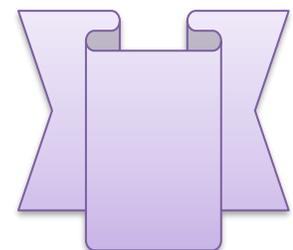
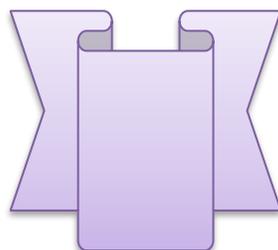
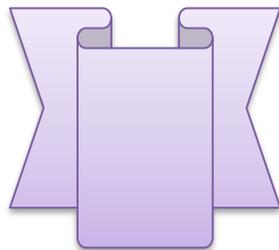
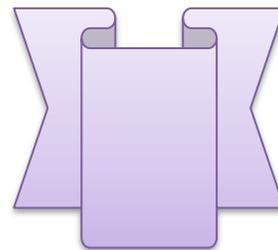
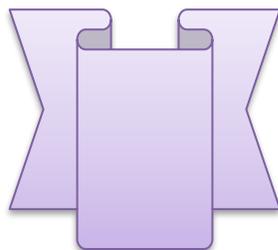
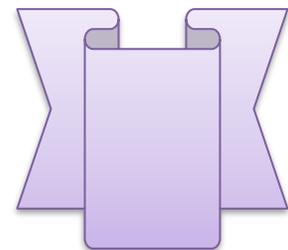
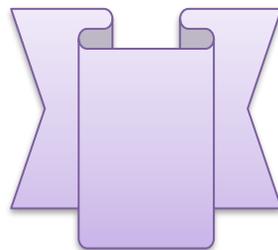
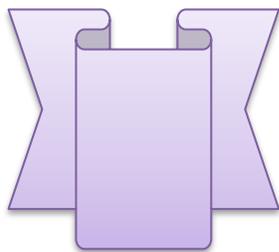


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Original Article

Ketamine versus Tramadol for Analgesia in Spontaneous Vaginal Delivery: A Randomized Clinical Trial

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ABSTRACT

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Background: The outcome of spontaneous vaginal birth is improved using analgesics during the three phases of labour. Both pharmaceutical and non-pharmaceutical approaches have been tried. Therefore, this study aimed to compare parenteral ketamine and tramadol regarding their analgesic effect and maternal and labor outcome.

Patients and Methods: This randomized clinical trial was conducted on 100 primigravida and multigravida women. The study population was randomized into two equal groups; ketamine group: received low dose ketamine 0.4 mg/kg body weight intravenous [IV] slowly over 30-60 seconds with maintenance dose at the rate of 1 mg/min in normal saline after 30 min of induction dose using an infusion pump and the tramadol group: 1 mg/kg iv slowly for 5-10 minutes then after 30 min we start maintenance by IV Tramadol 0.3 mg /kg/hr.

Results: Ketamine significantly decreased the time of onset analgesia [p=0.036] and VAS [p=0.002] than tramadol. Ketamine has a significant advance in patient satisfaction than tramadol. The duration of all 3 stages of labor, Apgar score after 1 min, Apgar score after 5 min, and the percentage of maternal complications did not exhibit any significant change between both groups.

Conclusion: In spontaneous vaginal delivery, ketamine and tramadol are considered safe drugs with low complications and similar Apgar scores after 1 min and also after 5 min with superiority of ketamine than tramadol regarding the earlier time of onset analgesia, lower VAS score and better patient satisfaction.

Keywords: Ketamine; Tramadol; Analgesia; Spontaneous Vaginal Delivery.



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INTRODUCTION

The pain felt during labor is one of the women's most excruciating experiences the women ever encounter. Fear of pain has been related to prolonged first and second stages of regular labor and dissatisfaction with the typical delivery process [1].

Pain during labor can be managed in several ways, including the inhalation of entonox or intravenous administration of ketamine or the oral administration of opioids like morphine, pethidine, or fentanyl [e.g., intravenous, inhalation, local, epidural anesthesia, and patient-controlled epidural] [2].

Tramadol is a mild opioid that suppresses nor-adrenergic and serotonergic transmission. Its analgesic effectiveness is comparable to other opioids, such as meperidine, although maternal sedation and infant respiratory depression are minimal. Tramadol can be administered orally, intravenously, intramuscularly, and epidurally with few adverse effects. It is a strong analgesic that can be administered to individuals in labor. Parenteral tramadol is less intrusive than oral intake. Obstetricians can also administer it [3, 4].

