Archives of Anesthesiology and Critical Care (In Press); x(x): xx-xx.

Available online at http://aacc.tums.ac.ir

Research Article

Propofol Target-Controlled Infusion (TCI) vs. Manual-Controlled Infusion (MCI)—Comparable Hemodynamic Stability with Reduced Propofol Consumption: Randomized Clinical Trial

Ira Ulil Inayah Wahid[1], Andi Muhammad Takdir Musba[1,2]*, Alamsyah Ambo Ala Husain[1], Muhammad Ramli Ahmad[1,2], Muhammad Rum[1], Madonna Damayanthie Datu[1,2]

[1]*Department of Anaesthesia, Intensive Care and Pain Management, Hasanuddin University, Makassar, Indonesia.*

[2]*Department of Anaesthesia, Intensive Care and Pain Management, Dr. Wahidin Sudirohusodo General Hospital, Makassar, Indonesia*.

ARTICLE INFO

Article history:
Received 12 March 2025
Revised 02 April 2025
Accepted 16 April 2025

Keywords:
Endoscopic retrograde cholangiopancreatography (ERCP);
Propofol;
Target controlled infusion (TCI);
Manual controlled infusion (MCI)

ABSTRACT

Background: The procedure of endoscopic retrograde cholangiopancreatography (ERCP) requires deep sedation for procedural success and patient safety. Propofol is commonly used due to its rapid onset and recovery, but its administration method significantly impacts its effectiveness and safety. This study compares Target Controlled Infusion (TCI) and Manual Controlled Infusion (MCI) of propofol in ERCP patients.

Methods: A single-blind randomized controlled trial was conducted with 22 ERCP patients, who were randomly assigned to either the TCI group (n=11) or the MCI group (n=11). In the TCI group, propofol was administered using the Schnider pharmacokinetic model, targeting effect sites, with an initial effect-site concentration set at 2.5 mcg.kg^{-1}. In contrast, the MCI group received an initial propofol bolus of 2 mg.kg^{-1}, followed by 20 mg increments every 10 seconds. The study analyzed propofol induction time, hemodynamic stability, and total propofol consumption, with hemodynamic parameters recorded every five minutes.

Results: The TCI group had a significantly longer induction time (10.00 ± 2.05 min vs. 3.45 ± 1.21 min; $p < 0.001$) but required a lower total dose of propofol (2.30 ± 0.43 mg.kg^{-1}.h^{-1} vs. 3.69 ± 0.69 mg.kg^{-1}.h^{-1}; $p < 0.001$). Hemodynamic stability was comparable between both groups.

Conclusion: TCI provides similar hemodynamic stability to MCI while reducing total propofol consumption. Despite a longer induction time, TCI may be a more cost-effective and controlled method for propofol administration in ERCP.

Introduction

ERCP is a complex procedure. Complications occurs around 5% of cases, including pancreatitis, infection or cholangitis, bleeding, and perforation. The mortality rate associated with ERCP is approximately 0.6%. To enhance procedural success, minimize adverse effects, and ensure patient comfort, ERCP is typically performed under deep sedation, following the sedation guidelines set by the American Society of Gastrointestinal Endoscopy (ASGE) [1-2].

Propofol is commonly utilized as a sedative in endoscopic procedures due to its rapid onset of action and short recovery time. It provides high-quality sedation and ensures adequate amnesia without elevating the risk of cardiopulmonary complications [1]. However, propofol can cause cardiorespiratory depression, so in some cases

The authors declare no conflicts of interest.
*Corresponding author.
E-mail address: takdir1974@yahoo.com

ventilation support is needed until propofol is metabolized, due to the absence of specific antagonists. Therefore, a balance between adequate depth of sedation and prevention of side effects must always be maintained to ensure patient safety during the procedure [3].

Intermittent bolus and continuous infusion represent alternative strategies for propofol administration. However, interindividual variability in response to propofol presents a significant challenge. During endoscopic procedures, achieving precise titration of the drug remains difficult, as inadequate dosing increased risk of severe hypoxia and prolonged sedation. Among the various systems available for propofol administration, total intravenous anesthesia (TIVA) can be used. TIVA is performed with the aim of achieving a balanced anesthetic state through the injection of a single drug or a combination of several drugs [4].

