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PREEMPTIVE KETAMINE FOR POSTOPERATIVE ANALGESIA FOLLOWING GENERAL ANESTHESIA-ASSISTED TOTAL ABDOMINAL HYSTERECTOMY (TAH)

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ABSTRACT

Background: The best way to deal with pain after surgery is to start treating it before it even happens, according to the theory of "pre-emptive analgesia." Postoperative pain following total abdominal hysterectomy can be effectively managed with preemptive low-dose Ketamine.

Objectives: This study set out to answer whether or not prophylactic low-dose Ketamine can be used to effectively treat acute postoperative pain in patients who had undergone general anesthesia for a total abdominal hysterectomy.

Study Setting: Khyber Teaching Hospital, Peshawar from January 2023 to June 2023.

Methods: Fifty-two women between the ages of 35 and 50 who hadcomplete elective Patients undergoing general anesthesia for abdominal hysterectomy were randomly divided into two groups, those with ASA physical status I and those with ASA physical status II. Group A patients were given a 60-90 second I/V infusion of 10 ml of normal saline before surgical incision. Within 60-90 seconds before incision, patients in Group B received 0.15 mg/kg ketamine (in 10 ml normal saline) I/V. Consistent anesthetic procedures and patient interviews became the norm. Information on pain, analgesic use, adverse events, and the degree of recovery was collected over 24 hours.

Results: Patients who were given Ketamine before surgery reported much less pain in the first 24 hours after the procedure than those who were given a placebo. First, analgesic requirements were significantly lower in group A (25.67±1.60) than in group B (57.3±32.97; p = 0.00). Opioid use was significantly higher in group A (290.00±9.09) than in group B (210.6±77.01) (p = 0.00). The urgency with which analgesia was required and the total amount utilized differed significantly between the groups. Neither group differed significantly from the other regarding hemodynamic variables or adverse effects.

Conclusion: Avoidance therapy with a low dose of intravenousKetamine is well-tolerated, non-opioid analgesia effective in coping with moderate-to-severe discomfort after surgery.

Keywords: Abdominal hysterectomy, Ketamine, and preventative analgesia

INTRODUCTION

As a frequent side effect of medical care, most patients will have to deal with pain. That is typically related to actual or potential tissue damage [1]. In reaction to a painful stimulus, whenever there is

tissue damage, whether from an accident or surgery, the body releases chemicals that cause pain. A hormonal reaction in the nervous system that decreases as pain increases [2].is often presents alongside acute postoperative pain. Preemptive analgesia is a theory put forth by academics who believe that preventing postoperative pain is preferable to dealing with it once it has already begun. It has been hypothesized that giving patients their analgesics before any nociceptive input may reduce the occurrence of sensitization and lead to better postoperative pain management [3]. Enough doses of opioids, Ketamine, nonsteroidal anti-inflammatory drugs (NSAIDs), or a central neuronal block can help with this. By stimulating C-fibers, painful stimuli increase the sensitivity of sensory neurons to peripheral inputs, a process known as central sensitization. Wind-up,6, which occurs after continuous stimulation of C- fibers, can also activate spinal sensory neurons [4-6]. An increase in c-fos appearance in sensory neurons makes sensitizations operate, which occurs as a result of the activation of N-methyl-D-aspartate (NMDA) receptors [7-9]. Opioids are highly effective painkillers, but they are underutilized because of their costly price tag and unpleasant side effects (drowsiness, respiratory depression, nausea, vomiting) [10]. Ketamine has analgesic properties because it blocks NMDA receptors. NSAIDs are a useful alternative to opioids for pain relief. Still, they come with their own set of risks, problems with platelet function, prolonged bleeding, decreased renal perfusion, and postoperative gastrointestinal bleeding is all examples. We have chosen Ketamine as a preventive analgesic medication just before skin incision to reduce the requirement for analgesics and the negative effects of opioids and NSAIDs [11-13]. Due to its widespread availability and inexpensive cost, Ketamine is increasingly being used. Before and after the administration of preventative Analgesic requirement, total 24-hour pethidine consumption, pain intensity, hemodynamic status, sedation score, recovery status, and complications including nausea, vomiting, hallucinations, delirium, etc. after low-dose (0.15mg/ kg) I.V. ketamine were assessed.