Ketamine is an antagonist of the N-methyl-D-aspartate [NMDA] receptor. Ketamine's analgesic, anesthetic and psychotomimetic actions result from NMDA receptor antagonism, which prevents central sensitization in dorsal horn neurons, resulting in analgesia. Ketamine interferes with spinal cord pain transmission [5].

Anesthesiologists are always searching for a painkiller that is effective and safe for both the mother and the fetus without interfering with the uterus's natural ability to contract. Therefore, this study aimed to evaluate the relative efficacy of parenteral tramadol and ketamine in reducing pain during delivery and for the mother's outcome.

PATIENTS AND METHODS

One hundred pregnant women from varying socioeconomic backgrounds participated in this randomized clinical investigation, admitted to the Department of Obstetrics and Gynaecology, Tertiary Care Hospital GNP hospital Khamis mushaira, Saudi Arabia, from June 2016 to June 2019.

The ethical committee approved the study. Signed consent was obtained from the patient.

Women with a cervical dilation of at least 4 cm who were in the active phase of labor with a single, healthy baby in a head-first position and who were at least 38 weeks along were eligible to participate in the trial.

Premature membrane rupture, Intrauterine growth retardation, a history of uterine scarring, a body mass index above 35, and repeated pregnancies were all excluding factors.

The included women were randomly assigned to the ketamine or tramadol group using a computer-generated random number in the parallel method. Because of the different infusion methods, this study was open labeled.

Ketamine group [n=50]: Patients were premedicated with 0.005 mg/kg of glycol-pyrrolate before receiving an IV infusion of 0.4 mg/kg of ketamine over 30-60 seconds. After 30 minutes of the induction dosage, a maintenance dose was begun via infusion pump at a rate of 1 mg/min in normal saline.

Tramadol group [n=50]: Iv administration of 1 mg/kg tramadol hydrochloride over 5-10 minutes, followed by IV maintenance injection 30 minutes later. 0.3 mg/kg/ hour of tramadol.

Full history taking and gynecological examination was done. A complete explanation of the Study design and purpose, as well as the visual analog scale [VAS], was instructed to the mother.

The study started at the active phase of labor, 4 cm cervical dilatation with effective uterine contraction [3 Contractions lasting for 40 to 50 sec in 10 minutes].

After administering ketamine and tramadol, the following values were recorded: Pain alleviation onset time [defined as the time interval between the introduction of the drug and any pain relief felt by the patient], The Apgar score at 1 and 5 minutes after birth, as well as the method of delivery, the length of labor's three phases, the presence of any complications or negative medication effects for the mother, and the VAS pain score were all recorded.

On an individual basis, patients were monitored. Partogram was preserved. Monitoring of labor included fetal monitoring with the use of Prenatal Non-Stress Test [NST] equipment, as well as maternal monitoring with a cardiac monitor measuring pulse, blood Pressure [BP], breathing rate, and blood oxygen level [SpO₂].

All required instruments for newborn resuscitation were stored on a stand. When the cervix attained complete dilation, the dosage was not raised. Even if she felt discomfort, the dose from the first stage was continued in the second. This allowed the patient to reach a light plane of analgesia when she could almost feel the diminished discomfort of uterine contractions and was instructed to bear down.

After birth, the infusion continued till the completion of the episiotomy suturing. This reduces the requirement for local analgesia during the episiotomy suturing process.

The primary outcome was the onset of pain relief, and the secondary outcomes were VAS score, type of delivery, duration of the 3 stages of labor, Apgar score at 1 minute and 5 minutes, maternal complication, and side effects of the drug.

Statistical analysis

SPSS v26 was used for statistical analysis [IBM Inc., Chicago, IL, USA]. Comparing the two groups using an unpaired Student's t-test, quantitative data were provided as mean and standard deviation [SD]. When applicable, qualitative variables were given as frequency and percentage [percent] and examined using the Chi-square test or Fisher's exact test. A two-

tailed $p < 0.05$ was deemed statistically significant.

RESULTS

No significant difference was detected in the demographic profile and gestational age. Both groups have no difference regarding age, weight, height, BMI, ASA physical status, and gestational age [table 1].

There is a significant decrease in time of onset analgesia between both groups, less in the ketamine group [P value=0.036] [figure 1].

