Journal Homepage: -www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/19807
DOI URL: http://dx.doi.org/10.21474/IJAR01/19807

RESEARCH ARTICLE

ANALGESIC EFFICACY OF TWO DIFFERENT DOSES OF NALBUPHINE 0.8 MG AND 1.6 MG AS AN ADJUVANT TO ROPIVACAINE 0.75% FOR ELECTIVE LOWER LIMB SURGERIES: RANDOMIZED DOUBLE-BLIND INTERVENTIONAL STUDY

Dr. Navdeep Chohan[1], Dr. Sunita Meena[2], Dr. Amrinderpal Singh[3] and Dr. Jeetam Singh Meena[4]

1. M.D Anaesthesia, Ex Resident SMS Medical College, Jaipur (Raj).
2. M.D. Anaesthesia, Professor SMS Medical College, Jaipur (Raj).
3. MBBS, MS Orthopaedics, Department of Orthpaedics, District Hospital, Fatehgarh Sahib, Punjab, India.
4. M.D. Paediatric Medicine, Associate Professor, SMS Medical College, Jaipur (Raj).

Manuscript Info

Manuscript History
Received: 31 August 2024
Final Accepted: 30 September 2024
Published: October 2024

Key words:-
Nalbuphine, Adjuvant, Intrathecal, Ropivacaine, Analgesia

Abstract

Background And Aim: Intrathecal Nalbuphine as an adjuvant with Ropivacaine providing profound analgesia with lesser side effects. We aimed to compare the analgesic efficacy of two different doses of intrathecal Nalbuphine (0.8mg versus 1.6mg) as an adjuvant to 0.75% isobaric Ropivacaine for elective lower limb Orthopaedic surgeries.

Material And Method: It was a Prospective Randomized Double-blind Interventional study in a total of 90 patients posted for elective lower limb surgeries under spinal anaesthesia, age 18-60 years, either gender, ASA I and II, weight 40-70 kg, height ≥ 145cm allocated in 3 groups, all of whom received 2.5ml total drug volume, Group A- Ropivacaine 2ml +0.5ml normal saline, Group B- Ropivacaine 2ml + 0.8mg Nalbuphinein 0.5ml normal saline, Group C- Ropivacaine 2ml+ 1.6mg Nalbuphine in 0.5 ml normal saline. We recorded the onset of sensory and motor block, total duration of analgesia, sedation, VAS (Visual Analogue Scale) and side effects.

Results: Onset of motor and the sensory block was earlier in Nalbuphine groups as compared to Ropivacaine alone. Analgesia was prolonged in 1.6mg Nalbuphine>0.8 mg Nalbuphine>Ropivacaine alone. VAS Score for rescue analgesia (>3) was achieved at 240 min in group B &C, and 210 min in groups A. Haemodynamic variables and sedation were comparable in all three groups and statistically non-significant. Hypotension, nausea and vomiting were higher in group C.

Conclusion: Nalbuphine dose 0.8mg and 1.6mg doses are equivalently effective as an intrathecal adjuvant in providing prolonged analgesia with isobaric Ropivacaine, but 0.8 mg is the optimal dose with lesser side effects.

Introduction:-

Spinal anaesthesia is a common and popular neuraxial anaesthesia technique for lower limb orthopaedic surgeries, as it provides intraoperative anaesthesia and extended analgesia in the postoperative period and good muscle relaxation. Various local anaesthetics are used for spinal anaesthesia and these areslowly being replaced by newer

Corresponding Author:-Dr. Navdeep Chohan
Address:-M.D Anaesthesia, Ex Resident SMS Medical College, Jaipur (Raj).

local anaesthetics like Ropivacaine.Ropivacaine use has shown a reduced risk of the central nervous system and cardiac toxicity, good quality of postoperative analgesia, early ambulation and discharge from the hospital.[1]A Local anaesthetic solely used provides good analgesia but for a limited duration in the postoperative period.Various adjuvants like clonidine, dexmedetomidine, opioids, magnesium sulphateand midazolam have been added to local anaesthetic for prolonged analgesia. Intrathecal opioids include morphine, fentanyl, buprenorphine and Nalbuphine. Nalbuphine is a semisynthetic opioid with mixed mu antagonist and k agonist properties.[2,3]Intrathecal Nalbuphine is a preferred opioid as compared to intrathecal morphine due to its minimum side effects like pruritus, hypotension, nausea, vomiting and respiratory depression.[4]Gupta K et al confirmed that intrathecal administration of Nalbuphine does not cause significant side effects, even at a dose of 2 mg.[5] Onlya few studies have compared the efficacy of two doses of Nalbuphine with Ropivacaine in spinal anaesthesia. In this study, we compared isobaric Ropivacaine with Nalbuphine 0.8 mg, 1.6 mg and Ropivacaine alone for spinal anaesthesia in lower limb orthopaedic surgeries.