Propofol TIVA control can be done manually, which is called manual controlled infusion (MCI), and target controlled infusion (TCI) [4]. The infusion rate of MCI is typically determined by the anesthesiologist based on their clinical expertise, patient-specific factors, and the observed hemodynamic response to various procedural stimuli. Decision-making in MCI, including rate adjustments, primarily relies on clinical judgment rather than objective pharmacokinetic and pharmacodynamic data. Due to individual variability in drug response, MCI may not consistently ensure optimal sedation quality and patient safety [5]. Meanwhile, TCI allows anesthesiologists to determine the target concentration of the drug in specific organs, specifically the concentration in the plasma (plasma concentration/pc) and the concentration of the drug in the brain (effect concentration/ec). The use of TCI technology in TIVA can provide various advantages, namely enabling better optimization of general anesthesia with a short extubation time, a decrease in the need for antispasmodics and fewer perioperative complications compared to standard anesthesia techniques. TCI provides a stable level of anesthesia, offering better anesthesia control, maintenance of spontaneous ventilation, and hemodynamic stability compared to bolus or continuous infusion techniques [6]. TCI results in faster induction of anesthesia, less propofol requirement, and more adequate depth of anesthesia when compared to TIVA MCI [4].

Various studies have been reported on the use of TIVA TCI compared to MCI in various procedures, but it is still rare in endoscopy, especially ERCP. In endoscopic procedures, the comparison of TCI and MCI has only been done by Sahu et al., who compared MCI and TCI in TIVA using a laryngeal mask airway (LMA) in ERCP procedures. The results showed that TCI resulted in earlier recovery than MCI [7]. However, the study did not compare hemodynamic response, induction time, and propofol requirements in ERCP procedures. This study aims to analyze the comparison of induction time, hemodynamic changes, and propofol requirements between TIVA propofol TCI and MCI in patients undergoing ERCP.

Methods

A single-blinded randomized controlled trial design was carried out between July and December 2024 at a tertiary care teaching hospital in Makassar, Indonesia. The study design was approved by the Ethics Commission of Biomedical Research (No: 520/UN4.6.4.5.31/ PP36/ 2A24).

Eligible patients were patients aged 18-50 years undergoing ECRP procedures using GA-TIVA, the American Society of Anesthesiologists (ASA) physical state I-II, and BMI 18-30 $kg.m^{-2}$. Patients with kidney failure, liver disorders, chronic opioid treatment, toothless with decreased mouth opening, Mallampati class III, facial deformities, obstructive sleep apnea, patients at greater risk of pulmonary aspiration, allergy to propofol, lipid emulsion or egg lecithin, and patients undergoing emergency ERCP were excluded in this study. Furthermore, patients who experienced surgical complications, procedures lasting more than two hours, and conversion from GA-TIVA anesthesia to general anesthesia dropped out of this study. After informed consent, samples were divided into 2 groups, which are MCI and TCI groups. Random allocation sequence using drawing lots methods by the team (Figure 1).

The patient is positioned semi-prone with standard monitors, including SpO_2, ECG, NIBP, capnography, and BIS. Oxygen is given via nasal cannula at 3 $L.min^{-1}$, and intravenous premedication with fentanyl 2 $mcg.kg^{-1}$ IV is administered, with an additional dose of 0.5 $mcg.kg^{-1}$ every 45 minutes if needed. Patients are then randomized into two groups, and propofol is given 3 minutes after fentanyl.

In the TCI group, propofol was administered using a Schnider pharmacokinetic model (targeting effect sites). The initial effect-site target concentration was set at 2.5 $mcg.ml^{-1}$ and was adjusted in increments of 0.5 $mcg.ml^{-1}$ every 2 minutes until the patient lost verbal contact or eyelash reflex and achieved a bispectral index (BIS) sedation level of 60–65. If the BIS score remained below 60 for 2 minutes, the target propofol concentration was reduced by 0.5 $mcg.ml^{-1}$, whereas if it exceeded 65, the target concentration was increased by 0.5 $mcg.ml^{-1}$.

