

Effects of low dose ketamine versus ketorolac on spinal headache and post-operative back & leg pain in patients undergoing elective cesarean section.

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Abstract- Objective: To find out the effects of low dose ketamine versus ketorolac on spinal headache and post-operative back & leg pain in patients undergoing elective cesarean section.

Methods: This is a double-blind randomized clinical trial. Convenient sampling was used and the patients who met the inclusion and exclusion criteria were randomly assigned to one of two groups: either low dose IV ketamine (group A) (32 patients) or IV ketorolac (group B) (32 patients), using a computer-generated random numbers table. In both groups, the incidence of headache and its severity at 01, 4, 12, and 24 hours postoperatively and back and leg pain within 2 weeks postoperatively were also recorded. The severity of the headache was measured using the numeric pain rating scale (NPRS) for pain, and for back and leg pain, low back pain rating scale.

Results: The mean age in ketamine group is 26.53 ± 4.53 and ketorolac group is 26.53 ± 4.00 . There was significant improvement (<0.005) in spinal headache and post-operative back and leg pain in ketamine group.

Conclusion: There is more improvement in spinal headache and post-operative back and leg pain in ketamine group and have more side effects as compare to ketorolac group.

Index Terms- Ketamine, ketorolac, spinal headache, cesarean

I. INTRODUCTION

Delivery is a completely natural process that requires preventive and supportive measures. Normal delivery applies to mothers who are unable to perform it, otherwise, a cesarean section may be used in cases where childbirth is not possible or if it may pose risks to the mother and infant.(1)Performing a cesarean section (CS) without medical reason has traditionally been considered as inappropriate. Nevertheless, many obstetricians are being increasingly confronted with women requesting an elective CS.(2) In recent years, a number of factors have been under consideration as possible influences on the rising cesarean rate. Changing risk profiles among increasingly older primiparae are often cited as a reason for the rise in cesarean deliveries. An increase in maternal request cesarean sections also plays a part. However, the rise in cesarean section rates should not be viewed in isolation from

changes in society.(3) The maternal mortality is higher than that associated with vaginal birth (5.9 for elective cesarean delivery v. 18.2 for emergency cesarean v. 2.1 for vaginal birth, per 100 000 completed pregnancies in the United Kingdom during 1994–1996). Cesarean section also requires a longer recovery time, and operative complications such as lacerations and bleeding may occur, at rates varying from 6% for elective cesarean to 15% for emergency cesarean. Having a cesarean delivery increases the risk of major bleeding in a subsequent pregnancy because of placenta previa (5.2 per 1000 live births) and placental abruption (11.5 per 1000 live births). Among term babies, the risk of neonatal respiratory distress necessitating oxygen therapy is higher if delivery is by cesarean (35.5 with a prelabour cesarean v. 12.2 with a cesarean during labour v. 5.3 with vaginal delivery, per 1000 live births).(4) The most important long-term maternal benefit of cesarean delivery is potential protection of the pelvic floor, reducing the incidence of incontinence of stool, flatus, and urine, as well as pelvic-organ prolapse. The lifetime risk of undergoing at least one operation for pelvic-organ prolapse and urinary incontinence is 11.1 percent overall(5)

Ketamine is a derivative of phencyclidine and is one of the intravenous drugs used in general anesthesia. The high solubility of this drug in fat guarantees its rapid onset. Ketamine is the only intravenous anesthetic drug that has an analgesic effect. The analgesic effect of this drug is administered at low doses (0.1 - 0.8 mg/kg) by inhibiting NMDA receptors (N-methyl D aspartate), which inhibits CNS pain transfer, which may be effective in preventing dura perforation headache.(1, 6). Another effect of ketamine is a mild increase in intracranial pressure, so since post-dural puncture headache (PDPH) causes intracranial pressure depletion, ketamine may be effective in preventing PDPH by compensating this decrease in pressure.(7) Ketorolac is a new non-opioid analgesic which has been shown in some studies to have analgesic activity which was not significantly different from that of morphine and pethidine. It has been used successfully in the treatment of postoperative orthopaedic pain, and other types of acute pain.(8)

II. MATERIALS AND METHODS

This double-blind randomized clinical trial was conducted from 1 March 2022 to 30 February 2023 in Services Hospital Lahore, Pakistan. The objective and protocol of the study were explained to the subjects who met the inclusion criteria in simple language and their informed consent was obtained in writing if they were willing to join the study. Participation in this research caused no disorder in diagnostic and therapeutic procedures and no additional costs were imposed on the patients.