Material and Methods:-

The study was carried out after approval from the institutional ethics committee and review board, CTRI registration and obtained written informed consent from the patients. Total Ninety patients with ASA physical status I and II, aged 18-60 years, weight 40-70 kg, height > 145cm, scheduled for lower limb orthopaedic surgeriesunder subarachnoid block were included in the study.sPatients in which SAB was contra-indicated, morbidobesity, patient refusal,pregnancy, history of convulsion, allergic to the drug used, bleeding disorder, severe neurological deficit, hypertensive, diabetic patients and with hepatic, cardiac or renal disease (ASA III or higher), patient receiving phenothiazine, hypnotics or other CNS depressants, and failed spinal anaesthesia, were excluded from the study. Patients were randomly allocated to one of the three groups (n=30), as presented in the consort flow chart (Figure 1). They received either normal saline 0.5ml(Group A), Nalbuphine 0.8mg in 0.5ml normal saline (Group B) or 1.6 mg in 0.5ml normal saline (Group C), mixed with 0.75% Ropivacaine 2ml (total volume 2.5 ml). Randomization was done by the sealed envelope method and double-blinding was done. An anaesthesiologist not involved in effect analysis did randomisation group allocation and study drug preparation without informing the patient. Another anaesthesiologist who was blinded to the group allocation did all other procedures and data collection.The routinepre-anaesthetic check-up was done one day before the surgery, and all the patients were kept nil orally for 6 hours. On the day of the surgery in the operation theatre securing i.v. access and attached all routine monitors (Pulse oximeter, ECG, NIBP) and lactated Ringer's solution was started. Airway management equipment and drugs for general anaesthesia/resuscitation were kept ready. Under all aseptic precautions, spinal anaesthesia was performed at L3-L4/L4- L5 interspace in the left lateral position or sitting position by using a 25-gauge Quincke needle. Free flow of cerebrospinal fluid was verified before injection of the anaesthetic drug, 2.5 mL volumewas administered according togroup allocation with blinding. All patients were placed in a supine position following the injection to achieve the level of a block of T10 dermatome after-that allpatients were placed in supine or lateral positions for surgery.Intraoperative haemodynamic parameters(SBP,DBP, MAPand HR)sensory and motor block assessment, VAS score, sedation score and side effects (hypotension, bradycardia, respiratory depression, nausea and vomiting), were recorded every 2 minutes for the first 10 minutes, every 5 minutes for the next 10–30 minutes, every 10 minutes until the surgery was completed, and every 30 minutes for the next 6 hours after SAB. The onset of sensory block was defined as the time from the intrathecal injection of the study drug to the time taken to achieve the T10 level of sensory block. Sensory block was assessed every 2 minutes by a pinprick test by using a 25 G blunted needle bilaterally in the mid-clavicular line until the level was stabilised for 4 consecutive tests. The onset of motor block was defined as the time from intrathecal injection of the study drug to the time taken to achieve a complete motor block (grade-1) according to the Modified Bromage scale.The total duration of sensory block was defined as two segment regression time from the highest sensory level achieved. The total duration of motor block was defined as the time taken from the onset of the complete motor block to regression to Modified Bromage grade I. The total duration of analgesia was defined as the time taken from intrathecal drug administration to the patient's first demand for rescue analgesia (on VAS 3). The quality of pain was assessed postoperatively using a visual analogue pain score (VAS) ranging from 0 to 10 (0 = no pain, 10 = most severe pain).It was assessed at every 30-minute interval until the patient demanded the first rescue dose of analgesia, Inj Diclofenac 75 mg IV (at VAS ≥3). Postoperatively, the degree of sedation was monitored by using the Four-point sedation scale(1=Awake and alert,2=Drowsy, responsive to verbal stimuli,3=Drowsy,arousable to physical stimuli,4=Unarousable). Hypotension was treated with InjMephentermine 6 mg IV and Nausea-vomiting with Inj Ondansetron 4 mg IV.

Statistical analysis

The statistical analysis of the data was done with SPSS (Statistical Package for the Social Science) version 20.0.0 (SPSS Inc., Chicago, Illinois, USA). The continuous variables (quantitative data) like age, weight, height, blood

pressure, heart rate, duration of analgesia and VAS score were presented as mean and standard deviation and analysed using the one-way ANOVA test. The categorical variables (qualitative data) like ASA grade and sedation score were presented in frequency and percentage and were analysed with the Chi-Square test (for nominal data). Probability (p-value) ≤0.05 was considered statistically significant in all the analyses. At an alpha-error of 0.05 and a study power of 80%, the sample size was calculated to be 22 subjects in each of the three groups, assuming a minimum detectable difference in the mean duration of analgesia of 22 (25) minutes as per the seed article.[6] Hence, 30 patients were taken in each of the three groups for study purposes.

