Comparison Of Intrathecal Bupivacaine With Clonidine Versus Intrathecal Bupivacaine With Fentanyl For Post-Operative Pain Treatment In Lower Limb Procedures

ABSTRACT

BACKGROUND: One of the anaesthesiologist's key goals during spinal anaesthesia is to keep the body physiology as close to normal as feasible. As we all know, subarachnoid block causes significant hemodynamic changes, especially in trauma and elderly individuals. Sympathetic nervous system denervation, skeletal muscle weakness, or loss of proprioception are not linked to neuraxial opioids. They primarily operate on the receptors found in the substantia gelatinosa of the spinal cord to exert their synergistic analgesic impact on visceral pain.Opioids and local anaesthetics delivered intrathecally have a powerful synergistic analgesic effect, according to studies. Clonidine, a 2 adrenergic agonist, is sometimes used as a local anaesthetic adjuvant with mixed effects. The effects of intrathecal Clonidine vs Fentanyl with 0.5 percent hyperbaric bupivacaine on postoperative analgesic duration and adverse effects were compared.

OBJECTIVES: The purpose of this study was to compare the efficacy of 0.5 percent hyperbaric bupivacaine with Clonidine (75 gs) vs Fentanyl (25 gs) for spinal anaesthesia in patients undergoing lower limb procedures, as well as the postoperative pain alleviation and adverse effects in both groups.

METHODS: This was a prospective study involving 80 patients who were scheduled for elective lower limb surgery under spinal anaesthesia. The participants were randomly assigned to one of two groups: Group C (15mg 0.5 percent bupivacaine + 75gs Clonidine) or Group F (15mg 0.5 percent bupivacaine + 25gs Fentanyl).

RESULTS: We discovered a time delay in the start of sensory and motor block in group C after assessing the outcomes of our investigation. In comparison to group F, group C's sensory and motor block lasted significantly longer. The average duration of analgesia in groups C and F was 234.7529.71 minutes and 170.8732.38 minutes, respectively. When compared to group C, the demand for rescue analgesics was higher in group F throughout the course of 24 hours. Bradycardia affected 12 individuals in group C, while pruritus affected 12 patients in group F. Five of the patients in group F experienced nausea.

CONCLUSION: In compared to 25gs Fentanyl, adjuvant use of Clonidine 75gs with hyperbaric bupivacaine prolongs the duration of both sensory and motor blockage, as well as the length of analgesia postoperatively, without generating substantial hemodynamic compromise or other side effects.

KEYWORDS: Spinal Anesthesia, Lower Limb Surgery, Clonidine

INTRODUCTION:-

"Pain is a more terrifying lord of people than death."[1]Albert Schwitzer. During the postoperative phase, the surgical stress response peaks and has significant effects on practically all bodily systems. Any surgical procedure with a pain-free postoperative phase minimises morbidity and death. Karl August Bierwas the first to put spinal anaesthetic into clinical practise in 1898.[2] Even after a century, spinal anaesthesia is still one of the most used approaches for both elective and emergency surgical procedures, such as Cesarean sections, lower abdominal surgery, orthopaedic, and urological procedures, to name a few.[3]For spinal anaesthesia, hyperbaric Bupivacaine, an amide local anaesthetic, is most usually utilised. A

tiny dosage of hyperbaric bupivacaine generates a brief spinal anaesthetic that could be beneficial in ambulatory surgical operations. However, for the majority of lower limb orthopaedic procedures, a higher-quality, longer-lasting analgesia is required on the operating side. Clonidine Hydrochloride is a 2-adrenergic agonistic imidazoline derivative with a selectivity ratio of 200:1 in favour of 2 receptors. Clonidine, unlike opioids, does not cause pruritus or respiratory depression.It also extends the sensory blockage[4]and minimises the quantity of local anaesthetic necessary for postoperative analgesia.[5]It has an opioid-independent mechanism for pain alleviation. Intrathecal clonidine, on the other hand, appears to be linked to bradycardia, relative hypotension, and sedation. Fentanyl is a synthetic opioid receptor agonist that is derived from phenylpiperidine. Because of its early start and brief duration of effect, it is chosen as an adjuvant in spinal anaesthesia. It also has a lower incidence of respiratory depression.[6,7]

The purpose of this study was to determine the efficacy, duration of pain relief, and incidence of adverse effects and complications when Clonidine or Fentanyl is combined with Bupivacaine for intrathecal injection in patients undergoing lower limb procedures.