There is a significant decrease in VAS between both groups, less in the ketamine group [P value=0.002] [figure 2].

Patient satisfaction was significantly higher in the ketamine group than in the tramadol group [figure 3].

Rate of CS was greater in tramadol group in compare with ketamine group [P value = 0.031] without significance in NVD and instrumental delivery [table 2].

There is no considerable change in the duration of all 3 stages of labor between both groups. There is no significant change between both groups in Apgar score after 1 min and 5 min. So, ketamine and tramadol are safe for the baby with no residual sedation effect [table 3].

No significant change in the percentage of maternal complications between both groups. The most common side effect is nausea and vomiting, but in a very low percentage, so ketamine and tramadol are considered safe drugs in normal delivery [table 4].

Table [1]: Patient's characteristics and gestational age of the studied groups

	Ketamine group [n = 50]	Tramadol group [n = 50]	P value
Age [years]	28.32 ± 4.78	26.6 ± 4.42	0.065
Weight [kg]	77.6 ± 8.34	80.08 ± 7.26	0.116
Height [m]	1.67 ± 0.06	1.69 ± 0.06	0.194
BMI [kg/m ²]	27.81 ± 3.34	28.16 ± 3.12	0.589
Gestational age [weeks]	38.86 ± 1.41	39.32 ± 1.45	0.111

Data are represented as mean ±SD or frequency [%], BMI: Body mass index, ASA: American society of anesthesiologists