MATERIALS AND METHODS

This clinical experiment was carried out in Khyber Teaching Hospital, Peshawar from January 2023 to June 2023. Before asking anyone to take part in the study, we made sure everyone knew exactly what we were trying to accomplish. We ensured we had approval from the ethical Clearance Committee before initiating this study. Sixty patients with elective full abdominal hysterectomy under general anesthesia, ages 35-50, weighing 45-65 kg, and classified as participants with an ASA physical status of I or II were randomly divided in half (30 in each group). In this experiment, we used a deck of cards to generate a random number. Patients were not allowed to participate if they had an allergy to Ketamine, were already on long-term painkillers for a condition like chronic pain syndrome, or had a history of conditions including high blood pressure, heart disease, valvular heart disease, neurological and behavioral issues, or substance abuse. To quantify the degree of discomfort felt after surgery, both a visual analog scale (VAS) and a verbal rating scale were used (VRS). The patient's pulse, blood pressure, and temperature were measured before the operation. Readings of the patient's pulse, respiration rate, and oxygen saturation were taken (SPO2). Group A patients were given a 60-90 second, 10-ml intravenous (I/V) infusion of normal saline before incision. Patients in Group B received 0.15 mg/kg of Ketamine (in 10 ml of normal saline) I/V 60-90 seconds before incision. The standard operating room monitor was hooked up to the I/V channel for regular infusion. The doctors could monitor patients' vitals, including their heart rate, blood pressure, and oxygen saturation levels (SPO2). All patients received general anesthesia in the same manner. After 3 minutes of preoxygenation with 100% O2, induction was achieved with intravenous thiopental sodium (5mg/kg) and fentanyl (2g/kg). 0.1mg/kg of vecuronium bromide was administered to facilitate tracheal intubation. Anesthesia continued with halothane, oxygen (70:30), and nitrous oxide. To get air into the lungs, a ventilator was utilized. Before beginning the procedure, the patient's pulse and blood pressure were checked every three minutes. No matter how often the vecuronium was administered, the muscle relaxation remained the same. To counteract the anesthetic and get the muscles working again after surgery, neostigmine (40 g/kg) and atropine (20 g/kg) were given. The tube was taken out as soon as the patient regained full consciousness. Once the patient had fully recovered from the

anesthetic, they were transferred to the postoperative ward. Intramuscular injections of pethidine (inj. pethidine) at a dosage of 1.5 mg/kg were given on demand to all patients after surgery. The rescue analgesic pethidine (10 mg through IV injection) was given when the VAS pain score was 20 mm or higher. Times from initial pain to the first request for analgesia (TFA) were recorded. Both groups' daily pethidine consumption was also tracked. Nurses interviewed all patients in the same way after their procedures, regardless of which medication was being studied. Every 15 minutes for the first hour, and then again at 2, 4, 6, 12, 18, and 24 hours after patients arrived in the postoperative ward, the pain was assessed using a visual analog scale (VAS). A scale from 1 (fully alert) to 5 (very sedated) was used to rate sedation levels during this time (deeply asleep but easily aroused). After surgery, the patient's vitals were recorded at regular intervals for 24 hours. This included monitoring the patient's respiration rate, heart rate, systolic blood pressure, diastolic blood pressure, and arterial oxygen saturation (SPO2). The frequency with which people experienced unwanted symptoms, such as feeling unwell or throwing up, was recorded. All data were summarised using means and standard errors or frequency counts. We gathered and analyzed the data using unpaired t-tests, Chi-square tests (x 2), and analysis of variance (ANOVA). Statistical significance was assigned to the results when the probability level was less than 0.05. (Confidence Interval CI- 95 percent).