Results:-

A total of 90 patients were enrolled and randomly allocated into three groups which showed in fig 1.All three groups were comparable concerningage, gender, weight, height, and duration of surgery which is depicted in table 1.Haemodynamic parameters (HR,MAP,SBP,DBP and MAP), and SPO_2 during intra-post operatively did not change statistically significant differences among the three groups (fig 2&3).

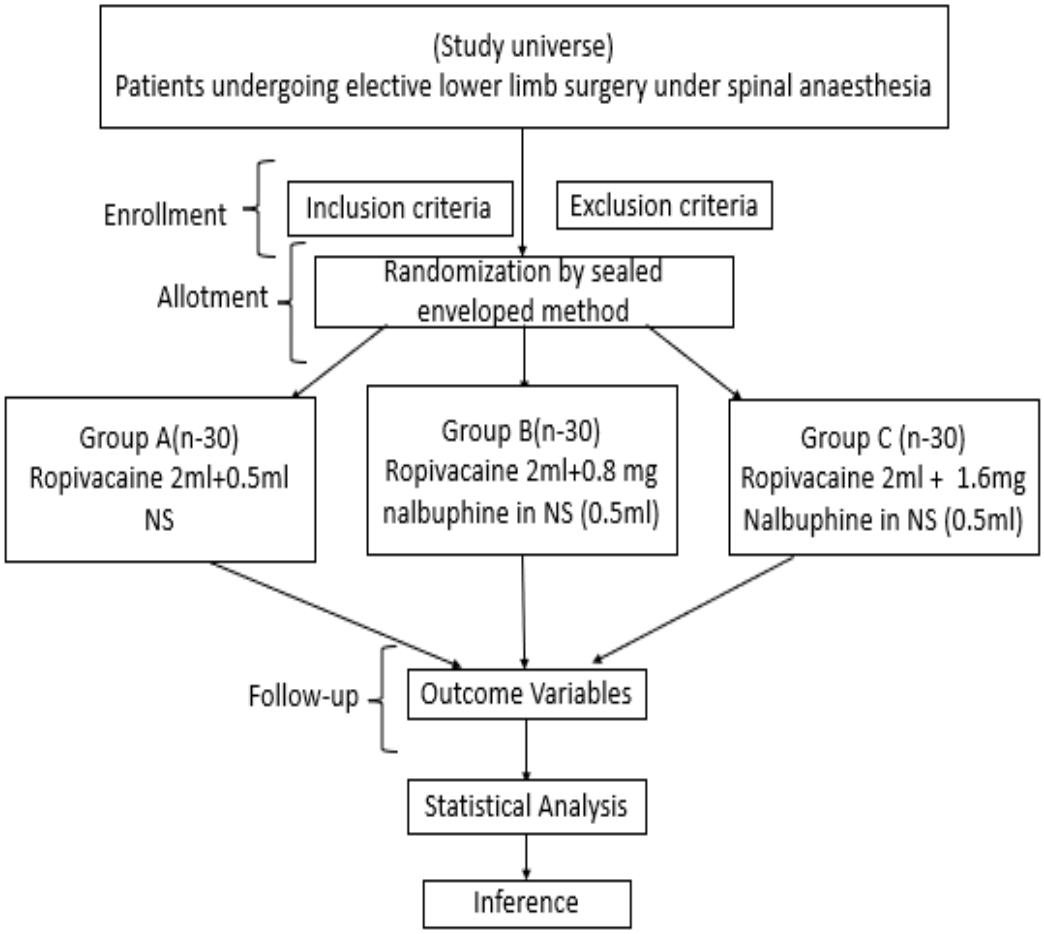


Fig. 1:- Consort Flow Chart.

Table 1:- Demographic and other characteristics of patients in three groups.

Variables	Group A	Group B	Group C	P value
Age(yrs) (Mean±SD)	37.5±13.27	37.9±12.98	37.5±13.27	0.99 (NS)
Height(cm)	159.6±5.3	160.6±5.7	161.6±5.26	0.59(NS)
Weight(kg)	60.71±7.06	61.56±7.56	60.89±7.71	0.71(NS)
Duration of surgery(min)	87±51.6	89.4±42.6	82.8±34.2	0.8(NS)
Gender(M/F) ratio	16/14	17/13	20/10	0.55(NS)

S-Significant, NS-Non-Significant

Fig 2:- Mean Arterial pressure (Inter group comparison) using ANOVA test.

