JPPIPA 11(4) (2025)

Jurnal Penelitian Pendidikan IPA

http://jppipa.unram.ac.id/index.php/jppipa/index

Optimizing Ketamine-Propofol Collaboration to Prevent SpO_2 Decrease in TIVA Patients at RSU Emanuel Banjarnegara

Rahmaya Nova Handayani[1*], Sakhfa Syesar Novaliyanto[2], Surtiningsih[3]

[1] Lecturer in Anesthesiology, Universitas Harapan Bangsa, Jawa Tengah, Indonesia.
[2] Faculty of Healty, Universitas Harapan Bangsa, Jawa Tengah, Indonesia.
[3] Midwifery Lecturer, Universitas Harapan Bangsa, Jawa Tengah, Indonesia

Received: December 13, 2024
Revised: February 26, 2025
Accepted: April 25, 2025
Published: April 30, 2025

Correspondence:
Rahmaya Nova Handayani
rahmayanova@uhb.ac.id

DOI: 10.29303/jppipa.v11i4.10982

Abstract: Introduction: Total Intravenous Anesthesia (TIVA) is a widely used anesthetic technique that relies entirely on intravenous agents. However, one of its challenges is the potential reduction in oxygen saturation (SpO_2) during induction. Ketamine and propofol are commonly used anesthetic agents and their combination is hypothesized to optimize hemodynamic stability and prevent SpO_2 decline. **Objectives**: This study aims to evaluate the effectiveness of ketamine-propofol collaboration in maintaining oxygen saturation during TIVA induction at RSU Emanuel Banjarnegara. **Methods**: This study was a quasi-experimental study with 50 TIVA patients who met the inclusion criteria**. Result:** The study found that patients receiving the ketamine-propofol combination exhibited a more stable SpO_2 level compared to those receiving propofol alone. The mean decrease in SpO_2 was significantly lower in the combination group ($p < 0.05$), indicating the protective effect of ketamine in preventing hypoxia. The combo group also maintained hemodynamic indicators including blood pressure and heart rate better. **Conclusion:** The simultaneous injection of Ketamine and Propofol is beneficial in preventing a drop in SpO_2 1 minute after induction of anesthesia compared to the combination of Propofol alone.

Keywords: Anesthesia; Ketamine; Oxygen saturation (SpO_2); Propofol; Total intravenous anesthesia (TIVA)

Introduction

Total intravenous anesthesia (TIVA) is a method of anesthesia that does not require inhalation agents by using intravenous medications for induction, maintenance, and recovery from anesthesia (Kampman et al., 2024). The advancement of TIVA in the field of anesthesia is gaining popularity due to its many advantages, ranging from rapid onset as well as short duration of action, precise control of anesthetic depth as well and rapid recovery making TIVA the right choice for patients with cardiovascular or respiratory comorbidities (Lone & Dar, 2023).

TIVA is conducted with a mixture of anesthetic medications to overcome the shortcomings of each agent (Watanabe et al., 2023). Using several classes of anesthetic medications in TIVA is important for complete and balanced anesthesia (Al-Rifai & Mulvey, 2016). The combination of anesthetic drugs will lower the single dose, therefore lowering the adverse effects of each anesthetic drug (Ali et al., 2023).

Oxygen saturation (SpO_2) is an important indicator that should be monitored while the patient is under anesthesia during a surgical procedure. The normal value of SpO_2 is 95% to 100%. Factors causing a decrease in SpO_2 when under anesthesia are respiratory depression due to the effects of anesthetic drugs, and hypoxia due to lack of oxygen in the blood. Administration of anesthetic drugs, especially hypnotic drugs can cause various events after anesthesia, Propofol is one of the drugs that can depress breathing (Arya et al., 2022).

How to Cite:
Handayani, R. N., Novaliyanto, S. S., & Surtiningsih. Optimizing Ketamine-Propofol Collaboration to Prevent SpO_2 Decrease in TIVA Patients at RSU Emanuel Banjarnegara. *Jurnal Penelitian Pendidikan IPA*, *11*(4), 216-223. https://doi.org/10.29303/jppipa.v11i4.10982

Based on research conducted (Prabowo et al., 2022) in 30 patients undergoing surgery using TIVA with a single Propofol, 23 patients (76.7%) experienced post-induction apnea using a dose of 2 mg/kg Propofol alone without a combination of other hypnotic drugs.