MATERIALS AND METHOD:-

The study was cross-sectional, prospective, and observational. The research was started once the Institutional Ethical Committee approved it. A complete clinical history and examination, as well as the necessary investigations, were all part of the pre-operative evaluation. The trial excluded patients with a height of less than 150 cm, any contraindication to regional anaesthesia, patient refusal, and any known drug allergy. The ten-point visual analogue scale was explained to all of the patients (VAS). The study comprised 80 patients with ASA (American Society of Anesthesiologists) status I or II who were scheduled for lower limb procedures.All patients signed a written informed consent form. Patients were divided into two groups of 40, one receiving 3.0ml injection Bupivacaine (H) + (75g) 0.5ml clonidine (Group C) and the other receiving 3.0ml injection Bupivacaine (H) + (25g) 0.5ml injection fentanyl (Group D) (Group F). The total volume of agents administered was 3.5 ml, and all of the study medications were injected intrathecally.

Monitors were linked to the patient in the operating room, and data such as heart rate, systemic arterial pressure, and peripheral arterial oxygen saturation were recorded. All of the patients were given 10ml/kg of Ringer lactate as a preload.Subarachnoid block was performed in the L3-L4 space with a 25G Quincke's spinal needle in a sitting position, following all aseptic precautions and using a midline approach. The drug was delivered into the appropriate group. The patient was placed in the supine position right away. Sensory analgesia and motor blockade onset were investigated. A pinprick test is used to determine the level of sensory anaesthesia, which is defined as the loss of keen sensation. The modified Bromage score was used to assess motor blockage. Every minute for the first 20 minutes, the time it took to complete a complete motor blockade was recorded.The time it took to reach the maximal sensory level was recorded. The patient's heart rate, blood pressure, respiratory rate, and oxygen saturation were monitored every minute for the first five minutes, then every five minutes for the next 30 minutes, and finally every ten minutes until the surgery was completed. The number of rescue analgesics provided, the duration for 2 segment regression, and the time for the first recue analgesia were all recorded. The postoperative pain reduction was measured using the Visual Analogue Scale. Injection Diclofenac 75mg was given intramuscularly as a rescue therapy at a score of 5.

Hypotension was defined as a drop in mean arterial pressure of less than 60mmhg from baseline in this trial, and it was treated with Injection Mephentermine IV. Atropine Sulphate 0.6mg IV injection was used to treat Bradycardia, which was described as a drop in pulse rate

to less than 50 per minute. For the next 24 hours, all patients were monitored. Any occurrence that occurred throughout the surgical and postoperative periods up to 24 hours was recorded and dealt with appropriately. The data was analysed statistically. The descriptive and inferential statistics were used in the statistical analysis, which included the student's paired and unpaired t test, as well as the chi-square test. The software used in the analysis were SPSS 17.0 version and GraphPad Prism 5.0 and $p<0.05$ is considered as level of significance ($p<0.05$).

Result:-

Table 1: Comparison of initial block characteristics in patients in both the groups

Initial Block Characteristics	Group C (n=40)	Group F (n=40)	t-value	p-value
OSB(sec)	96.25±16.66	87.75±14.40	2.44	0.017,**S**
DSB (min)	299±28.69	282.62±30.98	2.452	0.016,**S**
OMB(sec)	122.25±18.04	110.75±23.46	2.457	0.016,**S**
DMB(min)	234±27.36	219.12±28.34	2.388	0.019,**S**
T2SR(min)	138.50±20.45	127.92±23.75	2.13	0.036,**S**
TDA(min)	234.75±29.71	170.87±32.38	9.19	0.000,**S**