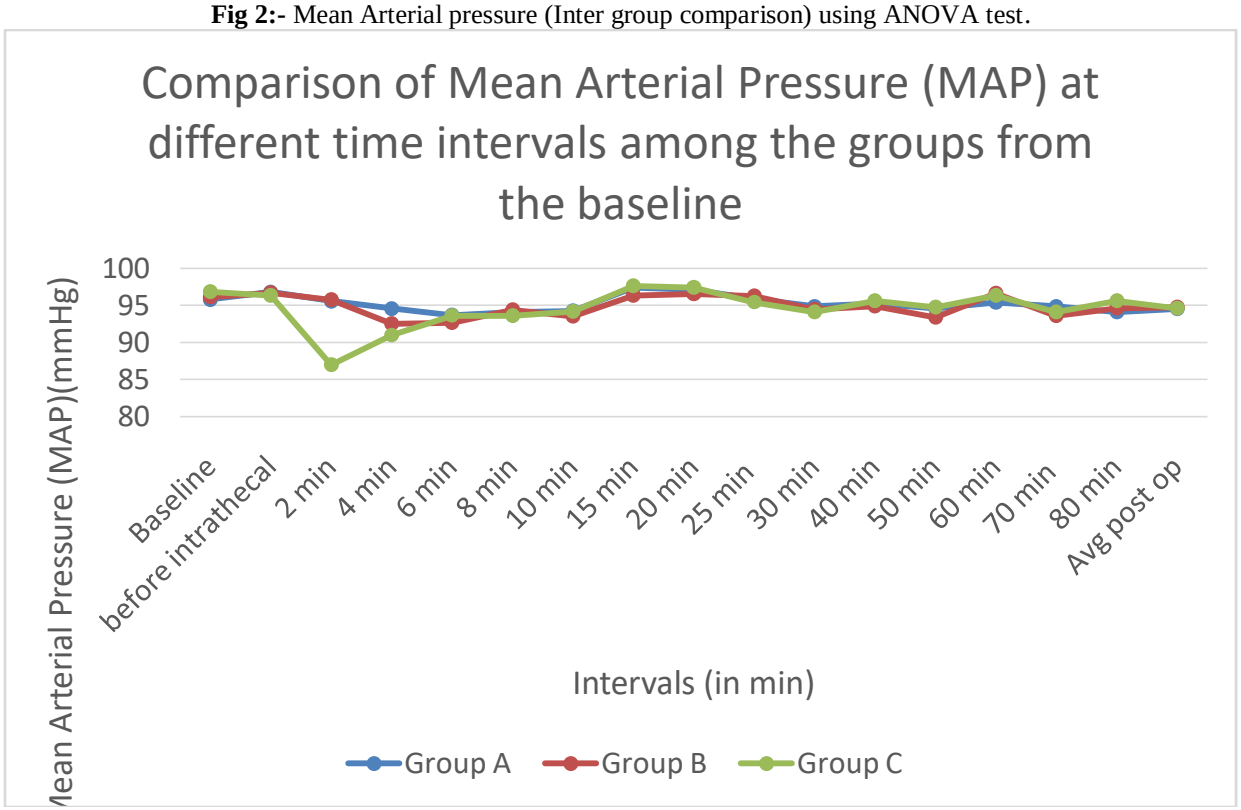
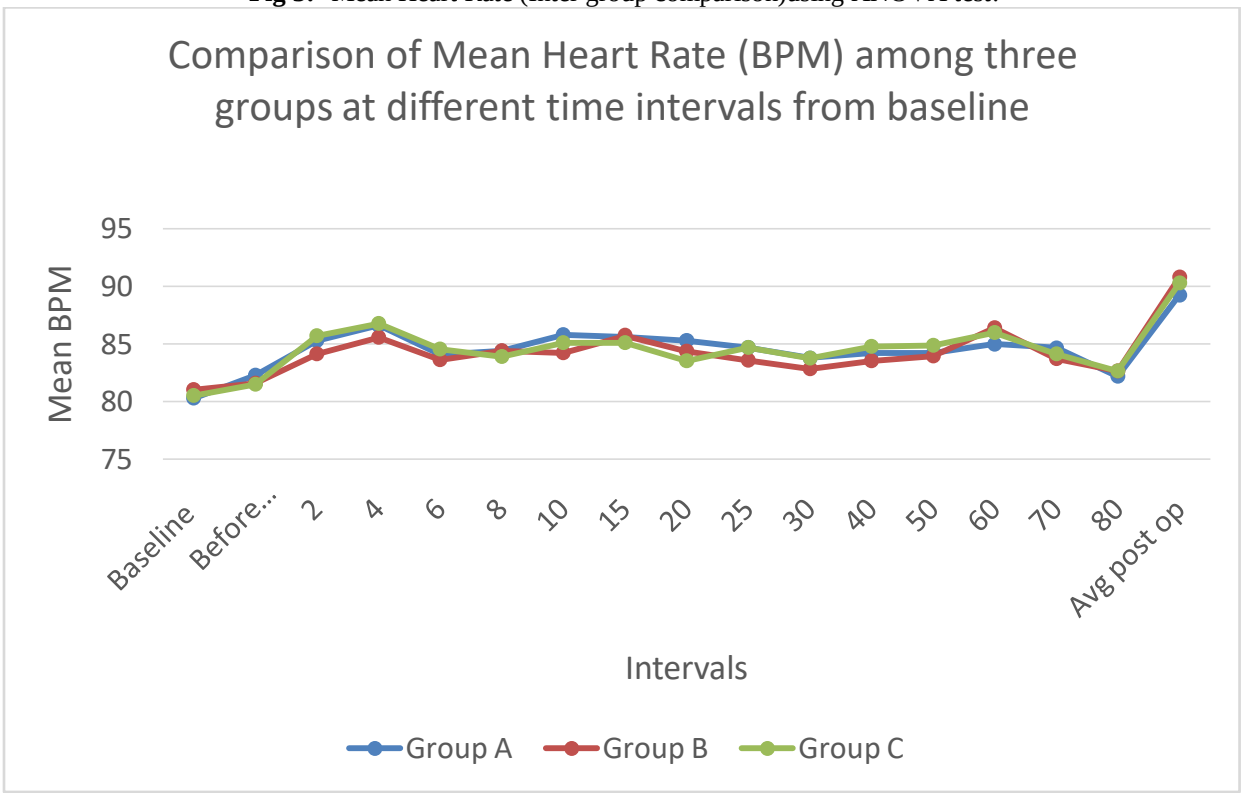