Propofol is an intravenous hypnotic that is frequently used to induce and maintain anesthesia (Sun et al., 2023). Its rapid onset and short duration of action make it the most widely used intravenous anesthetic drug in the past 30 years (Chiu et al., 2024). The main adverse effects of administering Propofol are related to cardiopulmonary physiology and include hypoventilation, loss of airway reflexes, and even apnea in high doses (Sahinovic et al., 2018). Propofol causes apnea by profoundly suppressing respiratory function at induction dosages (Yulia & Hadinata, 2022). Apnea may occur with an induction dose because propofol can induce respiratory depression (Ferrier et al., 2022).

Ketamine is a dissociative anesthetic agent with diverse pharmacological effects ranging from induction and maintenance of anesthesia to analgesic and sedative depending on the dose administered (Roy et al., 2019). Ketamine can be used singly or in combination with other drugs to enhance its efficacy. This drug has several advantages compared to other anesthetic drugs. In addition to providing a hyptonic effect Ketamine also has an analgetic effect and produces a bronchodilatory status, this allows it to be used as an option in the anesthesia of patients with asthma who experience acute bronchial constriction (Zhou et al., 2023). Its good hemodynamic profile also makes it the drug of choice for patients with unstable hemodynamics, such as shock or hypotensive patients. Relatively intact airway reflexes and a decreased risk of respiratory depression have also been linked to its use for anesthesia (Pathak et al., 2023). In addition to raising blood pressure, heart rate, and cardiac output, ketamine also activates the sympathetic nervous system, which enhances oxygenation by boosting lung blood flow (Nobre et al., 2024). This suggests that the addition of ketamine with other anesthetic drugs can result in better preoxygenation in patients who have asthma and acute bronchial constriction during induction (Chowdhury & Chakraborty, 2020).

Based on research conducted (Tusharbhai et al., 2022) reported that 40 patients who will undergo surgical procedures with TIVA were divided into 2 groups equally, in group A given Propofol-Ketamine induction and group B given Propofol-Fentanyl induction. The SpO_2 value before induction in group A was 98% and the value of group B was 99%. After the induction was performed, the SpO_2 value of group A was 99% and group B was 100%. A comparison of SpO_2 shows a higher value in group B both before induction and after induction is performed (Tusharbhai et al., 2022). This study aims to analyze the effectiveness of ketamine and propofol collaboration during induction in preventing a decrease in oxygen saturation (SpO_2) in patients with total intravenous anesthesia (TIVA).

Method

This study was conducted from July 15 to August 9, 2024. carried out in the central surgical installation of Emanuel Banjarnegara Hospital, Central Java Province. The author chose this hospital as a research site because the author found several incidents of decreased SpO2 after induction using Single Propofol on TIVA during Clinical Practice 5. Preparations made include submitting a research permit from the Faculty of Health, Harapan Bangsa University, Then submit a letter requesting permission to carry out research to the Emanuel Banjarnegara Hospital. The next step is to take secondary data (operation and anesthesia sheets) from TIVA patients to obtain data on patient hemoglobin levels, age, last vital signs and take primary data directly related to patient vital signs including blood pressure, Spo2 patients when entering the operating room according to predetermined criteria, namely hemoglobin levels within normal limits of 12-16 grams / dL, Adult patients ranging in age from 18 to 60 years, the patient's blood pressure is within the normal range of 90/60mmHg to 140/90mmHg, and the SpO2 value at pretest is within the normal range of 95% to 100%

In the research procedure carried out includes taking data on patient characteristics, namely age and gender, then taking the main data of this study. Recording data SpO_2 levels measured using a pulse oximeter before and after the induction of a combination of Ketamine and Propofol for induction in TIVA with a dose of Ketamine given is an analgesic dose of 0.1-0.6 mg / kg bw, and the dose of Propofol given is 1-2.5 / kg bw and SpO_2 levels measured using a pulse oximeter before and after the induction of a single Propofol collaboration for induction in TIVA with a dose of Propofol given 1-2.5 / kg bw. Then the data is entered in Microsoft Excel, to be further analyzed with SPSS.

Fifty patients receiving TIVA-assisted surgery are split into two groups for this quasi-experimental study, which employs a quantitative method of experimental research. Patients with TIVA induced with a combination of propofol and ketamine made up the experimental group in this study, while patients with TIVA induced with propofol alone made up the control group. A pretest-posttest control group design is used in this study. According to this research design, a pretest is administered first, followed by a posttest after treatment has been administered. The study began on July 15 and

ended on August 3, 2024. With code B. LPPM-UHB/900/09/2024, this study has been approved by Harapan Bangsa University's Health Research Ethics Committee.

This research design uses a pretest-posttest control group design. That is, a research design that gives an initial test (pretest) before being given treatment, after being given treatment, then gives a final test (posttest). The research design is presented in Table 1.

