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A RETROSPECTIVE STUDY TO COMPARE INFUSION OF PROPOFOL AND KETAMINE-PROPOFOL MIXTURE (KETOFOL) AS ANESTHETIC MAINTENANCE AGENTS IN PATIENTS UNDERGOING VARIOUS SURGICAL PROCEDURES IN TERTIARY CARE CENTRES

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Abstract

Introduction: The existing evidence suggests that the use of low doses and titers of ketamine can be effective in reducing the cardiovascular effects of propofol; nevertheless, this administration method can increase the chance of waking up during anesthesia. Some studies have reported the effect of anesthesia induction using a single propofol dose and low ketamine doses on the hemodynamic stability of patients in short-term outpatient operations in emergency departments. The aim of this study is to compare the effect of ketofol and propofol , to evaluate the intra and post-operative hemodynamic effects of ketofol infusion in comparison with propofol infusion.

Methods: This Retrospective study involved Prior Consent from the Hospital Authorities & was found to be within ethical standards. Data of 100 surgeries were selected which were managed with propofol (50 surgeries) & ketofol (50 surgeries) separately admitted to the local surgical units in last 5 years. The two groups were compared in terms of heart rate, systolic, diastolic and mean blood pressure, severity of pain and nausea, vomiting frequency and the doses of analgesics and antiemetic drugs used.

Results: 38 (76%) out of 50 of the patients were male in the propofol group and 31 (62%) out of 50 were male in the ketofol group and the difference was not Significant .The mean age of the patients was 39.68 ± 7.32 years in the ketofol and 34.14 ± 7.61 years in the propofol groups . There was no statistical difference between the two groups regarding age and sex distribution. There was no difference between the two groups regarding systolic, diastolic and mean arterial blood pressure before induction and after. The intensity of nausea was not significantly different between the two groups. Postoperative pain severity and drug dosage were not significantly different between the two study groups.

Conclusion: The infusion of a mixture of ketamine and propofol improves hemodynamic stability in addition to better analgesia compared to the infusion of propofol alone. But it led to heightened risk of nausea and vomiting. Future studies are recommended to address these issues. In addition, further studies are warranted to investigate the use of sub-hypnotic doses of ketamine + ketofol combination for infusion in surgical procedures. When these parameters are considered, ketofol might be used as an alternative to propofol.

Keyword: Ketofol, Propofol, Retrospective Study. Comparative study, Ketamine

Introduction

Propofol is one of the most commonly used drugs for the induction and maintenance of anaesthesia. Quick wakening up and short context-sensitive half-life after prolonged intravenous infusion are among the advantages of this drug, which in turn increase the tendency for using this drug for the maintenance of anaesthesia in outpatient operations, emergencies and intensive care units [1,2]. propofol is an agent that provides rapid induction and recovery, depresses airway reflexes, and is used for sedation and anesthesia. The fact that it causes dose-dependent hypotension and respiratory depression, limits the use of propofol.[3,4]

Cardiovascular complications caused by the administration of this drug including reduced cardiac contractility, decreased heart rate, reduced peripheral vascular resistance, suppression of baroreceptor reflex and sudden decrease in blood pressure, especially in elderly patients and those with an underlying cardiac disease, and shocks have limited the use of this drug [5,6,7].

If it is used as a single agent it can cause unwanted responses such as coughing, hiccups, laryngospasm, and movements.[8]

Ketamine is also a commonly used agent & In addition to its amnesic and analgesic properties, ketamine increases heart rate and blood pressure by activating the sympathetic nervous system.[9] It was observed that a combination of ketamine and propofol reduced consumption of propofol and opioids and ensured

better hemodynamic and respiratory stability in patients.[10,11,12]

Generally the Ketamine and propofol mixture (ketofol) is 5 mg/mL ketamine and 5 mg/mL propofol, 1:1 mixture in a 20-mL syringe. It is reported that if ketamine and propofol are mixed in a polypropylene syringe they are physically compatible and chemically stable, and that they can be stored at room temperature and under light.[13] Ketofol has successfully been used in brief, painful interventions in emergency departments; for sedation in pediatric cases; for regional anesthesia; and in anaesthesia applications in electroconvulsive therapy.[14,15,16]

The existing evidence suggests that the use of low doses and titers of ketamine can be effective in reducing the cardiovascular effects of propofol; nevertheless, this administration method can increase the chance of waking up during anaesthesia. Some studies have reported the effect of anaesthesia induction using a single propofol dose and low ketamine doses on the hemodynamic stability of patients in short-term outpatient operations in emergency departments. The aim of this study is to compare the effect of ketofol and propofol , to evaluate the intra and post-operative hemodynamic effects of ketofol infusion in comparison with propofol infusion.

Methedology

This Retrospective study involved Prior Consent from the Hospital Authorities / Medical Superintendent of the tertiary care hospitals to see the records of the patients & were found within ethical standards. Data of 100 surgeries were selected which were managed with propofol (50 surgeries) & ketofol (50 surgeries) separately admitted to the local surgical units in last 5 years .Subjects included both the genders , all age groups and all classes of socio economic strata. Randomization was done using computer tables in selecting data.

The exclusion criteria included patients with a recent history of upper respiratory tract infections, allergies to propofol-ketamine, psychosis, epilepsy, cardiac diseases, drug and alcohol abuse, uncontrolled diabetes, accelerated hypertension, opium addiction and history of postoperative nausea and vomiting.

It was observed in the obtained data that Heart rate and systolic, diastolic and mean blood pressure were measured prior to the induction of anaesthesia, immediately after the induction of anaesthesia, and at intervals until the end of the surgery. The severity of pain and nausea and vomiting frequency were recorded in both groups immediately after the operation and at intervals until 6 hours generally. Pain severity was evaluated immediately to 6 hours generally and in majority of the cases after the surgery at intervals based on the visual analog scale (VAS). The severity of nausea was also evaluated based on VAS, where the absence and highest severity of nausea were indicated by scores 0 and 10, respectively.