RESULTS

Age and BMI were comparable across the two groups (p=0.928 and p=0.477, respectively). The average number of analgesics needed by Group A was 25, while Group B averaged 57,33±2.97. In group A, the average daily opioid dose was 290.00±9.09, while in group B, it was 210.6±77.01. Statistical analysis revealed a disparity in the frequency with which an analgesic at the onset of pain and the number of times an analgesic was used between the (p0.001). Both groups similarly experienced postoperative nausea, vomiting, delirium, and hallucinations. Before extubation, there was no significant difference in heart rate between the two groups (Table IV) (p=0.008), although there was a significant difference in the second hour after the operation. Table V shows that there was a statistically significant difference (p = 0.016) in systolic blood pressure between the two groups at the time of incision. Table VI shows no statistically significant differences in diastolic blood pressure over time between the two groups. After extubation, there were statistically significant variations in VAS scores between the two groups between the first and fourth hours (table 1, p 0.05). (p = 0.375). As seen in table 2, there was a statistically significant difference in VRS between the two groups during the following extubation, exceptfor the 12-hour time point. (p = 0.713). Before the 18th hour following extubation, sedation levels were steady (p > 0.05; Table VII; p = 0.018).

Table.1. Quantitative analysis of demographic information

Variable	Group A (n=30)	Group B (n=30)	P-Value
Age years	41.37	41.47	0.928
Weight kg	55.47	54.30	0.447

T-tests were performed to compare the two groups' means and standard deviations. A value is considered statistically significant when p is less than 0.05.

Table.2. Initial pain relief required and total pethidine intake

Background	Variable A	Variable B	P-Value
First analgesic	25.67±1.60	57.33±2.97	0.000
Total consumption (mg) in 24 hours	290.00± 9.09	210.67± 7.01	0.000

The two groups were compared using T-tests, which calculated means and standard deviations. For statistical significance, a p-value of less than 0.05 is required.

Table.3. Problems (such as sickness and dizziness) experienced by the research subjects

Complications	Group A	Group B	P-Value
Vomiting	3.00	2	1
Nausea	3	4	1.00

T-tests were performed to compare the two groups' means and standard deviations. When the significance level is below 0.05, the value is marked as significant.

Table.4. Variations in heart rate (in beats per minute) across time for the groups under study

Group	Baseline	During incision	During induction	Extubation after 1 hr.	Extubation after 8 hr.	Extubation after 12 hr.	Extubation after 18 hr.	Extubation after 24 hr.
Group A	74.47	102.00	100.37	90.83	82.07	79.40	80.37	79.07
Group B	72.83	99.67	99.00	86.93	83.07	81.63	82.43	78.77
P-Value	0.333	0.148	0.313	0.008	0.489	0.225	0.182	0.810

Mean standard error of the mean is provided for values. A t-test was used to compare the two groups. An ANOVA was performed to analyze the interplay between the groups and the passage of time. When $p<0.05$, results are considered significant.

Table.5. Systolic blood pressure (mmHg) changes over time for the various study groups

Group	Baseline	During incision	During induction	Extubation after 1 hr.	Extubation after 8 hr.	Extubation after 12 hr.	Extubation after 18 hr.	Extubation after 24 hr.
Group A	120	147	112	129	125	124	125	`123
Group B	121	150	119	128	124	123	126	117
P-Value	0.947	0.307	0.016	0.887	0.474	0.547	0.655	0.082

Mean standard error of the mean is provided for values. A t-test was used to compare the two groups. An ANOVA was performed to analyze the interplay between the groups and the passage of time. When $p<0.05$, results are considered significant.

Table.6. The average percentage change in diastolic blood pressure (mmHg) over time for the various study groups

Group	Baseline	During incision	During induction	Extubation after 1 hr.	Extubation after 8 hr.	Extubation after 12 hr.	Extubation after 18 hr.	Extubation after 24 hr.
A	75	95	72	79	76	75	74	73
B	76	95	76	79	76	76	79	72
P	0.516	0.924	0.080	0.838	0.354	0.736	0.083	0.367

The mean, standard error of the mean is provided for values. A t-test was used to compare the two groups. An ANOVA was performed to analyze the interplay between the groups and the passage of time. When $p<0.05$, results are considered significant.