Table 1. The research design

Subject	Pre-test	Treatment	Post-test
K1	O1	X	O2
K2	O1′	X1	O2′

Description:
K1: Experimental group TIVA subjects/patients (induction using a collaboration of Ketamine and Propofol combination)
K2: Control group TIVA subjects/patients (induction using Propofol alone)
O1: SpO2 assessment in the experimental group
O1': SpO2 assessment in the control group
X: Treatment in the experimental group (induction using a collaboration of Ketamine and Propofol combination).
X1: Treatment in the control group (induction using a single Propofol collaboration).
O2: SpO2 assessment of the experimental group
O2': SpO2 assessment of the control group

Result

Table 2 shows that some respondents before induction using a combination of Ketamine and Propofol collaboration obtained the highest SpO_2 value of 100% and the lowest was 96%. The average SpO_2 value at pretest was 98.28%. With a median value of 98.00%, a value that often appears 99%, and a Standard Dervirasirnya of 1.137. Respondents who experienced changes in SpO_2 after induction using a collaboration of Ketamine and Propofol combinations obtained the highest value of 100% and the lowest was 96%. The average SpO_2 value at the posttest was 98.28%. With a median value of 98.00%, a value that often appears 99%, and a Standard Dervirasirnya of 1.137.

Table 2. Distribution of SpO_2 Values of Respondents Results of Pre-Test and Post-Test of Experimental Group

Experimental Group	Pre Test %	Post Test %
Maximum Value	100.00	100.00
Minimum Score	96.00	96.00
Average (mean)	98.28	98.28
Merdian	98.00	98.00
Mode	99.00	99.00
Standard Deviation	1.137	1.137

Based on table 3 shows that some respondents before induction using single Propofol collaboration obtained the highest SpO_2 value of 100% and the lowest was 97%. The average SpO_2 value at pretest was 98.56%. With a mean value of 98.00%, a value that often appears as 98%, and a Standard Dervirasirnya 1.121. Responders who experienced changes in SpO_2 after induction using a single Propofol collaboration obtained the highest value of 94% and the lowest 80%. The average SpO_2 value at the posttest was 89.36%. With a median value of 91.00%, the value that often appears is 91% and the Standard Dervirasir is 4.040.

Table 3. Distribution of SpO_2 Values of Respondents Results of Pre-Test and Post-Test of Control Group

Control Group	Pre Test %	Post Test %
Maximum Value	100.00	94.00
Minimum Score	97.00	80.00
Average (mean)	98.56	89.36
Merdian	98.00	91.00
Mode	98.00	91.00
Standard Deviation	1.121	4.040

Table 4. Shapiro Wilk Normality Test Shapiro Wilk Test Calculation Results Pre-Test Post-Test Experimental Group and Control Group

Group	Shapiro-Wilk		
	Statistic	Df	Sig.
Pre_Experiments	0.910	25	0.031
Post_Experiments	0.910	25	0.031
Pre_Control	0.859	25	0.003
POST_Control	0.864	25	0.003

a. Lilliefors Significance Correction

Based on table 4 demonstrates that the pre-test and post-test SpO_2 values of the experimental group acquire a pre-test significant value of 0.031 < 0.05 and post-test 0.031 < 0.05 it is demonstrated that the pre-test and post-test findings are not normally distributed. The pre-test and post-test findings were not normally distributed, as evidenced by the significant value of 0.003 <0.05 for the control group's pre-test SpO_2 value and 0.003 <0.05 for the post-test. The Wilcoxon Test will be used in the next test since the results of both are not normally distributed. To determine whether there was a difference between the experimental and control groups' pre-test and post-test SpO_2 values, the Wilcoxon test was used. The results of the calculation using the SPSS application obtained the results as follows.

Table 5. Wilcoxon Test to Find Out Differences Between Pair Data Wilcoxon Test Calculation Results Pre Test Post Test Experimental Group and Control Group

Variable	P value
Experimental	1.000
Control	0.000

Table 5 indicates that the experimental group's Post-Test SpO_2 value did not change following administration of a combination of ketamine and propofol, with the Wilcoxon test yielding a sig. Value of 1.000 <0.05.

Table 6. Respondent Homogeneity of Variance Test Homogeneity of Variance Test Results Experimental Group and Control Group

Grup	Levene Statistic	P value
Experimental Control	16.339	0.000

The following test is necessary because Table 6's sig. Value, which is based on the mean, is 0.000 <0.05, indicating that the experimental group's and the control group's Post-Test SpO_2 value data distribution is not homogeneous. The Mann-Whitnery test will be used for this. The SpO_2 Post-test values of the experimental group (Ketamine and Propofol) and the control group (Propofol alone) were subjected to the Mann-Whitney test; the findings are displayed in the Table 7.