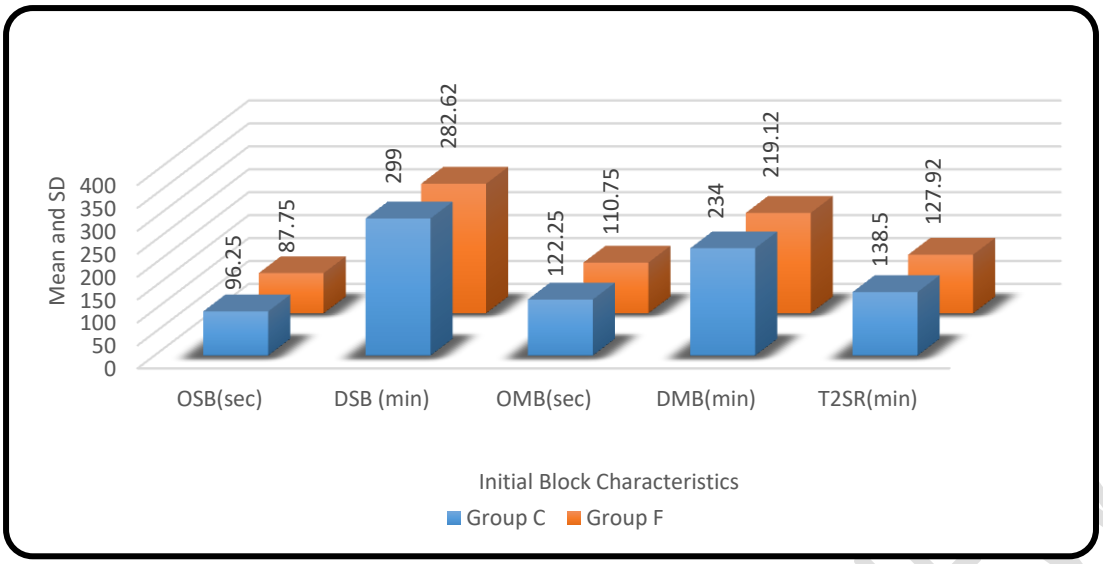
The comparison of initial block characteristics in both groups is shown in the table above. The clonidine group had a mean onset of sensory block of 96.25±16.66 seconds, while the fentanyl group had a mean onset of sensory block of 89.75±14.40 seconds (sec). In both groups, the mean onset of sensory block was significantly different (p-value 0.017). Similarly, the mean onset of motor block in the clonidine group was 122.25±18.04 (sec), while it was 110.75±23.46 (sec) in the fentanyl group. The difference was statistically significant (p-value 0.016), with the clonidine group having a faster onset of motor block.

The average duration of sensory block in the clonidine group was 299±28.69 minutes, while it was 282.62±30.98 minutes in the fentanyl group (p-value 0.016).Similarly, the average duration of motor blockade in the clonidine group was 234±27.36 minutes, while it was 219.12±28.34 minutes in the fentanyl group (p-value 0.019, S). When clonidine was compared to fentanyl, the difference was statistically significant.

In the clonidine group, the mean time for two segment regression was 138.50±20.45 (min), while in the fentanyl group, it was 127.92±23.75 (min) (min). There was a statistically significant difference (p-value 0.036, S).

In both groups, there was a statistically significant difference in overall analgesia duration. It was 234.75±29.71 (min) in group C and 170.87±32.38 (min) in group F. (p-value 0.000, S).

Graph 1.1: Comparison of initial block characteristics in patients in both the groups