The study population was primary pregnant women who were candidate for elective cesarean section with spinal anesthesia. According to Behdad et al. (6) study, the minimum sample size for each group was about 29 people with a 95% level of confidence. Taking into account a 20% drop, our study sample size was 32 per group. Convenient sampling was used to select patients from those who met the inclusion criteria. Checklists were used to gather patients' information such as demographic data (age, weight, and height), length of the operation and duration of hospital stay. All information was gathered and recorded in the recovery section.

In both groups, the incidence of headache and its severity at 01, 4, 12, and 24 hours postoperatively and back and leg pain within 2 weeks postoperatively were also recorded. The severity of the headache was measured using the numeric pain rating scale (NPRS) for pain, and for back and leg pain, low back pain rating scale(9, 10) used, which was taught to the patients before the surgery. In case of a headache greater than or equal to 4, diclofenac 100 mg suppository was administered. Primary pregnant women of 20 to 35 years who were candidate for elective cesarean section with spinal anesthesia who had ASA class 1 - 2, with no history of migraine or other types of headaches, psychological problems and seizures, coagulation disorders, and any drug addiction, were included in the study. The incidence of drug allergy, respiratory complications, severe bleeding, bronchospasm and laryngospasm, changes in anesthesia, and having more than once experience of spinal anesthesia, history of drug abuse, chronic diseases such as diabetes, history of previous cesarean section or any other abdominal surgery, abnormal bleeding during and/or following the surgery, allergic reaction to ketamine or ketorolac, psychological

disorders, high blood pressure, high intracranial pressure, history of seizure, and history of hallucination following taking ketamine and women with contraindications to spinal anesthesia were the exclusion criteria. The patients who met the inclusion and exclusion criteria were randomly assigned to one of two groups: either low dose IV ketamine (group A) (32 patients) or IV ketorolac (group B) (32 patients), using a computer-generated random numbers table. The method of blinding was that patients were unaware of the type of the drug received, and the drugs were prepared in encoded uniform syringes by one of the operating room nurses who was not involved in the study and assessor was also blind.

Before drug administration, one of the researchers assessed the initial headache severity using the numeric pain rating scale, The researchers used the Numeric Pain Rating Scale (NPRS) to measure patients' headache severity. The NPRS is a segmented numeric version of the visual analog scale (VAS) in which a respondent selects a whole number from 0 to 10 integers that best reflects the intensity of their pain. A score of zero indicates no pain and as the intensity of pain increases, the patient chooses a higher score. A score of five indicates average pain, and a score of ten means the worst possible pain(11) and back and leg pain using back pain rating scale. Then, ketamine at a dose of 0.6 mg/kg or ketorolac at a dose of 30 mg was administered by another person/nurse. In the next step, the same researcher who initially assessed the pain, re-assessed pain severity using the NPRS and the rate of adverse drug reactions at 01, 4, 12, and 24 hours after drug administration. Low back pain rating scale within 2 weeks post-operatively. The investigator, who was responsible for pain assessment, was kept blinded to the type of the administered drug. If pain was intolerable despite administration of ketorolac or ketamine and spinal headache was persistent, treatments included complete bed rest, adequate hydration, NSAID analgesics.

The headache scores and back pain were compared between the two groups using t-tests and Mann-Whitney U test. Chi-squared and Fisher's exact test were used to compare the frequency of side effects. The statistic software SPSS was used for all statistical analysis. For all analyses, a p-value of less than 0.05 was considered to be significant.

