Comparison of Target-Controlled Infusion vs. Manual Infusion of Propofol on Postoperative Recovery in Gynecological Endoscopic Procedures: An Open-Label Randomized Controlled Trial

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KEYWORDS
Propofol, Infusion pump, anaesthesia recovery time, total intravenous anaesthesia, target-controlled infusion.

ABSTRACT

Background: TIVA with propofol using a manually controlled infusion technique may cause delayed recovery or awareness due to overdosing or underdosing of an anaesthetic. However, TCI can optimally deliver anaesthetic by adjusting the infusion rates based on the pharmacokinetic profile of propofol. This study aimed to compare the recovery time after termination of propofol infusion in TCI with that of the manual infusion technique in patients undergoing gynaecological endoscopic procedures.

Methods: In this randomized trial, 100 female patients (18–65 years, American Society of Anesthesiologists (ASA - I/II) undergoing gynaecological endoscopic procedures were assigned to Manual or TCI propofol infusion. The Manual group (n=50) received propofol using the Bristol formula, while the TCI group (n=50) received a pump targeting 4 mcg/ml (Marsh model). Recovery time, total propofol dose, and post-induction MAP changes were measured with target BIS value of 40–60.

Results: The demographic data were comparable between the groups. The recovery time was faster with the TCI group (478.4±52.76 seconds) than the manual group (505.8±65.15 seconds) (p=0.0229). No significant difference was observed in total propofol consumption (p=0.199), with mean values of 14.47±1.24 mg/kg/hr in Group T and 14.12±1.46 mg/kg/hr in Group M. Patients in manual infusion group had better haemodynamic parameters than TCI group with less fall in mean arterial pressure post-induction. A significant difference was found in the percentage change in MAP (p=0.0003), with Group T showing a mean change of 9.18±2.6% and Group M 11.2±2.8%.

Conclusion: TCI offers significantly shorter recovery time and better post-induction haemodynamic parameters than manual propofol infusion in patients undergoing gynaecological endoscopic procedures.

1. Introduction

Total intravenous anaesthesia (TIVA) is a technique in which intravenous agents are used to induce and maintain general anaesthesia, thereby avoiding the use of inhalational anaesthetics. TIVA can be administered either by target-controlled infusion (TCI) or, more commonly, by intermittent boluses or manually controlled infusion systems. One of the key advantages of TIVA is its ability to titrate medications to achieve optimal anaesthesia levels. By adjusting the infusion rate of intravenous drugs, anaesthesiologists can tailor the level of sedation to meet the individual needs of each patient. This approach helps minimize the risk of under- or over-sedation, thus providing smoother recovery and improved overall patient outcomes. TIVA can be delivered with or without an airway device, and it may even be administered with oxygen alone.[1]

Propofol is the preferred hypnotic for TIVA and is often combined with short-acting opioids such as alfentanil or remifentanil for analgesia. Adjuncts, such as alpha2 agonists can enhance the effects of primary drugs. Medications with rapid onset and offset are ideal for achieving a balance between effective hypnosis, analgesia, and rapid recovery. Most intravenous drugs experience prolonged plasma concentrations over time, known as "context-sensitive half-time" (CSHT), which delays recovery. However, propofol and remifentanil have a minimal CSHT, making them superior to use in TIVA. Effective TIVA relies on precise combinations of hypnotics and analgesics to achieve the desired outcomes. The Fifth National Audit Project on Accidental Awareness during General Anaesthesia (NAP5) report highlights that inadequate knowledge of TIVA pharmacokinetics can lead to accidental awareness during general anaesthesia.[2] Therefore, a thorough understanding of TIVA/TCI pharmacokinetics is critical for safer practice.[3]

Target-controlled infusion (TCI) allows clinicians to input a desired drug concentration, with a computer calculating the necessary amounts for each bolus or infusion to reach that concentration. It continuously monitors tissue drug levels and adjusts infusion rates based on drug pharmacokinetics and patient factors. Modern TCI pumps include software for titrating the effect-site concentration, specifically in the brain. Monitoring the depth of anaesthesia, such as using the bispectral index, is crucial because individual responses

to anaesthetics can vary. Manual infusion of TIVA without TCI pumps requires extensive knowledge of drug pharmacokinetics.