Graph 1.2: Mean total duration of analgesia in patients in both the groups

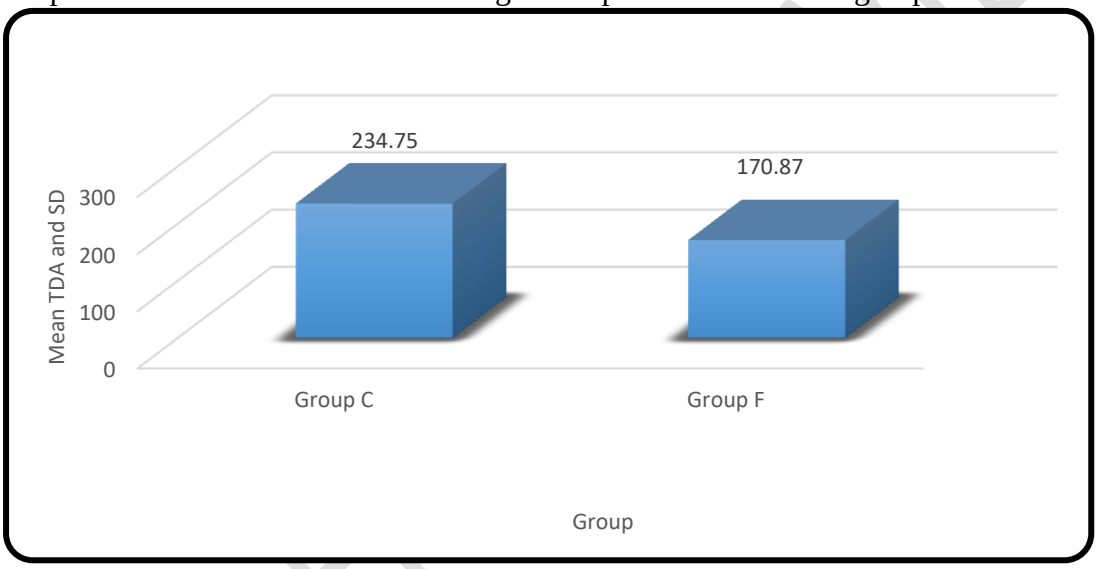
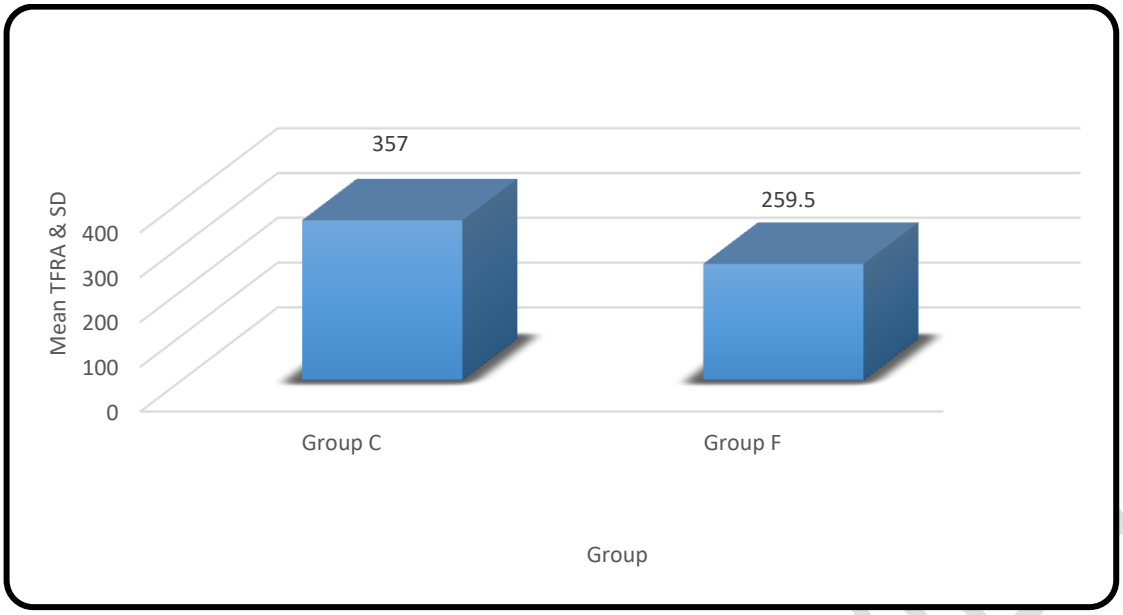


Table 2: Comparison of Time for Rescue Analgesia in both the groups

Group	N	Mean	Std. Deviation	Std. Error Mean	t-value	p-value
Group C	40	357.00	54.26	8.57	9.19	0.000 S,p<0.05
Group F	40	259.50	39.35	6.22		