In MCI group, patients initially received a propofol bolus of 2 $mg.kg^{-1}$, administered in 20 mg increments every 10 seconds until the loss of verbal contact or eyelash reflex and a BIS score of 60–65 was reached. If this was not achieved with the initial dose, an additional 0.5 $mg.kg^{-1}$ was administered and repeated every minute as needed. After induction, propofol was infused at 10 $mg.kg^{-1}.h^{-1}$ for the first 10 minutes, then reduced to 8 $mg.kg^{-1}.h^{-1}$ at the 10th minute, and further decreased to 6

$mg.kg^{-1}.h^{-1}$ at the 20th minute. Similar to the TCI group, if the BIS score remained below 60 for 2 minutes, the propofol concentration was reduced by 0.5 $mg.kg^{-1}$, whereas if it exceeded 65, the concentration was increased by 0.5 $mg.kg^{-1}$.

The primary endpoints were hemodynamic stability which include respiratory rate, heart rate, systolic and diastolic blood pressure, and oxygen saturation. A Bispectral Index (BIS) score is used to measure a patient's level of consciousness and brain activity. Hemodynamic parameters and BIS were recorded every 5 minutes. In addition, induction time, and total propofol requirement were also documented for further analysis.

Data analysis were made using Statistical Package for Social Sciences 26.0 (IBM Corp. Armonk, NY, USA). Participants' baseline characteristics were analyzed descriptively. Numerical variables are presented as mean and standard deviation. The data were tested for testing normality and homogeneity. The differences in numerical data between the two groups were analyzed using an independent t test or Mann–Whitney test. While categorical data is assessed using a chi-square test. A P value of <0.05 was considered statistically significant.

Results

This study included 22 samples consisting of 11 MCI samples and 11 TCI samples. There was no difference in baseline characteristics of the samples in both groups (Table 1). It was found that the total induction time in the TCI group (10.00 ± 2.05 minutes) was significantly longer than in the MCI group (3.45 ± 1.21 minutes) (p <0.001) (Table 2). The TCI group had a significantly lower mean volume of propofol use for induction (9.00 ± 1.73 mL) than the MCI group (12.18 ± 2.44 mL) (p = 0.002). The total volume of propofol was found to be significantly lower in the TCI group (24.91 ± 7.93 mL) than in the MCI group (35.00 ± 9.55 mL) (p = 0.014). Moreover, the TCI group received a significantly lower total dose of propofol compared to the MCI group (2.30 ± 0.43 mg/kg/hour vs 3.69 ± 0.69 mg/kg/hour; p<0.001). In this study, we found that the TCI and MCI groups had similar hemodynamic changes.