III. RESULTS

There was no significant difference between the both groups in participants' age and their height. There was significant difference between the two groups in term of weight, length of operation and hospital stay [Table 1]. All of the participants were primigravida

Table 1: Demographic Data

Characteristic	Group A (Ketamine)	Group B (Ketorolac)	P value
Age	26.53±4.53	26.53±4.00	1.00
Weight	85.43±7.99	79.46±9.48	0.008
Height	5.4±0.36	5.45±0.28	.592
Length of operation	47.37±10.93	52.84±8.90	0.032
Hospital stay	2.8±0.76	3.65±1.09	0.001

There was a significant difference between the two groups in headache pain scores at one, 4, 12 and 24 hours following surgery and back and leg pain. The headache pain scores were

significantly greater for the group B than the group A at all time intervals ($p < 0.001$) shown in table 2

Table 2: Between group comparison of headache and back pain

	Group A (Ketamine)	Group B (Ketorolac)	P value
Headache			
After 1 hour	2.71±0.68	3.53±0.5	<0.001
After 4 hours	3.09±0.81	5.12±0.75	<0.001
After 12 hours	2.56±0.50	5.68±0.82	<0.001
After 24 hours	2.34±0.60	4.09±0.89	<0.001
Back and leg pain			

Pain within 2 weeks	33.46±7.55	55.84±8.57	<0.001
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Table 3 summarizes the frequency of common side effects of surgery in the two groups. There was significant difference between the two groups in the occurrence of nausea ($p=0.001$). Although bloating was more common in the group B than the group A, the difference was significant ($p=0.000$). Vomiting was significantly more common in the group A than the group B ($p=0.01$). There was a significant difference between the two groups in hallucination ($p=0.000$), which was more common in the group A than the group B.

Table 3: Side effects in both groups in percentage

	Group A (Ketamine) (%)	Group B (Ketorolac) (%)	P value
Nausea	65.6	25	0.001
Vomiting	75	43	0.01
Hallucination	68.8	15.6	0.000
Itching	71.9	21.9	0.000
Confusion	68.8	12.5	0.000
Bloating	18.8	71.9	0.000

IV. DISCUSSION

This study was done to compare low-dose ketamine versus IV ketorolac in spinal headache and post-operative back and leg pain in patients undergoing cesarean section. According to the results of this study, low-dose ketamine was as effective as IV ketorolac in spinal headache and post-operative back and leg pain of these patients, but its use was associated with a higher rate of side effects. In the present study, ketamine and ketorolac were equally effective in controlling pain severity but the occurrence of complications like nausea, vomiting, confusion and hallucination was higher following ketamine administration and bloating is more common in ketorolac group.

Researchers who proposed the analgesic effects of ketamine at subdissociative low doses. However, after several years, the effectiveness of ketamine as an analgesic is still a matter of debate and discussion. Some researchers believe that its antihyperalgesic effects are stronger than its analgesic properties, and a number of studies are being conducted in this regard(12, 13). Postoperative pain is one of the most significant side effects of cesarean section(13). There are numerous methods for controlling postoperative pain. Opioids, such as morphine and pethidine, are the most commonly used medications; however, they usually cause multiple side effects(14) In an attempt to avoid the side effects of opioids, many scientists(14-16) have examined the effectiveness of different doses of ketamine administered in a variety of methods as an alternative approach for controlling postoperative pain following cesarean section. We examined the effect of low-dose intravenous ketamine at the dose of 0.6 mg/kg or ketorolac at a dose of 30 mg on postoperative pain in women undergoing caesarean section. Our results showed that the spinal headache and post-operative back and leg pain were significantly greater for the group B than the group A at one, 4, 12, and 24 hours following surgery indicating that participants in the group B experienced a greater level of postoperative pain than those in the group A. This finding was similar to reports by Sen and

colleagues(17) who showed that postoperative pain scores were significantly lower in elective cesarean section women who received low-dose intravenous ketamine (0.15mg/kg) than those who received an equal volume of normal saline intravenously (control group) and those who received intrathecal fentanyl. A similar findings was also found in another article which concluded that in ketamine group as compare to the control group there was significant improvement in terms of pain(18).

V. CONCLUSION

We conclude that administration of low-dose intravenous ketamine as compare to IV ketorolac following cesarean section with spinal anesthesia reduces postoperative back and leg pain and spinal headache and subsequently the need for analgesics. It also reduced the prevalence of side effects.

To fully understand the effect of ketamine in postoperative pain following cesarean section we recommend that future studies examine the effect of different doses of ketamine, alone and in combination with other medications to reduce its inevitable side effects (e.g., benzodiazepine to control hallucination). Furthermore, we recommend future studies use larger sample sizes to increase their power in detecting the true differences between the experimental and control groups.

Conflict of Interest

The authors declared that there is no conflict of interest.

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