Graph 2: Comparison of Time for Rescue Analgesia in both the groups

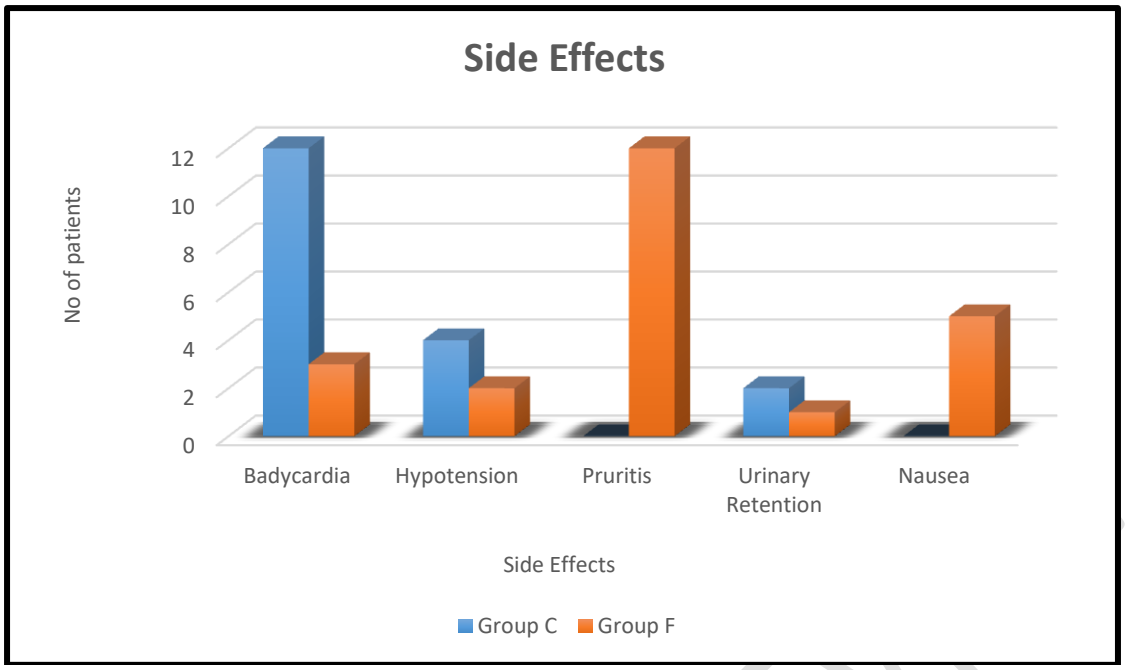


In both groups, the mean time required for rescue analgesia dose is shown in the table and graph above. The mean time for rescue analgesia in the clonidine group was 357.00 minutes, which was substantially longer than the 259.00 minutes in the fentanyl group (p-value>0.05, NS).

Table 3: Comparison of side effects in patients in both the groups

Complications	Clonidine		Fentanyl		א2-value
	No	%	No	%	
Bradycardia	12	30	3	7.5	15.72 P<0.0001,S
Hypotension	4	10	2	5	0.68 P=0.40,NS
Pruritus	0	0	12	30	12.77 P=0.0007,S
Urinary Retention	2	5	1	2.5	0.52 P=0.47,NS
Nausea	0	0	5	12.5	13.90 P=0.0002,S

Graph 3: Comparison of side effects in patients in both the groups



The percentage of adverse effects seen in both groups is shown in the table and graph above. Only 7.5 percent of patients in the fentanyl group exhibited bradycardia, compared to 30% in the clonidine group. In both groups, the difference was significant (p-value 0.05, S). Patients in the clonidine group had 10% hypotension, while only 5% of those in the fentanyl group had hypotension. In both groups, the difference was not significant (p-value 0.40, NS).Pruritus was not experienced by any of the patients in the clonidine group, whereas it was experienced by 30% of the patients in the fentanyl group. In both groups, the difference was statistically significant (p-value 0.0007, S). Urinary retention occurred in 5% of clonidine patients and 2.5 percent of fentanyl patients, a statistically insignificant difference (p-value 0.47, NS). Patients in the clonidine group did not experience nausea, whereas 12.5 percent of those in the fentanyl group did. In both groups, the difference was statistically significant (p-value 0.0002, S).