Table 7. Mann-Whitney Test to Compare First 1 Minute SpO_2 Value After Induction Of 2 Different Groups Mann Whitney Test Calculation Results Experimental Group and Control Group

Variable	P value
Experimental Control	0.000

Table 7 acquired sig. A value of 0.000 <0.05 indicates that patients who received a combination of Ketamine Propofol induction and those who had a single Propofol induction had different average SpO_2 values following induction.

Discussion

Based on Table 4 in this investigation, it was determined that there were no significant changes in SpO_2 values before and after induction with the collaboration of a combination of Ketamine and Propofol in TIVA patients.

Sub-dissociative doses of ketamine also referred to as analgesic doses of 0.1–0.3 mg/kg, have been used extensively in conjunction with hypnotic medications during induction. It is most frequently used in conjunction with propofol as the primary hypnotic because analgesic doses of ketamine serve as a strong bronchodilator, maintaining the upper respiratory tract and comparatively more awake respiratory reflexes, which helps overcome obstacles (Nikolin et al., 2023). The effects Propofol which can cause respiratory depression characterized by decreased SpO_2 values that usually occur after induction dosing, as well as replacing the role of opioids because they have an effective analgesic effect, especially in the TIVA technique which minimizes the use of opioids to get faster anesthetic recovery and avoids the incidence of respiratory depression (Motov et al., 2018).

Based on research Ramdev et al. (2015) role Ketamine produces bronchodilation so it is widely used in combination with hypnotic drugs which can mostly cause respiratory depression, the role of Ketamine in maintaining respiratory reflexes is very effective and is widely combined with Propofol to overcome the main side effects of giving induction doses of Propofol which can cause loss of respiratory reflexes (Rolfzen et al., 2024). The main purpose of the combination of anesthetic drugs is to overcome the effects of each drug and produce balanced anesthesia, especially in the TIVA technique which is expected to accelerate anesthetic recovery and minimize respiratory depression (Padhi et al., 2022).

This study is in line with Tusharbhai et al. (2022) who reported that the combination of Ketamine and Propofol can prevent a decrease in SpO_2 after induction because it was found that the SpO_2 value after induction with a combination of Ketamine Propofol did not decrease and could maintain a better SpO_2 value as long as the patient was under the influence of anesthesia (Abdildin et al., 2024). These findings are consistent with a study by Shirisha et al. (2024) that found that patients having surgery with the TIVA approach with induction using a mix of propofol and ketamine (Bakan et al., 2014).

Table 4 shows that SpO_2 levels in TIVA patients significantly change before and after induction with a single Propofol injection. These findings are consistent with Prabowo et al. (2022) research, which found that a single 1-2.5 mg/kb Propofol induction dose lowers SpO_2 values within the first minute following induction. This is because the patient's tidal volume decreases, which lowers minute volume and respiratory rate. Furthermore, the ventilatory response to hypoxia and hypercapnia can be suppressed by the concentration of propofol (Suneetha et al., 2023).

Propofol can cause respiratory depression, so apnea can be found after the administration of an induction dose of Propofol (Hashimoto et al., 2024). At subanesthetic doses for conscious sedation, Propofol can inhibit hypoxic ventilatory drive and suppress the respiratory response to hypercarbia (Molina et al., 2015). Propofol causes more airway reflex depression than Thiopental (Jansen et al., 2024). Propofol has a rapid onset, less than 30 seconds so the incidence of respiratory depression can be found in the first 1 minute after induction is carried out, this can cause a decrease in the patient's tidal volume and a decrease in minute volume and respiratory rate so that the incidence of

decreased SpO_2 values can occur after induction is carried out (Bajwa et al., 2010; Prabowo et al., 2022).

Based on Jansen et al. (2024); Yesua et al. (2019) the incidence of drunkenness in post-anesthetic recovery using a single Propofol is milder when compared to Thiopental or Ketamine, but Propofol can cause respiratory depression which is often found apneu after induction dosing (Lii et al., 2023). So a combination of anesthetic drugs is needed to reduce the side effects of each drug and also to achieve balanced anesthesia.

Based on Table 6, it can be said that there is a substantial difference in SpO_2 values between the experiment group (a collaboration of Ketamine and Propofol combinations) and the control group (single Propofol collaboration) (Denomme & Heifets, 2024). Therefore, it can be said that in patients with TIVA, the combination of ketamine and propofol is more effective for induction as a preventive measure against decreasing SpO_2 than the use of propofol alone (Linassi et al., 2024).