Advancements in TIVA have come through various methods, specialized infusion sets, and mobile applications to ensure safety.[4] TCI technology is continually improving, with advancements in drug delivery devices, pharmacokinetic models, and computer systems. Advanced closed-loop anaesthesia delivery systems (CLADS) use controllers that allow manual or automatic dosage adjustments based on clinical or physiological monitors. This feedback is vital for accurate dosing, improving hemodynamic stability, and speeding recovery.[5] The goal of TCI advancements is to provide reliable feedback through physiological or processed electroencephalogram monitoring. We conceptualised this study to compare postoperative recovery between patients who undergo gynecologic endoscopic procedure under TCI with manually controlled infusion.

1.1. Aim

This study aimed to compare the recovery time after termination of propofol infusion in TCI with that of the manual infusion technique in patients undergoing gynaecological endoscopic procedures.

2. Materials and Methods

This prospective, single-blinded, randomized study included 100 patients who underwent gynaecological endoscopic procedures at the SRM Medical College Hospital and Research Centre. The study received approval from the Institutional Ethics Committee (SRMIEC-ST1122-276 dated 22.02.2023) and was done conforming to Helsinki guidelines. The study was registered in the Clinical Trial Registry of India (CTRI/2023/03/050936) on 26/04/2021, and informed consent was obtained from all enrolled patients.

2.1 Inclusion criteria:

The study included patients aged 18 to 65 years with American Society of Anaesthesiologists (ASA) physical status I or II, who had fasted for clear liquids for at least two hours and solids for a minimum of six hours.

2.2 Exclusion criteria:

Patients with uncontrolled comorbid illnesses, hypersensitivity or allergy to propofol, psychiatric disorders, opioid dependency, or refusal to provide consent were excluded from the study.

2.3 Method

The patients were informed about anaesthesia technique and consent was obtained. Patients were pre-medicated with tablet alprazolam 0.25 mg, ranitidine 150 mg, and metoclopramide 10 mg on the morning of surgery with sips of water. On arrival in the theatre, standard monitors, including pulse oximetry, non-invasive blood pressure, electrocardiogram and BIS (Bispectral Index) were connected. The patients were allocated to either Group T (TCI group) or Group M (manual infusion group) by computer generated random numbers in sealed envelope.

All patients were pre-medicated with an Inj.Glycopyrrolate 0.2 mg iv and fentanyl (2 µg/kg IV). Patients in Group T (n=50) were administered propofol using a TCI pump (Perfusor® Space® Infusion Pump, B. Braun, Germany) using a marsh model with a target propofol concentration of 4 µg/ml. Patients in Group M (n=50) were administered propofol based on the Bristol formula (10 mg/kg/h for the first 10 min, followed by 8 mg/kg/h infusion for the next 10 min, followed by 6 mg/kg/h for the rest of the surgery). The airway was secured with an LMA of an appropriate size in both groups following induction. The BIS values were measured in both groups using the BIS Monitor. If the BIS value was > 60, the target was increased by 1 µg/ml in Group- T and a Propofol bolus of 1 mg/kg was administered in Group M to ensure a target BIS of 40-60.

The patient's haemodynamic status, spO2, and EtCO2 were monitored throughout the procedure, and the LMA was removed at the end of the procedure. The recovery time, total dose of propofol administered (mg/kg/h), and change in Mean Arterial Pressure (MAP) at five minutes post-induction (%) were recorded and compared.

2.4 Statistical analysis

Data are presented as mean and standard deviation. Normality was checked using the Shapiro-Wilk test. Continuous variables were compared using an independent-sample t-test. Significance was defined as p values less than 0.05 using a two-tailed test. Data analysis was performed using IBM-SPSS version 21.0 (IBM-SPSS Corp., Armonk, NY, USA).

