Comparison of Analgesic Requirement and Pain Intensity in Lower Segment Cesarean Section (LSCS) with Ketofol and Conventional Induction of General Anesthesia

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ABSTRACT
Objective: to compare the analgesic requirement and pain intensity in LSCS with ketofol and conventional induction of general anesthesia.
Study Type: randomized controlled trial
Study Place and Duration: department of Anesthesiology at Ghazi Medical College & Teaching Hospital, Dera Ghazi Khan, from 1st January 2019 to 30th June 2019.
Material and methods: 100 adult participants (20–40 years) ASA physical status 1 and 2, with no previous case of neurologic or cardiovascular undergoing LSCS operations were enlisted in a randomised prospective comparative study after receiving approval from the ethical research committee. Patients were divided into two groups, each with 50 patients: group P (propofol) and group KP (Ketamine) (ketofol). The surgeon picked a closed envelope as the method of randomization. Visual analogue scale was used to assess the postoperative pain where, 0 means no pain, 1-3 means mild pain, 4-7 means moderate pain, and 8-10 means severe pain using a visual analog scale, where 0 means no pain, 1-3 means mild pain, 4-7 means moderate pain, and 8-10 means severe pain. Furthermore, the need for postoperative analgesia was examined, including the need for fentanyl.
Results: The majority of the patient's Group P and Group KP had 0 VAS scores12 (56.0%) and 26 (52.0%), respectively, (p=0.475). Intra operation fentanyl was required 3 (6.0%) in Group P and 1 (2.0%) in Group PK, (p=0.307). While, post-operation fentanyl was required 7 (14.0) in Group P and 4 (8.0) in Group PK, (p=0.338).
Conclusion: Ketofol as an induction agent can be used as an alternative which is relatively safe and show less side effects in comparison to propofol alone.

Keywords: Ketamine, propofol, ketofol, pain intensity, analgesia requirement, conventional induction, general anesthesia

INTRODUCTION
In the 1960s, An IV anesthetic ketamine with MOA causing dissociative anesthesia was manufactured from phencyclidine. Advantages i.e. analgesic and amnesic effects, protection of reflexes of the respiratory tract, spontaneous respiration, and muscle tone maintenance contributed to the start of ketamine. On the other hand, there are many side effects of ketamine (i.e. its sympathomimetic effects cause vomiting, development of hallucinations, nausea, rise in B.P., and heart rate and it is argued that it may cause an increase in intracranial pressure) that prohibited its frequent use. In Europe during the 1970s, the drug propofol (2,6-Diisopropylphenol), which is more and more utilized in the USA over the past 20 years. General anesthesia is produced by the promotion of the GABA effect (neurotransmission inhibition). Recovery, rapid induction, anticonvulsant effects, and antiniemics are its major advantages. In this case, major disadvantages are respiratory depression and hypotension which are dose-dependent.

It was suggested that the combination of both drugs may develop a mixture comprising additive properties of each drug in such a way that we can reduce the dosage of each of the drugs and on one hand, reduce the disadvantages caused by either of the drugs; and on the second hand, profit from advantages concerning analgesia, hemodynamic stability, hypnosis, and amnesia. The mixture formed is considered to be a sedative agent named ketofol and produces encouraging results in the emergency departments. In the current study, we aim to obtain conclusive ketofol, in the case of hemodynamic parameters, and hypnotic criteria, by clinical assessment and the incidence of adverse effects of both ketamine and propofol in comparison to ketofol.

MATERIAL AND METHOD
This study was conducted at department of Anaesthesiology, at Ghazi Medical College & Teaching Hospital, Dera Ghazi Khan, from 1st January 2019 to 30th June 2019. It is a randomized controlled trial.100 adult participants (20–40 years) ASA physical status 1 and 2, with no previous case of neurologic or cardiovascular undergoing LSCS operations were enlisted in a randomised prospective comparative study after receiving approval from the ethical research committee at Nishtar Hospital, Multan and acquiring written informed consent. Patients were not given any premedication, and no drugs were authorised within 12 hours of operation. Pre-oxygenation was initiated for 5 minutes after the patient arrived in the operating theater. Patients were divided into two groups, each with 50 patients: group P (propofol) and group KP (ketamine) (ketofol). The surgeon picked a closed envelope as the method of randomization. To reduce the pain, all the patients are administered 2 ml of lidocaine IV before induction.