Based on the aforementioned research findings, it can be said that a combination of ketamine and propofol used both before and after induction effectively prevents a drop in SpO_2 during the first minute following induction. The primary adverse effects of administering a single induction dosage of propofol can be mitigated by administering a 0.1–0.3 mg/kg dose of ketamine analgesic, which acts to promote bronchodilation and maintain respiratory reflexes. The primary goal of combining anesthetic medications is to counteract their respective effects and create balanced anesthesia, particularly when using the TIVA technique, which is anticipated to hasten anesthetic recovery and reduce respiratory depression (Motov et al., 2018). The obvious side effect of Propofol can cause respiratory depression so apnea can be found after giving an induction dose of Propofol. At subanesthetic doses for conscious sedation, Propofol can inhibit hypoxic ventilatory drive and suppress the respiratory response to hypercarbia (Landoni et al., 2019). Propofol causes more airway reflex depression than Thiopental. Propofol can cause respiratory depression which is often found in apnea after induction dosing. So a combination of anesthetic drugs is needed to reduce the side effects of each drug and also to achieve balanced anesthesia (Morgan, 2022).

The findings of this study are consistent with those of Tusharbhai et al. (2022) who demonstrated that induction with a mixture of propofol and ketamine was effective in halting a drop in SpO_2 following induction. This conclusion is consistent with the findings of Shirisha et al. (2024). which also showed that the combination group of ketamine and propofol was more successful than the propofol and fentanyl group in preventing a drop in air SpO_2 following induction. This investigation supports the conclusion that in patients with TIVA, the combination of ketamine and propofol is more beneficial for the induction and prevention of SpO_2 decrease than the use of only propofol (Sahinovic et al., 2018).

All things considered, it may be said that the combination of ketamine and propofol works better than either drug alone to keep SpO_2 from dropping as soon as induction is complete (Yang et al., 2024). The combination of ketamine and propofol during induction was very successful in preventing the reduction of SpO_2, according to the effectiveness that was interpreted in the non-inferior SpO_2 group (Sodickson & Urman, 2015). Based on the aforementioned findings, hierpotersa H3 — which states that ketamine and propofol work better together to induce and prevent SpO_2 drop in patients with TIVA than propofol alone — is acknowledged (Han et al., 2025).

Conclusion

This investigation finds that patients receiving Ketamine + Propofol had a different average SpO_2 value than those receiving Propofol alone. This means that the administration of Ketamine and Propofol in the experimental group is significantly more effective in preventing a decrease in SpO_2 value in the first 1 minute after induction compared to the control group given a single Propofol. SpO_2 values showed that in the experimental group (Ketamine and Propofol), there was no significant decrease in the mean SpO_2 value from 98.96% before intervention to 98.28 after intervention. Meanwhile, in the control group (Propofol alone), the mean SpO_2 value decreased from 98.56% to 89.44%. The larger decrease in the control group demonstrates that ketamine and propofol working together during induction is more effective than propofol by itself at preventing a drop in SpO_2 in TIVA patients. The combined administration of Ketamine and Propofol is effective in preventing a decrease in SpO_2 1 minute after induction of anesthesia, as evidenced by the control group's average decrease in SpO_2 of 89.44% while the experimental group's average decrease in SpO_2 was smaller than the control group's average.

Acknowledgments

The researcher would like to thank the campus of Universitas Harapan Bangsa for supporting the research team in this research. This research is anindependent research conducted by a collaborative research team between study programs at Harapan Bangsa University.

Author Contributions

All authors have collaboratively contributed to every stage of this research, from conceptualization, data collection, analysis, and interpretation, to the final writing of this article. Each

author has played an integral role in ensuring the accuracy and integrity of the findings presented in this study.

Funding
This research did not receive any external funding.

Conflicts of Interests
The author's interest in publishing this article is for the purpose of research output in the form of publication in a scientific journal as evidence of required performance. There is no conflict of interest.