Fig 3:- Mean Heart Rate (Inter group comparison)using ANOVA test.



We observed that Intergroup comparison of characteristics of spinal anaesthesia in among the groups,onset of sensory and motor blockade, two segments regression time,duration of motor blockadeand total duration of analgesia among group A with group B and C showed statistically significant difference (p = 0.001) whereasthe difference between group B and group C was statistically non-significant (table 2).

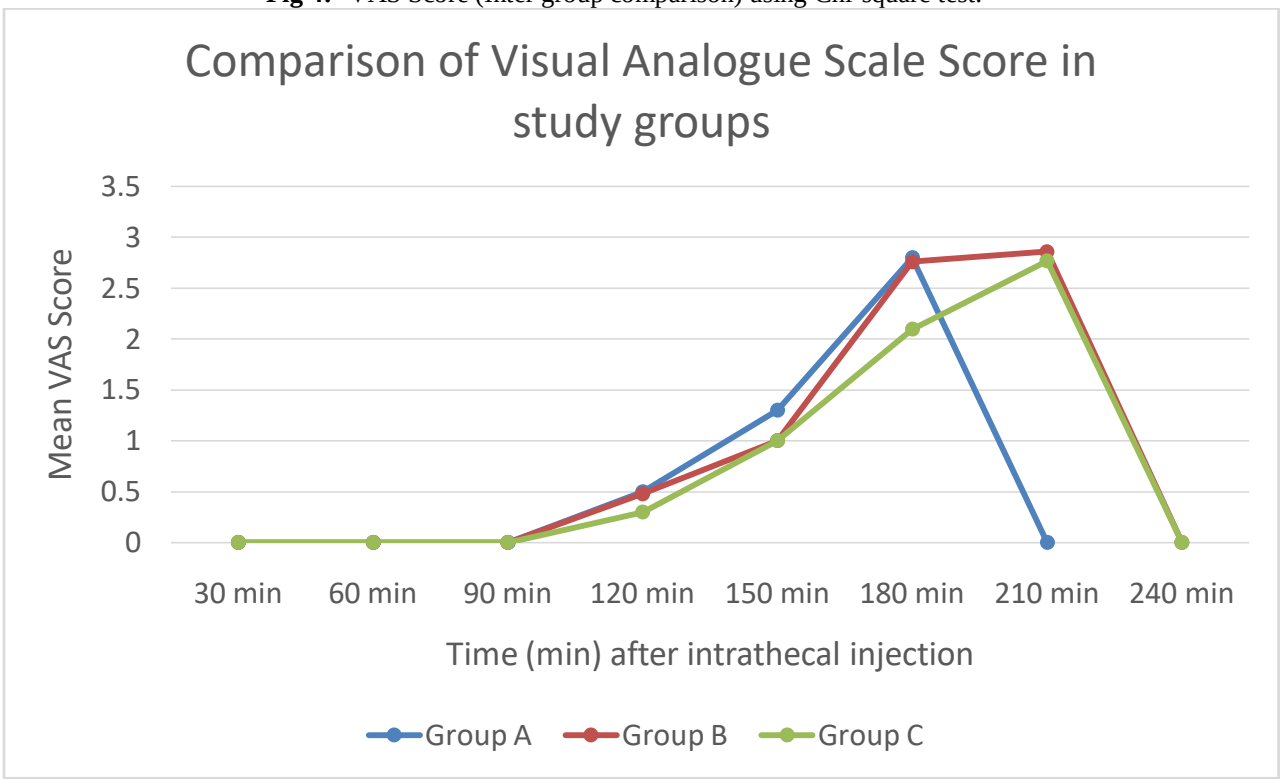
Table2:-Characteristics of spinal anaesthesia- Onset and duration of motor and sensory block and total duration of analgesia.