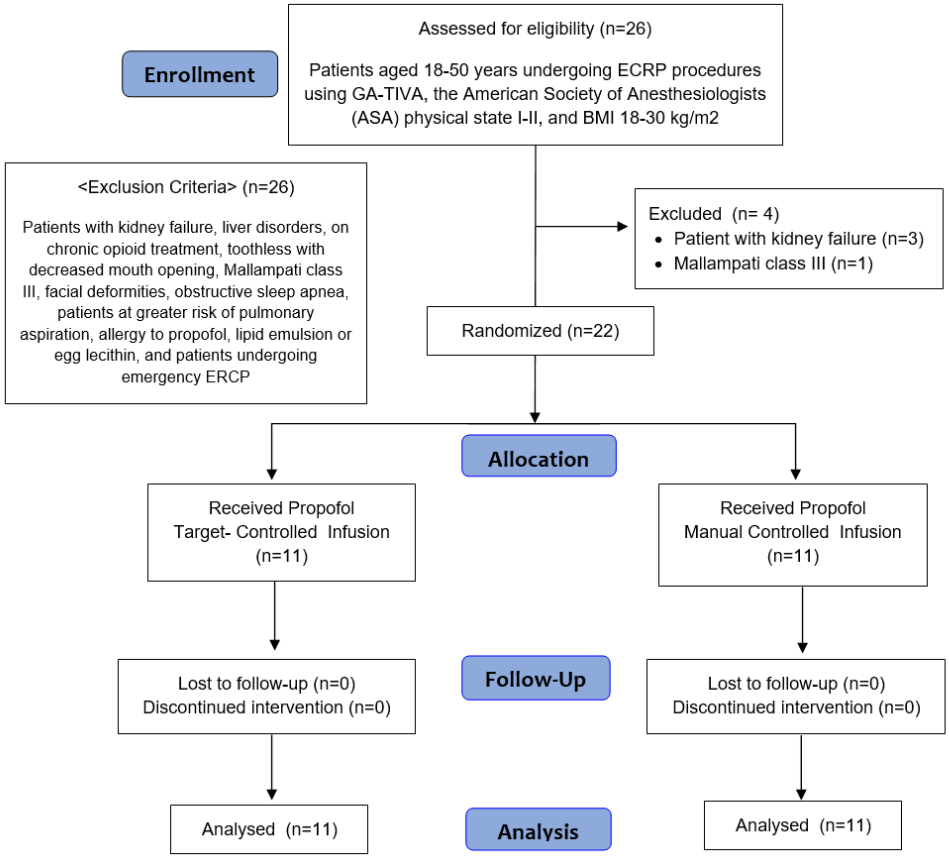

Figure 1- Sample Group

Table 1- Patient characteristics between two groups

Characteristics	TCI (n=11)	MCI (n=11)	P value
Sex			
Female (%)	5 (45.5%)	5 (45.5%)	1.000[a]
Male (%)	6 (54.5%)	6 (54.5%)	
Age (years)	49.63 ± 7.67	44.45 ± 6.56	0.104[b]
Body mass index (kg/m^2)	23.20 ± 2.60	23.43 ± 3.45	0.865[b]
ASA class			
I (%)	2 (18.2)	3 (27.3)	0.611[a]
II (%)	9 (81.8)	8 (72.7)	
Length of procedure (minutes)	32.27 ± 11.94	27.90 ± 10.64	0.376[b]

(a) Chi-square test; (b) Independent T-test

Table 2- Result

Variable	TCI (n=11) (Mean ± SD)	MCI (n=11) (Mean ± SD)	P value
Duration of induction of anesthesia (min)	10.00 ± 2.05	3.45 ± 1.21	< 0.001[a†]
Volume propofol use for induction (mL)	9.00 ± 1.73	12.18 ± 2.44	0.002[a*]
Total volume of propofol (mL)	24.91 ± 7.93	35.00 ± 9.55	0.014[a*]
Total dose of propofol (mg/kg/hour)	2.30 ± 0.43	3.69 ± 0.69	< 0.001[a†]
Hemodynamic Change			
Systolic blood pressure (mmHg)			
Baseline	124.27 ± 9.37	129.72 ± 8.16	0.161[a]
Induction	112.91 ± 10.75	119.55 ± 12.86	0.204[a]
Beginning of procedure	112.36 ± 8.18	113.09 ± 9.69	0.851[a]
End of procedure	113.00 ± 10.87	113.45 ± 8.05	0.912[a]
Awake	118.00 ± 6.26	110.81 ± 8.98	0.088[a]
Diastolic blood pressure (mmHg)			
Baseline	81.00 ± 10.85	78.73 ± 5.64	0.545[a]
Induction	73.63 ± 9.83	73.00 ± 6.84	0.862[a]
Beginning of procedure	72.91 ± 11.41	72.45 ± 4.13	0.903[a]
End of procedure	71.45 ± 13.69	73.27 ± 6.74	0.697[a]
Awake	74.18 ± 9.38	75.00 ± 9.72	0.843[a]
Heart rate (times/min)			
Baseline	83.00 ± 10.38	81.45 ± 13.20	0.847[b]
Induction	78.09 ± 12.48	80.91 ± 11.26	0.584[a]
Beginning of procedure	77.47 ± 9.87	79.59 ± 9.41	0.613[a]
End of procedure	77.73 ± 10.48	78.09 ± 9.06	0.931[a]
Awake	78.27 ± 9.89	78.55 ± 9.98	0.949[a]
Respiratory rate (times/min)			
Baseline	17.27 ± 1.27	17.72 ± 2.24	0.567[a]
Induction	15.55 ± 2.25	16.09 ± 3.14	0.519[b]
Beginning of procedure	15.21 ± 1.32	16.40 ± 1.59	0.053[b]
End of procedure	15.81 ± 1.40	16.73 ± 1.90	0.217[a]
Awake	16.45 ± 1.63	16.54 ± 1.44	0.949[b]
Oxygen saturation (%)			
Baseline	99.64 ± 0.50	99.45 ± 0.93	0.898[b]
Induction	99.00 ± 1.00	99.45 ± 1.21	0.243[b]
Beginning of procedure	99.13 ± 0.67	99.08 ± 1.27	0.562[b]
End of procedure	99.27 ± 0.90	99.09 ± 1.14	0.797[b]
Awake	99.91 ± 0.30	99.64 ± 0.92	0.699[b]