References

Abdildin, Y., Tapinova, K., Nemerenova, A., & Viderman, D. (2024). The impact of ketamine on outcomes in critically ill patients: a systematic review with meta-analysis and trial sequential analysis of randomized controlled trials. *Acute and Critical Care*, *39*(1), :34-46. https://doi.org/10.4266/ACC.2023.00829

Al-Rifai, Z., & Mulvey, D. (2016). Principles of total intravenous anaesthesia: practical aspects of using total intravenous anaesthesia. *BJA Education*, *16*(8), 276–280. https://doi.org/10.1093/bjaed/mkv074

Ali, S., Athar, M., & Ahmed, S. M. (2023). Basics of CPB. *Indian Journal of Anaesthesia*, *49*(4), 257–262. https://doi.org/10.4103/ija.IJA

Arya, J. R., Sojitra, B. H., & Pandya, M. J. (2022). Comparison of Two Drug Combinations in Total Intravenous Anaesthesia: Propofol-Ketamine and Propofol-Fentanyl. *National Journal of Medical Research*, *12*(04), 77–82. https://doi.org/10.55489/njmr.12042022937

Bajwa, S. S., Bajwa, S., & Kaur, J. (2010). Comparison of two drug combinations in total intravenous anesthesia: Propofol-ketamine and propofol-fentanyl. *Saudi Journal of Anaesthesia*, *4*(2), 72. https://doi.org/10.4103/1658-354x.65132

Bakan, M., Topuz, U., Umutoglu, T., Gundogdu, G., Ilce, Z., Elicevik, M., & Kaya, G. (2014). Remifentanil-based total intravenous anesthesia for pediatric rigid bronchoscopy: Comparison of adjuvant propofol and ketamine. *Clinics*, *69*(6), 372–377. https://doi.org/10.6061/clinics/2014(06)01

Chiu, W. C., Wu, Z. F., Lee, M. S., Chen, J. Y. H., Huang, Y. H., Tseng, W. C., & Lai, H. C. (2024). Propofol-based total intravenous anesthesia is associated with less postoperative recurrence than desflurane anesthesia in thyroid cancer surgery. *PLoS ONE*, *19*(1 January), 1–14. https://doi.org/10.1371/journal.pone.0296169

Chowdhury, S., & Chakraborty, P. pratim. (2020). Universal health coverage - There is more to it than meets the eye. *Journal of Family Medicine and Primary Care*, *6*(2), 169–170. https://doi.org/10.4103/jfmpc.jfmpc

Denomme, N., & Heifets, B. D. (2024). Ketamine, the First Associative Anesthetic? Some Considerations on Classifying Psychedelics, Entactogens, and Dissociatives. *American Journal of Psychiatry*, *181*(9), 784–786. https://doi.org/10.1176/appi.ajp.20240644

Ferrier, D. C., Kiely, J., & Luxton, R. (2022). Propofol detection for monitoring of intravenous anaesthesia: a review. *Journal of Clinical Monitoring and Computing*, *36*(2), 315–323. https://doi.org/10.1007/s10877-021-00738-5

Han, F., Dong, S., Chen, Z., Ye, C., Dong, C., Du, Y., Shi, H., & Lu, G. (2025). The global trend of intravenous anesthesia and tumors : a bibliometric and visualized study. *Perioperative Medicine*. https://doi.org/10.1186/s13741-025-00513-z

Hashimoto, K., Zhao, M., Zhu, T., Wang, X., & Yang, J. (2024). Ketamine and its two enantiomers in anesthesiology and psychiatry: A historical review and future directions. *Journal of Anesthesia and Translational Medicine*, *3*(3), 65–75. https://doi.org/10.1016/j.jatmed.2024.07.001

Jansen, S. C., van Lemmen, M., Olofsen, E., Moss, L., Pergolizzi, J. V., Miller, T., Colucci, R. D., van Velzen, M., Kremer, P., Dahan, A., van der Schrier, R., & Niesters, M. (2024). Reversal of Propofol-induced Depression of the Hypoxic Ventilatory Response by BK-channel Blocker ENA-001: A Randomized Controlled Trial. *Anesthesiology*, *140*(6), 1076–1087. https://doi.org/10.1097/ALN.0000000000004915

Kampman, J. M., Hermanides, J., Hollmann, M. W., Gilhuis, C. N., Bloem, W. A., Schraag, S., Pradelli, L., Repping, S., & Sperna Weiland, N. H. (2024). Mortality and morbidity after total intravenous anaesthesia versus inhalational anaesthesia: a systematic review and meta-analysis. *EClinicalMedicine*, *72*, 102636. https://doi.org/10.1016/j.eclinm.2024.102636

Landoni, G., Lomivorotov, V. V., Nigro Neto, C., Monaco, F., Pasyuga, V. V., Bradic, N., Lembo, R., Gazivoda, G., Likhvantsev, V. V., Lei, C., Lozovskiy, A., Di Tomasso, N., Bukamal, N. A. R., Silva, F. S., Bautin, A. E., Ma, J., Crivellari, M., Farag, A. M. G. A., Uvaliev, N. S., Zangrillo, A. (2019). Volatile Anesthetics versus Total Intravenous Anesthesia for Cardiac Surgery. *New England Journal of Medicine*, *380*(13), 1214–1225. https://doi.org/10.1056/nejmoa1816476