Parameters	Group A	Group B	Group C	F test	P value	Post hoc p value		
						A vs B	A vsC	B vs C
Onset of sensory block (min)	2.89±0.18	1.99±0.1	1.96±0.09	2.89	0.001(S)	0.001(S)	0.001(S)	0.79
onset of motor block(min)	5.44±0.08	5.01±0.12	5.09±0.04	5.27	0.001(S)	0.001(S)	0.001(S)	0.81
Two segment regression time of sensory block (min)	142.50±11.65	156±8.13	160±11.81	751.6	0.001(S)	0.001(S)	0.001(S)	0.56
Total duration of motor block(min)	185±14.56	202±14.23	210±15.92	126.87	0.001(S)	0.001(S)	0.001(S)	0,73
Total duration of analgesia(min)	189±15.39	208±12.704	214±15.22	413.57	0.001(S)	0.001(S)	0.001(S)	0.81

S-Significant, NS-Non-Significant

VAS score noted at different time intervals, we found at 180 min VAS was comparable in all three groups but higher in group A than group B&C,which was 2.8±0.47,2.76±0.56,2.1±0.96 respectively (Fig 4).At 210 min VAS was in group B & C, 2.86±0.61, 2.77±0.78 respectively. Rescue analgesic was given when VAS score was≥3.Demand of first rescue of analgesia wasin group A at 210 min while in group B & C at 240 min after spinal anaesthesia.

Fig 4:- VAS Score (Inter group comparison) using Chi-square test.



Four-pointRamsay sedation score was observed and noted that all patients of three groups showed sedation score 1 which was non-significant. Side effects like nausea, vomiting,hypotension, bradycardia, pruritus and others were also noted and foundthat only group C had nausea and vomiting (80%) and hypotension (10%) which was statistically significant (p value0.01) in comparison to group A and B.

Discussion:-

Sub-arachnoid block is the most commonly favouredneuraxial technique among anaesthesiologists in lower limb surgeries.Local anaesthetics agents are available with different mechanisms and duration of action with different levels of safety margin.Variousintrathecal adjuvants are added to local anaesthetics for early onset of sensory and motor blockade and prolonged postoperative analgesia without affecting the autonomic functions. The administration of opioids in intrathecal space as an adjuvant to local anaesthetic was found to provide very good analgesia in various surgical procedures.[7,8]The scientific explanation behind the combination of opioids and local anaesthetics intrathecally is, that these two drugs act at different sites and hence provide better analgesia than administration of an individual drug alone.[9]Local anaesthetics produce their effects by acting on nerve axons and opioids at their receptors in the spinal cord.[9] This combination provides better haemodynamic control and fewer side effects than used alone.[9]Nalbuphine is an opioid agonist-antagonist with structural similarities to Oxymorphone and Naloxone that binds to μ-receptors as well asκ and delta receptors, so it providing good analgesia with minimum side effects like pruritus, hypotension, nausea, vomiting and respiratory depression.Madhuri SK et al showed intrathecal use of Ropivacaine, 0.75% glucose-free isobaric Ropivacaine in the dose range of 3.5-4.5ml successfully and found safe in patientsundergoing spinal anaesthesia for lower limb and lower abdominal surgery.[10]

Scarcity of review of literature on different doses of Nalbuphine with 0.75% isobaric Ropivacaine in the subarachnoid block so we planned the present study designed to compare the duration of analgesia and VAS score between two different doses of Nalbuphine (0.8mg and 1.6 mg) with 0.75% isobaric Ropivacaine and Ropivacaine alone in the subarachnoid blockfor lower limb surgeries. Demographic data (age, gender, weight, height) and haemodynamic variables(HR, SBP, MAP) between the study groups were comparable and the difference observed was statistically non-significant in the three groupsthroughout the perioperative period. Our study demonstrates that 0.8 mg and 1.6 mg Nalbuphine as an adjuvant are superior in prolonging anaesthesia when compared to Ropivacaine alone, with the duration of analgesia and side effects(nausea, vomiting, hypotension) being higher in 1.6 mg Nalbuphine group.

GS Karthik et al[11], Borah TJ et al[6] and Shekar S et al[12]studied similar drug combinations of drugs in subarachnoid block in different surgeries with different doses and theyhave concluded that addition of Nalbuphine with Ropivacaine provided better sensory and motor block along with prolonged postoperative analgesia.

Our findings, given haemodynamic variability during the perioperative period,were comparable and stable in all three groups,these results were similar to studies done by G.S. Karthik etal[11], Borah TJ et al [6]and Shekar S et al[12].The reason behind this because these both individual drug properties like Ropivacainemore cardio stable and Nalbuphine with lesser side effects as compare other opioids due to agonistic and antagonistic property.

