & Intensive Care, Vol. 6 No. 1, Janauary-March 2019.
2. Babu KV, Kumar GP, Harinath G. Evaluation of the Efficacy of Intrathecal Fentanyl versus Intrathecal Nalbuphine as Adjuvants to 0.75% Ropivacaine for Post-operative Pain Relief in Cesarean Section: A Double-Blind Randomized Comparative Study. Int J Sci Stud 2017;5 (1):5-10.
3. Gupta K, Rastogi B, Gupta PK, Singh I, Bansal M, Tyagi V. Intrathecal nalbuphine versus intrathecal fentanyl as adjuvant to 0.5% hyperbaric bupivacaine for orthopedic surgery of lower limbs under subarachnoid block: A comparative evaluation. Indian J Pain 2016;30:90-5.
4. Bindra TK, Kumar P, Jindal G. Postoperative analgesia with intrathecal nalbuphine versus intrathecal fentanyl in cesarean section: A double-blind randomized comparative study. Anesth Essays Res 2018;12:561-5.
5. Tarangini Das *et al.,* Sch. J. App. Med. Sci., Jun 2017; 5(6E):2388-2392.
6. Prabhakaraiah UN, Narayanappa AB, Gurulingaswamy S, Kempegowda K, Vijaynagar KA, Hanumantharayappa NB, *et al.* "Comparison of nalbuphine hydrochloride and fentanyl as an adjuvant to bupivacaine for spinal anesthesia in lower abdominal surgeries:" A randomized, double-blind study. Anesth Essays Res 2017;11:859-63.
7. Jaideep Singh, Aditya Agarwal, Ajay Vatal. Intrathecal nalbuphine an effective adjuvant for post operative analgesia (a comparitive study with

fentanil). International Journal of Contemporary Medical Research 2017;4(1):39-42.
8. Shehla Shakooh, Pooja Bhosle, INTRATHECAL NALBUPHINE: AN EFFECTIVE ADJUVANT FOR POST OPERATIVE ANALGESIA, Innovative Journal of Medical and Health Science 4 : 2 March – April (2014) 79 - 82.
9. Ahmed F, Narula H, Khandelwal M, Dutta D. A comparative study of three different doses of nalbuphine as an adjuvant to intrathecal bupivacaine for postoperative analgesia inabdominal hysterectomy. Indian J Pain 2016;30:23-8.
10. Jyothi B, Shruthi Gowda, Safiya I Shaikh, A comparison of analgesic effect of different doses of intrathecal nalbuphine hydrochloride with bupivacaine and bupivacaine alone for lower abdominal and orthopedic surgeriesIndian Journal of Pain | January-April 2014 | Vol 28 | Issue 1.
11. Shagufta Naaz et al., A Comparative Study of Analgesic Effect of Intrathecal Nalbuphine and Fentanyl as Adjuvant Journal of Clinical and Diagnostic Research. 2017 Jul, Vol-11(7): UC25-UC28.
12. Olfat Abdelmoniem, Ibrahem Amin, Mohamed Abdel-moniem, Ibrahem Dina Abdelhameed Elsadek Salem, Anesthesia and Journal of Pain Research 2020:13 1369–1376.
13. Bisht S, Rashmi D. Comparison of intrathecal fentanyl and nalbuphine: A prospective randomized controlled study in patients undergoing total abdominal hysterectomy. Anaesth Pain & Intensive Care 2017;21(2):194-198.
14. Rajeev Sharma & Rajendra Prasad Jatolia., SAS J. Med., May 2018; 4(5): 64-68.
15. Kumaresan and Raj: Intrathecal Nalbuphine as an Adjuvant to Spinal Anaesthesia: What is Most Optiμ -m Dose? International Journal of Scientific Study | April 2017 | Vol 5 | Issue 1.
16. Hala Mostafa Gomaaa,Nashwa Nabil Mohameda, , ,Heba Allah Hussein Zoheira, A comparison between post-operative analgesia after intrathecal nalbuphine with bupivacaine and intrathecal fentanyl with bupivacaine after cesarean section. Egyptian Journal of Anaesthesia ;30(4);405-410.