DISCUSSION:

The effects of adding clonidine and fentanyl to Bupivacaine were studied in order to determine which additive was the best by weighing effects versus side effects. Adding Clonidine to bupivacaine, even in very tiny dosages, considerably increases the onset and duration of sensory block, according to several studies. Clonidine's anti-nociception activity is mediated through post-junctional adrenoreceptor-mediated noradrenaline release in the dorsal horn (Eisenach et al, 1996).[8]Clonidine (Group C) provided greater early postoperative analgesia, as evidenced by a considerable delay in the first request for analgesia, less need for rescue analgesic diclofenac, and a lower VAS score. In a study by van Tuijl et al.[9] using 75µgs clonidine, the duration of analgesia was reported to be up to 120 (min), in contrast to the current study, where the mean duration of analgesia remained for 234.75±29.71 minutes, which is substantially longer than the previous study.

The duration of analgesia with Fentanyl was 170.87±32.38 (min), which is consistent with previous investigations by Biswas et al[10] and Belzarena[11]; 12.5g Fentanyl caused analgesia that lasted 248±11 minutes. (Biswas et al)[10]and 305±89 minutes (Belzarena, 1992)[11].In this study, the Fentanyl group had a faster onset of sensory block (87.75±14.40 sec) than the Clonidine group (96.25±16.66 sec) ($p<0.017$).

Sensory and motor block lasted 299±28.69mins and 234±27.36mins in the clonidine group, and 282.62±30.98mins and 219.12±28.34mins in the fentanyl group, respectively. There was a statistically significant difference.

In our trial, the average time for rescue analgesia in the clonidine group was 357 minutes, while it was 259 minutes in the fentanyl group. At VAS values of 5 or higher, the rescue analgesic Diclofenac 75mg was given intramuscularly. Two doses of rescue analgesic were necessary in the Fentanyl group, whereas only one dosage was required in the clonidine group.Our findings matched those of Chandrashekharappa k et al[12], who found that the period for initial rescue analgesia was 169.57 minutes in patients given 0.5 percent (2.5mg) hyperbaric bupivacaine and 30g clonidine. Though there is a substantial difference in time for initial recue analgesia when compared to our data, this could be due to the fact that our trial used a higher volume of local anaesthetic and clonidine, resulting in a longer period of analgesia.

The most prevalent side effects associated with the use of intrathecal Clonidine are hypotension and bradycardia. Hypotension was observed in this investigation, however it was not statistically significant. (p=0.94).This finding was similar to that of **Van Tuijet al[9]** who found that while mean arterial pressure (MAP) reduced with 75g intrathecal Clonidine, it was not clinically significant. In the Fentanyl group, 12 patients complained pruritus and 5 patients reported nausea. PONV (postoperative nausea and vomiting) is a well-known side effect of opioid therapy. Our findings are consistent with those of **Biswas BN et al[10]** who identified a 5% incidence of nausea and vomiting in their research. Some of the related studies on different combinations in anaesthesia were reviewed[13-18]. Clonidine can cause nausea and vomiting, however these are uncommon side effects. No one in our Clonidine group felt nauseous. The side effect of opioid administration has been observed to be pruritus. It happens as a result of opioids migrating cephalad in the CSF and interacting with opioid receptors in the trigeminal nucleus. Patients with minor pruritus with Fentanyl, but with self-limiting symptoms, were found by **Biswas BN et al[10]** in their trial, which was similar to ours.

CONCLUSION:

The current study found that combining intrathecal Clonidine 75 mg or Fentanyl 25 mg with hyperbaric Bupivacaine 15 mg increases the onset and duration of sensory and motor block while maintaining relative haemodynamic stability. Both medicines had minor adverse effects that could be effectively handled, despite Fentanyl having a lower frequency of side effects. Clonidine came in second. There were no negative side effects to be concerned about. The technique's cost-effectiveness and simplicity add to these benefits.

Despite the fact that Fentanyl is a good adjuvant, our research demonstrates that Clonidine is a better medicine in terms of anaesthetic quality and post-operative pain relief duration. As a result, we would like to propose Clonidine as a safe adjuvant for spinal anaesthesia, providing that the user is aware of the drug's effect-side effect profile and follows rigorous protocol when performing the procedure. The patients must be monitored by competent people after surgery.

As a result, we would like to suggest Clonidine as a safe adjuvant for spinal anaesthesia in patients having lower limb surgery.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of

the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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