In our study, the onset of sensory and motor blockade was earlier and statistically significant in Nalbuphine groups as compared to plain Ropivacaine group but the statistically nonsignificant difference between two dosesof Nalbuphine as an adjuvant with Ropivacaine. G.S. Karthik etal[11]studied effects of Nalbuphine 1 mg as an adjuvant to Ropivacaine in TURP surgery and observed that onset of sensory block early in Nalbuphine than Ropivacaine alone. Studies done by Ahluwalia Pet al[13] and Basunia SR et al[14] found thatthe onset time of sensory and motor block was significantly faster in Nalbuphine with Bupivacaine groups as compared to Bupivacaine alone. Whereas similar study done by Borah TJ et al[6] and Shekar S et al[12] found that statistically nonsignificant difference in the onset time of sensory and motor blockade after addition of Nalbuphine with Ropivacaine.

In our study two segment regression time of sensory block in group A142.50±11.65,in group B 156±8.13and in group C160±11.81,statistically significant difference between plain group and both Nalbuphine groups. These findings correspond to Borah TJ et al[6] two segment regression time of sensory block lesser in plain Ropivacaine group as compared to Nalbuphine groups.

In our study, duration of analgesia prolonged in group B 208±12.704 min and group C 214 ±15.22 as compared to plain isobaric Ropivacaine group A 189± 15.39 (p value 0.001).Our findingswere consistent with Borah TJ et al[6],

conducted a dose finding study of different doses 0.4mg,0.8 mg & 1.6 mg of Nalbuphine as an adjuvant with isobaric Ropivacaine 0.75% in spinal anaesthesia. They also found that duration of analgesia highest in Ropivacaine with Nalbuphine 1.6 mg followed by 0.8,0.4 and plain 0.75% Ropivacaine (P <0.05). Our study findings also corelate with G.S. Karthik etal[11] and, Shekar S et al[12] that use of Nalbuphine as adjuvant with Ropivacaine prolonging and potentiating analgesic efficacy of isobaric Ropivacaine in spinal anaesthesia

Our findings correspond with other studiesby Culebras et al[4], ShakooshS et al[15], Borah J et al [16]and Ahluwalia P et al [13],they also found that0.8 mg of Nalbuphine to 0.5% bupivacaine provides excellent analgesia with prolonging of action.

Mavaliya et al compared intrathecal fentanyl and Nalbuphine with 0.75% isobaric Ropivacaine and concluded that Nalbuphine prolongs the duration of postoperative analgesia as compared to fentanyl.[17]

We found no statistically difference between all three study groups at any time point postoperatively concerning sedation score.Our study findings are consistent with Gupta K et al[5] and Shah MS et al[18] sedation was not observed in Nalbuphine groups.

In our study finding VAS score was comparable (p-value>0.05) up to 180 min after intrathecal block. We observed that demand of first rescue analgesia (VAS≥ 3), at 210 min in Ropivacaine group while both Nalbuphine groups at 240 min after intrathecal block.The requirement of first Rescue analgesia was earlier in the plain Ropivacaine group than in both Nalbuphine groups. Our findings correlate with the study of Borah TJ et al[6]and G.S Karthik et al[11] also observed that RopivacaineNalbuphine group patients had low VAS score and reduced analgesic requirements as compared to Ropivacaine group.

In our study in all the three groups we found that only the Nalbuphine 1.6 mg grouphad nausea andvomiting in 24 patients (80%) and hypotension in 3 patients (10%) which was statistically significant (p value0.01) than plain Ropivacaine and 0.8 mg Nalbuphine group.Our findings were similar to the multiple studies likeBasunia SR et al[14],Naaz S et al[19],G.S. Karthik etal[11], Borah TJ et al [6]and Shekar S et al[12].

Limitations

The scarcity of literature in this study with the same drug dose combination (Ropivacaine with Nalbuphine 0.8mg and 1.6mg) of drugs used intrathecally, limited our knowledge. Being a single-centre study and smaller samplesize (n=30) it was not feasible to validate our conclusion. To strongly prove our conclusion, a larger sample size could help in future studies

Conclusion:-

Nalbuphine is a good alternative to other opioids as an adjuvant intrathecally with isobaric Ropivacaine since it is easily available, affordable, early onset of action, and prolonged sensory and motor blockade without any significant side effects. We conclude from our study findings that Nalbuphine dose 0.8 mg and 1.6 mg are equally effective as adjuvant with isobaric Ropivacaine 0.75% (2 ml) as compared to isobaric Ropivacaine alone, in patients undergoing lower limb surgery. Using 1.6 mg dose does not provide any extra advantage over 0.8mg dose in providing prolonged analgesia with more side effects.