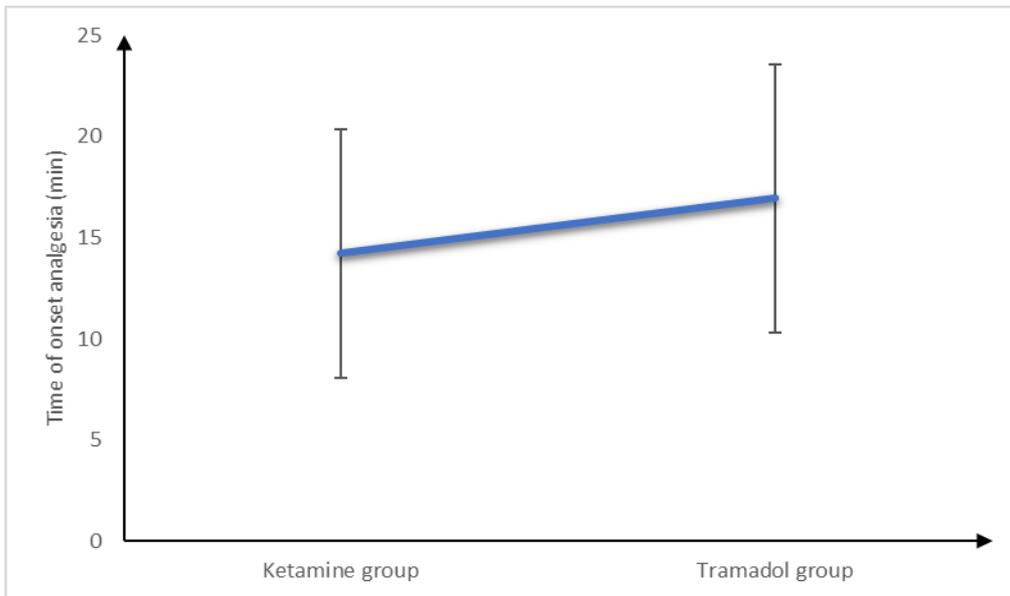


Figure [1]: Time of onset analgesia of the studied groups

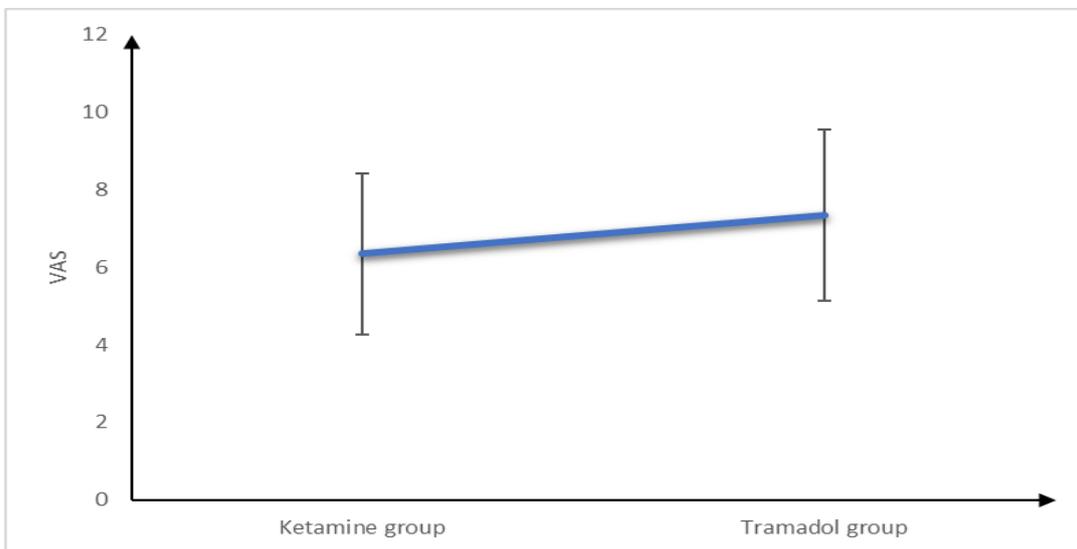


Figure [2]: Visual analog scale [VAS] during labor period of the studied groups

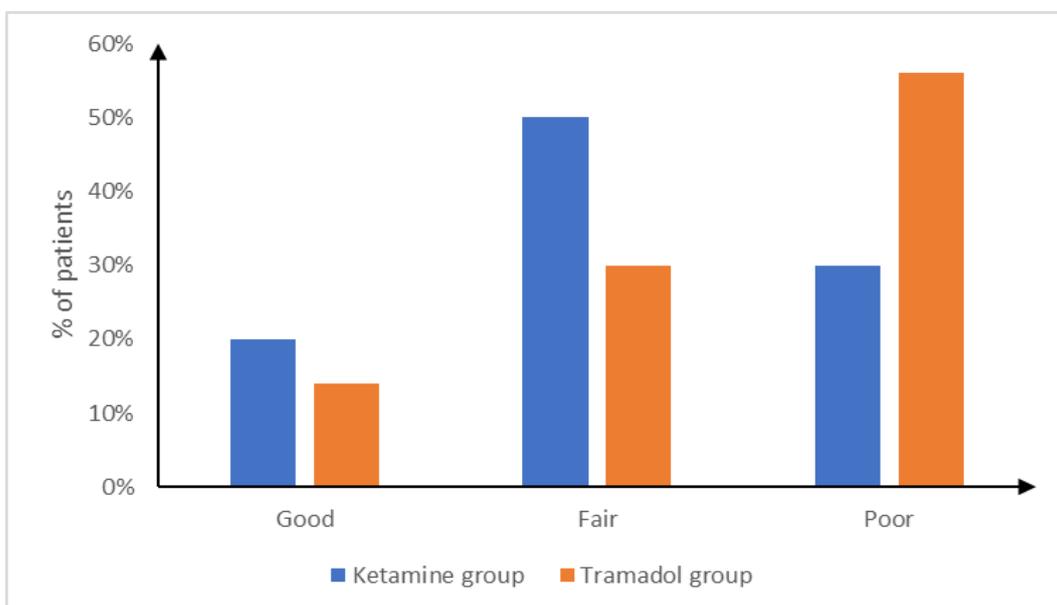


Figure [3]: Patient satisfaction of the studied groups

Table [2]: Type of delivery of the studied groups

Type of delivery	Ketamine group [n = 50]	Tramadol group [n = 50]	P value
Normal vaginal delivery	48 [96%]	41 [82%]	0.051
LSCS	1 [2%]	8 [16%]	0.031*
Instrumental	1 [2%]	1 [2%]	1.000

Data are represented as frequency [%]. LSCS: Lower [uterine] segment caesarean section. * significant as P value <0.05

Table [3]: Duration of 1st, 2nd, 3rd stage of labor and APGAR score of the studied groups

	Ketamine group [n = 49]	Tramadol group [n = 48]	P value
Duration of 1 st stage of labor [min.]	123.06 ± 35.82	117.08 ± 31.65	0.386
Duration of 2 nd stage of labor [min.]	16.43 ± 8.6	18.13 ± 9.03	0.346
Duration of 3 rd stage of labor [min.]	11.84 ± 6.82	9.38 ± 6.16	0.065
APGAR score after 1 min.	8 [7-9]	8 [7-10]	0.791
APGAR score after 5 min.	8 [8-9]	9 [7-10]	0.563