The two groups were compared in terms of heart rate, systolic, diastolic and mean blood pressure, severity of pain and nausea, vomiting frequency and the doses of analgesics and antiemetic drugs used.

Data was filled in Microsoft Excel & analysed using a computer software Epi Info version 6.2 (Atlanta, Georgia, USA) & SPSS. Normality of the distribution within the groups was measured by Shapiro-Wilk test. Differences between the groups were assessed by independent samples *t* test and Mann-Whitney *U* test. P value of 0.05 and less was considered as statistically significant.

Results

Overall, in the selected / obtained data , 38 (76%) out of 50 of the patients were male in the propofol group and 31 (62%) out of 50 were male in the ketofol group and the difference was not Significant .The mean age of the patients was 39.68 ± 7.32 years in the ketofol and 34.14 ± 7.61 years in the propofol groups . There was no statistical difference between the two groups regarding age and sex distribution.

There was no difference between the two groups regarding systolic, diastolic and mean arterial blood pressure before induction and after. Heart rate showed the same trend in both groups.

The severity of pain and nausea was compared .None of the participants in the ketofol group had nausea immediately and uptil 6 hours after the surgery. The intensity of nausea was not significantly different between the two groups. With the exception of four patients in the propofol group, until 6 hours after surgery, none of the participants had vomiting during the follow-up However, compared to the propofol group, the ketofol group reported more pain at the outset of follow up, which improved by the end of follow-up. Postoperative pain severity and drug dosage were not significantly different between the two study groups.

Adverse effects such as excessive secretion, hallucination, bradycardia, or muscular rigidity was not observed in any patients.

Discussion

Rapid onset of action and short duration of action have made propofol a desirable drug for the induction and maintenance of anaesthesia [17]. However, the cardiovascular effects of this drug have limited its use, especially in patients with cardiac diseases and haemorrhagic emergency. Based on the available studies, the use of drugs such as ketamine as an anaesthetic induction agent can reduce the suppressing hemodynamic

effects of propofol, in addition to reducing the need for high propofol doses [18]. To the best of our knowledge, most studies have investigated the use of a single ketamine dose in the induction of anaesthesia, while the use of this drug in infusion has not been examined except in cases of local anaesthetic procedures requiring sedation. In the present study, we compared he hemodynamic effects of ketamine + propofol infusion in relation to propofol infusion alone for the maintenance of anaesthesia in 100 patients undergoing various surgeries.

In this study, systolic, diastolic and mean blood pressures were comparable in the two groups before and after anaesthesia induction as well as immediately after intubation. On the other hand, the values of these variables were significantly higher in the ketofol group than in the propofol group until the end of the operation.

Tang et al. [19] compared the effects of addition of low dose ketamine to propofol-fentanyl and propofol-fentanyl alone for sedation in 80 patients who were candidates for gynaecologic diagnostic laparoscopy. They observed that mean blood pressure was consistently higher in the Ketamine group, as sympathomimetic effects of ketamine might have overcome the cardiovascular effects of propofol, thereby maintaining hemodynamic stability in these patients compared to the propofol-treated patients. In contrast with our findings, a study performed by Singh et al. [20,21] comparing the cardiovascular effects of propofol alone and in combination with ketamine or fentanyl for sedation in patients undergoing endoscopic ultrasonography showed no significant differences in the mean blood pressure or heart rate at any time point among the groups.

Although there was a higher incidence of nausea in the Ketofol group, there was no significant difference between the two groups in terms of the incidence and severity of nausea and vomiting in the present study. Inconsistent with this finding, another study comparing the administration of a bolus dose of ketofol, compared to fetofol (fentanyl + propofol) showed significantly higher severity of nausea in the ketofol group than in the Fetofol group[22].

Based on the available literature, nausea and vomiting are the known complications of ketamine [23,]. In contrast, propofol has anti-nausea and vomiting effects; therefore, considering the longer recovery time in the ketamine-treated group than in the propofol group, the higher incidence of nausea and vomiting in patients receiving the combined bolus regimen of propofol and ketamine seems logical after administering a single dose. On the other hand, since propofol + ketamine combination was used in our study for intraoperative infusion, it probably increases the metabolism of context-dependent propofol, resulting in its elevated plasma levels and recovery time in comparison with its single dose. On the other hand, this can overlap the recovery time of ketamine and propofol, thereby reducing the nausea-inducing effects of ketamine. Also, the infusion of a low dose of ketamine probably has less pre-emetic effects [24]. In our study, the severity of postoperative pain at the outset of follow-up (immediately after surgery and 2 hours later) was higher in the ketofol group than in the propofol group, which decreased in the ketofol group compared to the propofol group in the next follow ups. However, none of these changes were significant in the two groups. The results of another relevant study revealed that the ketamine + propofol combination led to better analgesia compared to propofol alone.[25,26,27]

Conclusion

It can be concluded that the infusion of a mixture of ketamine and propofol improves hemodynamic stability in addition to better analgesia compared to the infusion of propofol alone. Nevertheless, it led to heightened risk of nausea and vomiting. We did not investigate the effect of ketofol infusion on opiate doses and the recovery time. Therefore, future studies are recommended to address these issues. In addition, further studies are warranted to investigate the use of sub-hypnotic doses of ketamine + ketofol combination for infusion in surgical procedures.

Concerns regarding ketamine are increased secretion, delay of recovery, and emergence of reactions but We did not see these adverse effects in our study. Those adverse effects might be reduced by the presence of propofol.

When these parameters are considered, ketofol might be used as an alternative to propofol.

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