References:-

1. Sultan MA, Ali Shams TM, Mageed NA, El-ebidy MG. Intrathecal hyperbaric Ropivacaine versus hyperbaric bupivacaine in geriatric hypertensive patients. Benha M J 2005;22:479

[2] Chen JC, Smith ER, Cahill M, Cohen R, Fishman JB. The opioid receptor binding of dezocine, morphine, fentanyl, butorphanol and Nalbuphine. Life Sci 1993; 52:389–96.

[3] Pick CG, Paul D, Pasternak GW. Nalbuphine, is a mixed kappa 1 and kappa 3 analgesic in mice. J Pharmacol Exp Ther 1992; 262:1044–50.

[4] Culebras X, Gaggero G, Zatloukal J, Kern C, Marti R. Advantages of intrathecal Nalbuphine, compared with intrathecal morphine, after caesarean delivery: An evaluation of postoperative analgesia and adverse effects. AnesthAnalg2000; 91:601-5

[5] 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 orthopaedic surgery of lower limbs under subarachnoid block: A comparative evaluation. Indian J Pain 2016; 30:90-5.
[6]Borah TJ, Dey S, Yunus M, Dev P, Karim HMR, Bhattacharyya P. Effect of different doses of intrathecal Nalbuphine as an adjuvant to Ropivacaine in elective lower limb surgeries: A dose-finding study. Indian J Anaesth 2018;62(11):865-70.
[7]Wilwerth M, Majcher J-L, Van der Linden P. Spinal fentanyl vs. sufentanil for post-operative analgesia after C-section: a double-blinded randomised trial. Acta Anaesthesiol Scand 2016;60(9):1306–13.
[8] Chakraborty S, Chakrabarti J, Bhattacharya D. Intrathecal tramadol added to bupivacaine as spinal anaesthetic increases analgesic effect of the spinal blockade after major gynaecological surgeries. Indian J Pharmacol 2008; 40:4180–2.
[9] Raghuraman M. S. Intrathecal Nalbuphine – Will it gain wider acceptance? – A narrative review, Egyptian Journal of Anaesthesia 2017; 33(3:, 289-293, DOI: 10.1016/j.egja.2017.04.003
[10] Madhuri SK, Anjali KB. Use of Ropivacaine intrathecally. J Anaesthesiol Clin Pharmacol. 2010 Oct;6(4):5641
[11] Karthik G.S., Sudheer R.S., Rangalakshmi,Shruthishree, Singh U. Effects of intrathecal Nalbuphine as an adjuvant to Ropivacaine in patients undergoing Transurethral resection ofprostate.Indian J Anaesth Analg.2018;5(8):1330-38.
[12] Shekhar S,Rautela R S,ChaudharyS, Sony S.Comparison of two different doses with isobaric Ropivacaine in patients undergoing lower segment caesarean section under subarachnoid block: A Randomized Controlled Trial. Cureus 17 June 2023;15(6): e40558.DOI 10 .7759/Cureus .40558
[13] Ahluwalia P, Ahluwalia A, Varshney R, Hakur S, Bhandari S. A prospective randomized double-blind study to evaluate the effects of intrathecal Nalbuphine in patients of lower abdominal surgeries under spinal anaesthesia. Int J Sci Stud 2015;3(3);19-23
[14] Basunia SR, Chattopadhyay S, Das A, Laha B, Bhar D, Pal R. A prospective, double-blind dose-ranging study of intrathecal Nalbuphine in the lower abdominal and lower limb surgeries. Indian J Pain 2016; 30:198-203.
[15] Shakooh S, Bhosle P. Intrathecal Nalbuphine: An effective adjuvant for post-operative analgesia. Innovative J Med Health Sci 2004; 4:79-82 38.
[16] Borah J, Shruthi Gowda, Safiya Shaikh. A comparison of analgesic effect of different doses of intrathecal Nalbuphine hydrochloride with bupivacaine and bupivacaine alone for lower abdominal and orthopaedic surgeries. Indian J Pain 2014; 28:18-23
[17] Mavaliya V, Babita, Tak ML, Singh B, Gurjar SS. Comparison of Nalbuphine versus fentanyl as an adjuvant to 0.75% isobaric Ropivacaine in subarachnoid block for orthopaedic surgery of lower limbs: A randomized, doubleblind study. Bali J Anaesthesiol2020; 4:161-5.
[18] Shah M S, Masoodi T, Hussain S Y, et al. (May 16, 2022) Nalbuphine as an Intrathecal Adjuvant to 0.5% Hyperbaric Bupivacaine in Two Different Doses for Postoperative Analgesia After Abdominal Hysterectomy: A Prospective, Randomized, Double-Blind Control Study. Cureus 14(5): e25044.
[19] Naaz S, Shukla U, Srivastava S, Ozair E, Asghar A. A comparative study of analgesic effect of intrathecal Nalbuphine and fentanyl as adjuvant in lower limb orthopaedic surgery. J Clin Diagn Res 2017;11: UC25-8.