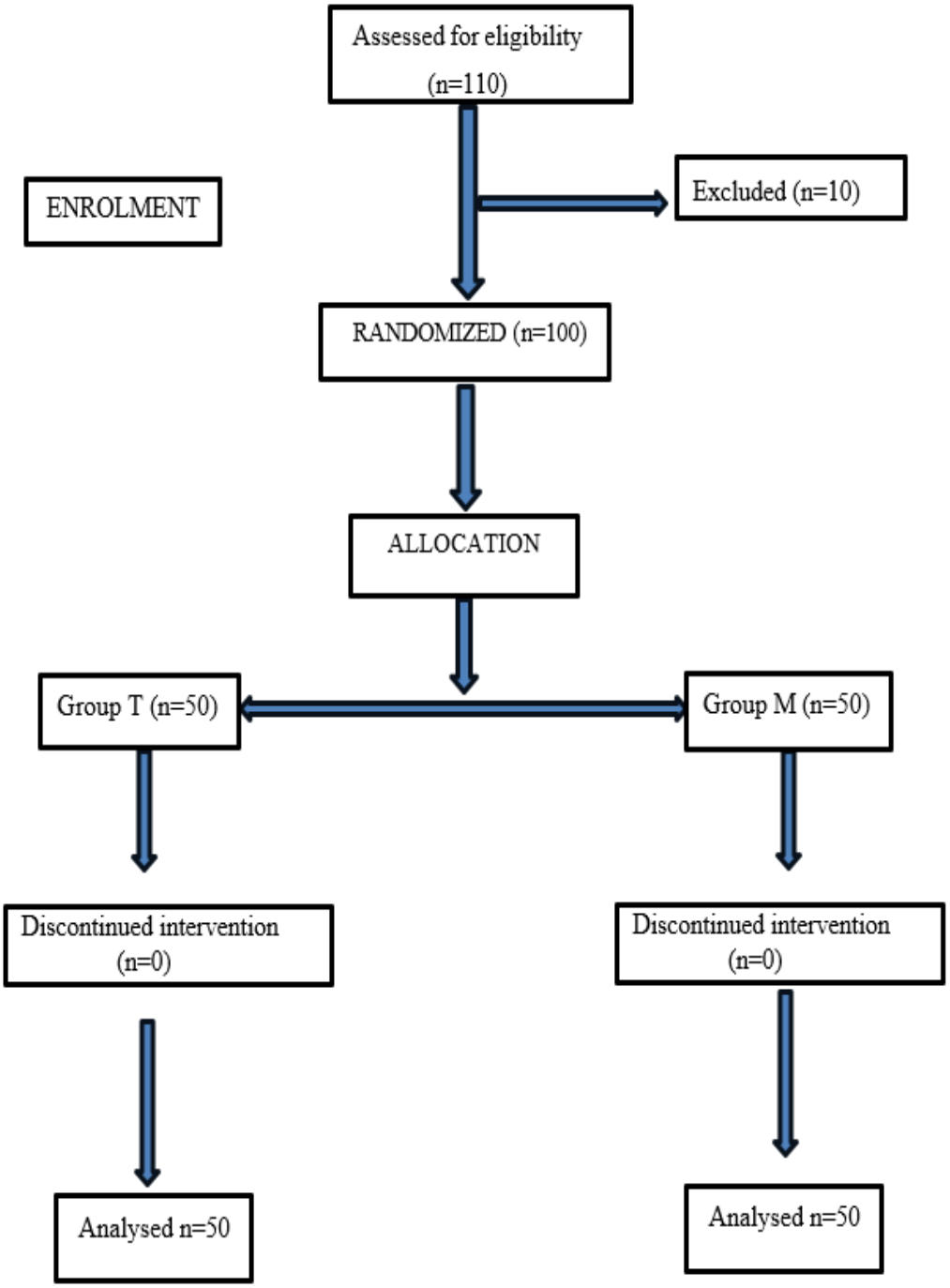

Figure 1: CONSORT flow chart

3. Results

The mean age of Group T was 40.04±12.82 years, and that of Group M was 43.66±10.45 years with no significant difference (p=0.125). The mean weight of Group T was 61.64±10.78 kg, and that of Group M was 61.52±12.00 kg with no significant difference (p=0.958).