DISCUSSION

Despite an annual total of 23 million procedures, postoperative pain treatment is typically insufficient. An analgesic regimen is delivered before the commencement of unpleasant stimuli, a new concept in a clinical practice known as preemptive analgesia, to prevent the nervous system from becoming sensitized to following stimuli, which could increase pain perception. Because of the predictable pattern of painful stimuli, preemptive analgesia is especially useful in the surgical situation. Intravenous opiates, nerve blocks, subarachnoid blocks, and epidural blocks can relieve postoperative pain for up to a year if given to the correct patients. The best perioperative analgesic regimes are those that can prevent nervous system sensitization from occurring. Preemptive low-dose Ketamine

(0.15mg/kg delivered I/V soon before (60-90 sec) surgical incision to minimize central sensitization before tissue harm may play an important function as an adjuvant to opioids in the management of acute postoperative pain. After a little dose of Ketamine was added to the general anesthesia administered to patients undergoing total abdominal hysterectomy, the amount of pethidine needed to keep them asleep during the procedure decreased dramatically.

Group A waited an average of 25 minutes and 67 seconds, while Group B waited an average of 57 minutes and 2.97 seconds. Initial analgesic requirements did not differ from the control group at the 0.000 level of significance. Group A consumed 290.00±9.09 mg of pethidine during 24 hours, while Group B consumed only 210.6±77.01 mg (a difference of roughly 27 percent). This study demonstrates that Ketamine has strong opioid-sparing benefits and is useful as preventive analgesia. Patients having cholecystectomy who received low-dose Ketamine (0.15mg/kg) in addition to general anesthesia experienced a nearly 40% reduction in their cumulative dose of morphine, according to research by Roytblas et al.9. In patients undergoing inguinal herniorrhaphy, Tvers Koy et al.10 found that preemptive ketamine administration at a dose of 20 g/kg followed by a continuous infusion rate of 20 g/kg/min decreased wound hyperalgesia. Ketamine was found to considerably lower cumulative morphine consumption over 24 hours when compared to placebo (WMD [weighted mean difference] = -15.7 mg; Elia et al. Not only did he find the morphine's unpleasant side effects to be unaffected by the Ketamine treatment, but he also found out that there was no benefit to the treatment. Patients in group A (the control group) reported significantly higher pain levels than patients in group B (the experimental group) within the first few hours after surgery (the study group). Members of Group B were significantly less likely to be dissatisfied than those in Group A. (P 0.05). In 21 of 30 studies, rescue analgesics' usage was either reduced or less effective when Ketamine was provided first. The following are signs of elevated sympathetic activity: Some examples include the patient's pulse, blood pressure, peripheral resistance, and cardiac output. In this study, we could not find any evidence of a statistically significant difference in either blood pressure or heart rate. There was no statistically significant difference between the two groups concerning respiratory rate, sedation, or arterial oxygen saturation (SPO2). Elia's study comparing 391 ketamine-treated patients to 284 placebo-treated persons found no decrease in PONV [14-15]. And colleagues observed that 705 patients treated with Ketamine had significantly less nausea and vomiting than 578 people given a placebo [16]. One possible explanation for the decreased incidence of PONV is the pethidine-sparing effect. No statistically significant difference in the occurrence of PONV was seen between the two groups in this study. Neither set of patients had any hallucinations, delirium, or bad dreams. There was no evidence of that psychomimetic phenomenon. Roytblat L et al. discovered a finding that agrees with this one. It has been discovered that combining Ketamine with other substances reduces psychomimetic symptoms. Some methods of inducing anesthesia include thiopental, halothane, nitrous oxide, and benzodiazepines [17]. This study did not miss a single detail.

CONCLUSION

The results of this study show that patients undergoing elective total abdominal hysterectomies under general anesthesia who surgical incision and a mild dosage of Ketamine (0.15mg/kg) experienced a preemptive analgesic effect that significantly reduces their need for additional pain medication after surgery.

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