Lii, T. R., Smith, A. E., Flohr, J. R., Okada, R. L., Nyongesa, C. A., Cianfichi, L. J., & Heifets, B. D. (2023). Randomized trial of ketamine masked by surgical anesthesia in patients with

depression. *Nature Mental Health*, *1*(11), 876-886. Retrieved from https://www.nature.com/articles/s44220-023-00140-x

Linassi, F., Troyas, C., Kreuzer, M., Spano, L., Burelli, P., Schneider, G., Zanatta, P., & Carron, M. (2024). Effect of ketamine on the bispectral index, spectral edge frequency, and surgical pleth index during propofol-remifentanil anesthesia: an observational prospective trial. *Anesthesia & Analgesia*, *XXX*(00), 1–10. https://doi.org/10.1213/ANE.0000000000007255

Lone, J. A., & Dar, M. T.-T. (2023). Recent Advancements in Total Intravenous Anaesthesia (TIVA) and Anaesthetic Pharmacology. *International Journal of Health Sciences and Research*, *13*(11), 365–376. https://doi.org/10.52403/ijhsr.20231145

Molina, A. M., Moyano, M. R., Serrano-Rodriguez, J. M., Ayala, N., Lora, A. J., & Serrano-Caballero, J. M. (2015). Analyses of anaesthesia with ketamine combined with different sedatives in rats. *Veterinarni Medicina*, *60*(7), 368–375. https://doi.org/10.17221/8384-VETMED

Morgan. (2022). *Morgan & Mikhail's: Clinical Anesthesiology* (7 th editi). McGraw Hill LLC.

Motov, S., Drapkin, J., Likourezos, A., Doros, J., Monfort, R., & Marshall, J. (2018). *Sub-dissociative dose ketamine administration for managing pain in the emergency department*. *9*(4), 16–19. https://doi.org/10.5847/wjem.j.1920

Nikolin, S., Rodgers, A., Schwaab, A., Bahji, A., Zarate, C., Vazquez, G., & Loo, C. (2023). Ketamine for the treatment of major depression: a systematic review and meta-analysis. *EClinicalMedicine*, *62*, 102127. https://doi.org/10.1016/j.eclinm.2023.102127

Nobre, M. de O., Gehrcke, M. I., Boff, G. A., de Lima, C. M., & Iepsen, L. B. (2024). Total intravenous anesthesia with propofol, ketamine, and lidocaine associated with dexmedetomidine or xylazine for ovariohysterectomy surgery in female dogs. *Ciencia Rural*, *54*(6), 1–9. https://doi.org/10.1590/0103-8478cr20220323

Padhi, P. P., Yeeda, S., Nayak, L. K., & Das, S. (2022). Procedural Sedation Using Two Different Proportions of Ketamine-Propofol Combination in Short Gynecological Procedures: A Randomized Controlled Trial. *Cureus*, *14*(1), 1–8. https://doi.org/10.7759/cureus.21393

Pathak, S., Gupta, P., Kaushal, A., & Biswas, K. (2023). Effect of Ketamine and Dexmedetomidine as Adjuvant to Total Intravenous Anesthesia on Intraoperative Cranial Nerve Monitoring in the Patients Undergoing Posterior Fossa Craniotomies—A Randomized Quadruple Blind Placebo-Controlled Study. *Asian Journal of Neurosurgery*, *18*(03), 587–596. https://doi.org/10.1055/s-0043-1772762

Prabowo, A. D., Yudono, D. T., & Maryoto, M. (2022). Gambaran Pemberian Terapi Propofol pada Pasien General Anestesi di RSUD Hj. Anna Lasmanah Banjarnegara. *Seminar Nasional Penelitian Dan Pengabdian Kepada Masyarakat (SNPPKM) ISSN*, *2809*, 2767.