Data are represented as mean ±SD or median [IQR], APGAR: Appearance, Pulse, Grimace, Activity and Respiration

Table [4]: Maternal complications of the studied groups

Maternal complications	Ketamine group [n = 50]	Tramadol group [n = 50]	P value
Nausea	2 [4%]	2 [4%]	1.000
Vomiting	2 [4%]	1 [2%]	1.000
Hallucination	0 [0]	0 [0]	---
Headache	1 [2%]	0 [0]	1.000
Apnea	0 [0]	0 [0]	---
Allergy	0 [0]	0 [0]	---

Data are represented as frequency [%].

DISCUSSION

Controlling and reducing labor pain is one of the most difficult tasks for anesthesiologists, as any procedure or substance utilized for this pain has adverse effects on the mother or the infant [6].

Neuraxial block [epidural block] provides a high average success rate for analgesia but increases the rate of instrumental delivery and CS due to motor weakness [7].

Opioid as morphine and pethidine is a good alternative analgesia for normal labor. However, it increases the risk of respiratory apnea, drowsiness, and newborn respiratory depression up to three days after birth [8].

Parenteral opioids give considerable pain relief during childbirth. The impact is not long-lasting, according to a Cochrane evaluation of 7,000 parturient, but long-acting opioids have long-lasting effect. Common adverse maternal effects were sleepiness, nausea, and vomiting [9].

In the current investigation, the induction dosage of ketamine was 0.4 mg/kg, and the maintenance dose was 1 mg/min using a continuous infusion pump. Ketamine lowers pain and maternal fatigue; hence, the patients were quite cooperative during birth. It has an

oxytocin impact [10]. Additionally, it has increased uterine contractions and cervical dilatation, resulting in a significant decrease in VAS in 16 % of the ketamine group to 3-4 and 40 percent to 5-6 with 5-15 [min], with no effect on the second and third stages of labor compared to tramadol, which has a lack of oxytocin effect.

In contrast to our findings, **Ahmadi et al.** [11] reported that 12 % in the tramadol group experienced a reduction in VAS score to 3-4, 34 % to 5-6, and 16% to 7-8. Patient satisfaction increased from poor to good at 14 percent and fair satisfaction at 40%, which is a good result. However, compared to the other group [ketamine], the tramadol group has a greater percentage reduction in VAS score and greater patient satisfaction [20 % good and 50 % reasonable].

Regarding the beginning of analgesia, the ketamine group considerably reduces the time required to obtain a decent level of satisfaction and the lowest VAS, indicating that ketamine has a brief duration of action. **Kushtagi and Surpaneni** [3] compared various dosages of tramadol and pethidine and discovered that tramadol 100 mg is as effective as meperidine as a labor analgesic with less maternal and perinatal adverse effects.

Sun ^[12] reported shortened second stage to 17.5 minutes compared to the usual [45 mins]. Our investigation showed no discernible difference between the groups after less than 20 minutes. These results agreed with a study by **Singh and Tamta** ^[13].

No particular maternal complications associated with our medications were recorded in the trial, and there was no significant difference between the two groups in the incidence of side effects such as nausea and vomiting. We will advise premedication with an antiemetic such as ondansetron in the future.

There was no significant difference in the Apgar score between the two groups regarding fetal complications.

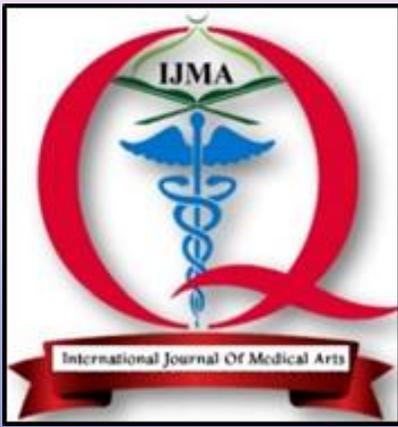
Women using tramadol and ketamine had comparable rates of instrumental vaginal and cesarean birth, regardless of duration or style of labor.

Conclusion: In a spontaneous vaginal birth, ketamine and tramadol are considered safe drugs with a low incidence of complications and identical Apgar scores after 1 and 5 minutes, with ketamine being superior to tramadol regarding analgesic onset time, VAS score, and patient satisfaction.

Conflict of Interest and Financial Disclosure: None.

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