(a) Independent T-test; (b) Mann-Whitney test; *: significant at $p < 0.05$; †Significant at $p < 0.001$

Discussion

The use of TCI leads to a longer induction time than MCI in ERCP patients, consistent with findings from other studies on elective surgeries [8-9]. This phenomenon can be explained by the fact that TCI administration begins with a higher initial propofol infusion rate, typically lasting 20–30 minutes. As the procedure progresses, the infusion rate gradually decreases and may even reverse in prolonged applications within the TCI group. Consequently, the Induction phase in the TCI system takes longer than in the MCI system [10]. This is because TCI is designed to maintain a stable blood propofol concentration up to a selected higher or lower target concentration, which cannot be achieved with the manual regimen used [11].

This study observed comparable hemodynamic changes between TCI and MCI in ERCP patients, consistent with findings from other studies on elective surgeries [12]. However, these results contrast with another study that found TCI induction with propofol offered greater hemodynamic stability compared to manual induction [13]. Another study also suggests that TCI pumps deliver propofol more accurately than manual methods, leading to better hemodynamic stability and lower induction doses [14]. In contrast, different research indicates that MCI offers better hemodynamic stability compared to TCI [8]. A lower dose of propofol can cause a higher pulse rate due to less cardiovascular depressant effect. Administration of higher concentrations of propofol can reduce consciousness but cause hemodynamic side effects [8]. Meanwhile, slow infusion of propofol increases heart rate [15]. In this study, the hemodynamic stability of MCI and TCI was similar because TCI had lower induction and total propofol requirements than MCI but the induction time of TCI was longer than MCI.

In the TCI group, propofol administration is regulated to achieve a theoretically targeted concentration in the blood or brain, calculated based on the patient's age, weight, and height using a computer-assisted algorithm. In contrast, MCI delivers propofol at a fixed dose and rate proportional to body weight, which may increase the risk of hypotension, particularly in patients with compromised cardiovascular function. This occurs because continuous infusion following an initial manual bolus can lead to a progressive rise in blood concentration. Conversely, the TCI system eliminates the need for manual infusion rate adjustments by automatically titrating the dose to meet individual patient requirements, resulting in a more stable hemodynamic profile during anesthesia induction. However, hemodynamic responses may still vary among patients due to differences in induction dose, infusion duration, administration technique, and individual physiological characteristics [10,13].

In this study, the TCI group had lower propofol induction and total propofol requirements than the MCI group. Similar results were found in other studies that the total dose of propofol tends to be smaller in TCI than in MCI in elective surgery [8-9]. These results can be attributed to the fact that, following intravenous administration, the onset of clinical effects is influenced by a decrease in blood flow along the route leading to the target site. The speed of blood/brain equilibrium is very important in drug administration. In manual infusion, a faster effect can occur but it takes longer to wake up because the prediction of the concentration of the propofol effect site is inaccurate and it is impossible to maintain a constant concentration [9]. Thus, the TCI group requires less propofol than the MCI group, indicating that TCI is more cost-effective than MCI. This corresponds with findings that the cost of anesthetic drugs, particularly propofol, is higher in the MCI group compared to the TCI group [16].

This study has several limitations. This study does not assess other aspects such as pain level, mobilization and length of hospitalization as well as the cost-effectiveness of using total intravenous anesthesia propofol target controlled infusion with manual controlled infusion.

Conclusion

Total intravenous anesthesia – propofol target controlled infusion in patients undergoing ERCP has a longer total induction time, lower propofol requirements, and a hemodynamic profile similar to the manual controlled infusion method.