The mean height of Group T was 157.14±4.78 cm, and that of Group M was 156.94±5.80 cm, showing no significant difference (p=0.851). The mean BMI of study participants in Group T was 24.94±4.16 kg/m^2, and that of Group M was 24.88±4.18 kg/m^2 with no significant difference (p=0.943) (Table 1).

Table 1: Baseline characteristics between groups

	Group T	**Group M**	**P value**
Age	40.04±12.82	43.66±10.45	0.125
Weight (kg)	61.64±10.78	61.52±12.00	0.958
Height (cm)	157. 14±4.78	156. 94±5.80	0.851
BMI (kg/m^2)	24.94±4.16	24.88±4.18	0.943

The mean recovery time in Group T was 478.4±52.76 seconds, while in Group M, it was 505.8±65.15 seconds, showing a significant difference (p=0.023). The mean propofol consumption was 14.47±1.24 mg/kg/hr in Group T and 14.12±1.46 mg/kg/hr in Group M with no significant difference (p=0.199). The mean change in MAP in Group T was 9.18±2.6% and in Group M was 11.2±2.8%, with a significant difference (p=0.0003) (Table 2).

Table 2: Comparison of recovery time, propofol consumption, and MAP changes between the groups

	Group T	**Group M**	**P value**
Recovery time (seconds)	478.4±52. 76	505.8 ± 65.15	0.023
Total propofol consumption (mg/kg/hr)	14.47±1.24	14. 12±1.46	0.199
Changes in MAP (%)	9.18±2.6	11 .2±2.8	0.0003

4. Discussion

In our study, time taken by patients in the TCI group to obey simple commands was significantly shorter than the time it took patients in the manual infusion group (p=0.022). Similar results were reported by **Sahu et al.**, who found that patients in TCI group had a significantly shorter recovery time compared to the TIVA group (p<0.001), and concluded that TCI, guided by BIS, would be a safer method for sedation in patients who undergo ERCP procedures with LMA gastro.[6] A study by **Laso et al.** concluded that induction with propofol using TCI is similar to manually delivered propofol. However, the anaesthesia recovery time was statistically significantly shorter in the TCI group.[7] **Mu et al.** conducted a study on children undergoing elective surgeries and found that the time to achieve extubation was quicker in the TCI group.[8]

The study by **Passot et al.** concluded that the TCI group had shorter recovery times compared to the manual infusion group.[9] Another trial conducted by **Chiang et al.** revealed that TCI of propofol combined with alfentanil was associated with a faster recovery time and better hemodynamic and respiratory stability than MCI in same-day bidirectional endoscopy procedures.[10] A study by **Jasper et al.** showed that the recovery time was better with the manual group, which contradicts our study.[11]

In our study, we observed that the total propofol dose consumed in the TCI group was comparable to that consumed in the manual infusion group, with no significant differences (p=0.199). Similar results were reported by **Kateliya et al.,** who revealed a significant increase in propofol consumption in the TCI group and concluded that TCI resulted in improved depths of anaesthesia despite higher propofol consumption.[12] In the study by **Breslin et al.,** the total propofol consumed in the TCI group was significant compared to the manual group. The emergence times and recovery endpoints were similar in both groups.[13] The study by **Mu et al.** concluded that, in comparison to manual infusion, the use of TCI led to larger propofol doses without lengthening the recovery period in children.[8] Studies by **Servin et al.** and **Sahu et al.** concluded that the rate of propofol administration was significantly higher in the TCI group.[6,14]