The procedure for inducing general anesthesia began with Group P receiving in 20 seconds IV 1% propofol (2mg/kg), with 10mg/ml propofol and so for every 5 kilograms 1 ml propofol syringe. Intravenous ketofol was administered to Group KP. Postoperatively, when the Alderete score reached 10 the patients were discharged after they were transported to the PACU (post-anesthesia care unit) and discharged. Time is required to recover from the lack of verbal interaction. Time is required for the disappearance of the eyelash reflex. Before induction, 2 minutes after initiation, post-intubation, 5 minutes post-intubation, and every 15 minutes until the completion of the surgery, hemodynamic data (mean heart rate and B.P.) were collected. In the PACU, all patients were queried about their memories of events or consciousness, and euphoria and hallucinations were assessed. The occurrence of apnea, as well as postoperative nausea and vomiting, was tracked. Visual analogue scale was used to assess the postoperative pain. Furthermore, the need for postoperative analgesia was examined, including the need for fentanyl.

The Chi-squared (v2) test was used with Yates correction to compare qualitative data. A P-value of less than 0.05 was used to indicate statistical significance. All of the data were examined using SPSS 15.0.
RESULTS
In total, 100 patients were enrolled in this investigation. Patients for the trial were randomly assigned to either Group P or Group KP. The distribution of age, height, weight, and ASA status of both the groups were almost equal, (p=0.050). (Table I). The majority of the patient's Group P and Group KP had 0 VAS scores/28 (56.0%) and 26 (52.0%), respectively, (p=0.475). Intra operation fentanyl was required 3 (6.0%) in Group P and 1 (2.0%) in Group KP, (p=0.307). While, post-operation fentanyl was required 7 (14.0) in Group P and 4 (8.0) in Group PK, (p=0.338). (Table II). The average blood pressure MAP in mmHg was displayed in Table III. The differences were statistically significant, (p=0.050). The average time for loss of verbal contact of Group P was less than the Group KP, 32.08±2.62 and 39.69±4.01, respectively, (p=0.000). Similarly, the time for loss of eyelash reflex was shorter than the Group KP, of37.76±1.47 and 48.13±2.55, respectively, (p=0.000). (Table IV).

DISCUSSION
For many years, anesthesiologists have used a combination of propofol and ketamine with great effectiveness. In comparison to propofol and ketamine alone, there is very little information in the scientific research about the usage of ketofol as an induction drug10. Frey et al.,11 discovered that utilising ketofol resulted in a lesser time till sedation achieved compared to propofol. The difference between our results and theirs may be due to the fact that we used an equal dose of propofol and ketamine in this investigation.

If we compare the result with other groups, the KP group had more stable vitals in this study. Arora et al.,12 for investigated 10 adults (more than 18 years of age) patients for the proposed method of sedation with ketofol in a 1:1 ratio and found that the mixture was hemodynamically stable. Akin et al.,13 also discovered ketofol's hemodynamic stability in youngsters undergoing cardiac catheterization. These findings are similar with the findings of Hui et al.,14 who reported that utilizing different combinations of propofol and ketamine enhanced cardiovascular stability when compared to using either drug alone.

In a 2005 study by Akin et al.,20% of patients experienced apnea at a dosage of 1.5 mg/kg of propofol. Since it has already been established that potential side effects are dose-dependent and might be decreased when both drugs are used together, apnea was not noticed in any of the cases with ketofol. Montero and colleagues15 found that combining low-dose ketamine with propofol sedation decreased the effects of propofol on hypoventilation while preserving the integrity of laryngeal and pharyngeal reflexes and ventilatory response to CO2. Propofol's antiemetic properties were evident in the mixture in the case of PONV, as evidenced by the decrease in the number of patients experiencing vomiting and nausea from two in the K group to zero in the KP group. No vomiting was reported by Willman and Andolfatto in 200717 when they gave 114 patients intravenous ketofol (1:1 mixture of ketamine and propofol, each 10 mg/mL) for procedural sedation and analgesia for predominantly orthopaedic procedures in an emergency department. There were no reported cases of nausea or vomiting in Singh et al.,16's study as well.

The results gathered are convincing for the usage of such an induction agent with minimal side effect, the only limitation we faced was the small number of patients. We should also search for the optimum combined dosages of the drugs used in the combination.

No significant differences in post-operative pain and analgesia requirements were seen between the two groups. A prior study found that postoperative pain was higher in the ketofol group than in the propofol group at 0 and 2 hours postoperatively, but it was reduced at 4 and 6 hours in the ketofol group as compared to the propofol group, but the difference was statistically insignificant at both events17. Similar findings have also been published18-20.

CONCLUSION
Ketofol as an induction agent can be used as an alternative which is relatively safe and show less side effects in comparison to propofol alone.

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