References

[1] De Vico P, Biasucci DG, Aversano L, Polidoro R, Zingaro A, Millarelli FR, et al. Feasibility and safety of deep sedation with propofol and remifentanil in spontaneous breathing during endoscopic retrograde cholangiopancreatography: an observational prospective study. BMC Anesthesiol. 2023;23(1): 260.

[2] Salama HZ, Alnajjar YA, Owais TA, Jobran AWM, Safi R, Bahar M, et al. Endoscopic retrograde cholangiopancreatography utilization and outcomes in the first advanced endoscopy center in Palestine at Al-Ahli Hospital: a retrospective cohort study. BMJ Open. 2023;13(12): e077806.

[3] Sarraj R, Theiler L, Vakilzadeh N, Krupka N, Wiest R. Propofol sedation in routine endoscopy: a case series comparing target controlled infusion vs manually controlled bolus concept. World J Gastrointest Endosc. 2024;16(1):11-17.

[4] Simanjuntak VE, Oktaliansah E, Redjeki IS. Perbandingan waktu induksi, perubahan tekanan

darah, dan pulih sadar antara total intravenous anesthesia profopol target controlled infusion dan manual controlled infusion. Jurnal Anestesi Perioperatif. 2013;1(3).

[5] Chiang MH, Wu SC, You CH, Wu KL, Chiu YC, Ma CW, et al. Target-controlled infusion vs manually controlled infusion of propofol with alfentanil for bidirectional endoscopy: a randomized controlled trial. Endoscopy. 2013;45(11):907-14.

[6] Motiaa Y, Bensghir M, Jaafari A, Meziane M, Ahtil R, Drissi Kamili N. Anesthesia for endoscopic retrograde cholangiopancreatography: target-controlled infusion versus standard volatile anesthesia. Ann Gastroenterol. 2016;29(4): 530-535.

[7] Sahu A, Tripathy D, Gupta B, Talawar P, Gupta R. Recovery time in target controlled infusion versus manual infusion of propofol in total intravenous anesthesia for endoscopic retrograde cholangio-pancreatography procedure using laryngeal mask airway-gastro: a randomized comparative study. Indian J Anaesth. 2023;67(14): S120-S125.

[8] Jasper A, Efe BP, Philomina Nosa E, Simbo AB. Total intravenous anesthesia with propofol-a comparison of target-controlled infusion (TCI) with manual controlled infusion (MCI). A randomized study. [Journal name if available]. 2022;[Volume(Issue):Pages].

[9] Laso F, López-Picado A, Olea E, Fuente L, Mendiguren Murua A, Sánchez-Castro C, et al. Manual vs. target-controlled infusion induction with propofol: an observational study. Rev Colomb Anestesiol. 2016;[Volume(Issue):Pages].

[10] Arslan G, Sezen Ö. Comparison of target controlled infusion and manual infusion of propofol for sedation in spinal anesthesia. Ain-Shams J Anesthesiol. 2020;12(1).

[11] Russell D, Wilkes MP, Hunter SC, Glen JB, Hutton P, Kenny GNC. Manual compared with target-controlled infusion of propofol. Br J Anaesth. 1995;75(5):[pages if available].

[12] Gale T, Leslie K, Kluger M. Propofol anesthesia via target controlled infusion or manually controlled infusion: effects on the bispectral index as a measure of anesthetic depth. Anaesth Intensive Care. 2001; 29(6):579-84.

[13] Yildirim SA, Dogan L, Sarikaya ZT, Ulugol H, Gucyetmez B, Toraman F. Hypotension after anesthesia induction: target-controlled infusion versus manual anesthesia induction of propofol. J Clin Med. 2023; 12(16):5280.

[14] Anderson BJ, Houghton J. Total intravenous anesthesia and target-controlled infusion. In: A Practice of Anesthesia for Infants and Children. Elsevier; 2018. p.177-98.

[15] Fabus MS, Sleigh JW, Warnaby CE. Effect of propofol on heart rate and its coupling to cortical slow waves in humans. Anesthesiology. 2024; 140(1):62-72.

[16] Yeganeh N, Roshani B, Yari M, Almasi A. Target-controlled infusion anesthesia with propofol and remifentanil compared with manually controlled infusion anesthesia in mastoidectomy surgeries. Middle East J Anesthesiol. 2010; 20(6):785-93.