Ramdev, B., Bansal, S., Sharma, D. K., Sharma, S. R., Sodhi, G. S., & Kaur, J. (2015). Comparison Of Two Total Intravenous Anaesthesia Techniques : Propofol-Ketamine vs Propofol-Fentanyl In Minor Surgeries On Quality Of Induction And Haemodynamic Changes During Induction. *International Journal of Advances in Health Sciences (IJHS)* *2*(2), 234–240. Retrieved from https://www.ijhsonline.com/index.php/IJHS/article/view/59

Rolfzen, M. L., Palanca, B. J. A., & Bartels, K. (2024). Rethinking ketamine as a panacea: adverse effects on oxygenation and postoperative outcomes. *British Journal of Anaesthesia*, *132*(4), 635–638. https://doi.org/10.1016/j.bja.2023.12.030

Roy, S. D., Ritvik Rajat, & Hriday Kumar. (2019). A comparative study of ketamine and propofol versus fentanyl and propofol in total intravenous anaesthesia for short surgical procedures. *MedPulse International Journal of Anesthesology*, *12*(3), 238–243. https://doi.org/10.26611/10151235

Sahinovic, M. M., Struys, M. M. R. F., & Absalom, A. R. (2018). Clinical Pharmacokinetics and Pharmacodynamics of Propofol. *Clinical Pharmacokinetics*, *57*(12), 1539–1558. https://doi.org/10.1007/s40262-018-0672-3

Shirisha, N., Murthy, T. K. K., & Gangadhar, S. B. (2024). Comparative Evaluation of Propofol-Ketamine , Propofol Fentanyl and Propofol-Dexmedetomidine in Terms of Hemodynamic Variables and Recovery Characteristics in Upper Abdominal Surgeries under General Anaesthesia. *International Journal of Pharmaceutical and Clinical Research*, *16*(8), 17–25. Retrieved from https://impactfactor.org/PDF/IJPCR/16/IJPCR, Vol16,Issue8,Article4.pdf

Sodickson, A., & Urman, R. D. (2015). Total intravenous anesthesia. *Essential Clinical Anesthesia Review: Keywords, Questions and Answers for the Boards*, *2*(November), 166–168. https://doi.org/10.1017/CBO9781139584005.050

Sun, D., Li, K., Chai, Z., Wang, L., Gu, S., Sun, N., Zhang, Y., Wang, Y., & Wang, T. (2023). Effects of propofol intravenous general anesthesia and inhalational

anesthesia on T-lymphocyte activity after breast cancer surgery: A meta-analysis. *Journal of Research in Medical Sciences*, *28*(1), 1–9. https://doi.org/10.4103/jrms.jrms_336_23

Suneetha, D., Rajaratnakumar, N., Kumar, S. B., Athmakuri, K. S., Quadri, S. F., & Vani, S. (2023). Comparison of hemodynamic stability of propofol ketamine versus etomidate ketamine during induction in peritonitis cases posted for emergency surgery. *EUREKA: Health Sciences*, *2*, 33–39. https://doi.org/10.21303/2504-5679.2023.002914

Tusharbhai, D. M., Baliga, M., Kamath, S., & Mishra, A. (2022). Comparison of Propofol-Fentanyl Versus Propofol-Ketamine Combination as Total Intravenous Anesthesia in Maxillofacial Surgical Procedures - A Prospective Randomized Controlled Study. *Biomedical and Pharmacology Journal*, *15*(2), 935–944. https://doi.org/10.13005/bpj/2428

Watanabe, Y., Obara, S., & Inoue, S. (2023). Total intravenous anesthesia management with simultaneous use of remimazolam and propofol: A case series of three patients. *SAGE Open Medical Case Reports*, *11*, 1–7. https://doi.org/10.1177/2050313X231204574

Yang, Y., Liao, B., Deng, R., Ren, L., Sun, Y., Xiong, S., & Wu, X. (2024). Comparison of anaesthesia strategies on postoperative nausea and vomiting in laparoscopic sleeve gastrectomy: a randomised controlled trial. *BMC Anesthesiology*, *24*(1), 1–8. https://doi.org/10.1186/s12871-024-02577-8

Yesua, I. N., Rahardjo, P., & Edwar, P. P. M. (2019). Keamanan Penggunaan Propofol Auto-Coinduction Dibandingkan Dengan Midazolam Coinduction Berdasarkan Perubahan Hemodinamik Pada Induksi Anestesi Pasien Yang Dilakukan General Anestesi. *JAI (Jurnal Anestesiologi Indonesia)*, *11*(1), 1. https://doi.org/10.14710/jai.v11i1.22039

Yulia, M., & Hadinata, Y. (2022). Total Intravenous Anesthesia (TIVA) pada Bedah Jantung Koroner. *JAI (Jurnal Anestesiologi Indonesia)*, *14*(1), 69–77. https://doi.org/10.14710/jai.v0i0.41418

Zhou, N., Chen, C., Liu, Y., Yu, Z., & Chen, Y. (2023). Efficacy of intraoperative subanesthetic dose of ketamine/esketamine in preventing postoperative cognitive dysfunction: a systematic review and meta-analysis. *Therapeutic Advances in Psychopharmacology*, *13*, 1–12. https://doi.org/10.1177/20451253231200261