In our study, we found that the change in MAP at five minutes post-induction (%) was 11.2±2.8% in the manual group compared to 9.18±2.6% in the TCI group, which was highly significant (p=0.0003). Our results are different from the research done by **Niewiadomski et al.**, which showed a comparable change in MAP in manual group to that of the TCI group following endotracheal intubation.[15] **Yildirim et al.** also concluded that propofol induction with TCI prevents post-induction hypotension better than manual anaesthesia induction. However, administering propofol by a slow manual infusion may produce results similar to those of TCI during induction.[16] The study by **Passot et al.** showed that the hemodynamic stability was best achieved in the TCI group. [9]

5. Limitations

As it compared the two approaches to propofol infusion, blinding the anaesthesiologist to group allocation was not possible, potentially introducing bias. The Marsh pharmacokinetic model, targeting plasma-site concentration, was used in the TCI group instead of the Schneider model, which targets effect-site concentration and affects results. Additionally, we did not measure the actual plasma or serum concentrations of propofol, which could have provided a clearer understanding of pharmacokinetic differences. This study did not assess the time to hospital discharge, which is a conventional parameter for evaluating recovery and efficiency. Future studies that address these aspects are required for a more comprehensive analysis.

6. Conclusion

Our study concluded that TCI offers a significantly shorter recovery time and better haemodynamics post-induction than manual propofol infusion in patients undergoing gynaecological endoscopic procedures.

References

[1] Chokshi T, Channabasappa S, Vergheese DC, Bajwa SJS, Gupta B, Mehdiratta L. Re-emergence of TIVA in COVID times. Indian J Anaesth 2020;64: S125–31. https://doi.org/10.4103/ija.IJA_554_20.

[2] Pandit JJ, Andrade J, Bogod DG, Hitchman JM, Jonker WR, Lucas N, et al. Royal College of Anaesthetists; Association of Anaesthetists of Great Britain and Ireland. 5th National Audit Project (NAP5) on accidental awareness during general anaesthesia: summary of main findings and risk factors. Br J Anaesth 2014; 113:549–549. https://doi.org/10.1093/bja/aeu313.

[3] Nimmo AF, Absalom AR, Bagshaw O, Biswas A, Cook TM, Costello A, et al. Guidelines for the safe practice of total intravenous anaesthesia (TIVA): Joint Guidelines from the Association of Anaesthetists and the Society for Intravenous Anaesthesia: Joint Guidelines from the Association of Anaesthetists and the Society for Intravenous Anaesthesia. Anaesthesia 2019; 74:211–24. https://doi.org/10.1111/anae.14428.

[4] Bajwa SJS, Vinayagam S, Shinde S, Dalal S, Vennel J, Nanda S. Recent advancements in total intravenous anaesthesia and anaesthetic pharmacology. Indian J Anaesth 2023; 67:56–62. https://doi.org/10.4103/ija.ija_1022_22.

[5] Puri GD, Kumar B, Aveek J. Closed-loop anaesthesia delivery system (CLADSTM) using bispectral index: A performance assessment study. Anaesth Intensive Care 2007; 35:357–62. https://doi.org/10.1177/0310057x0703500306.

[6] Sahu A, Tripathy DK, Gupta B, Talawar P, Gupta R. Recovery time in target-controlled infusion versus manual infusion of propofol in total intravenous anaesthesia for an endoscopic retrograde cholangiopancreatography procedure using laryngeal mask airway-gastro: A randomised comparative study. Indian J Anaesth 2023;67: S120–5. https://doi.org/10.4103/ija.ija_484_22.

[7] Laso LF, López-Picado A, De La Fuente EO, Murua AM, Sánchez-Castro C, Ruilope LP. Valero-Martínez C. Manual vs. target-controlled infusion induction with propofol: An observational study. Colomb. J. Anesthesiol 2016; 44:272–7. https://doi.org/10.1016/j.rcae.2016.06.005.

[8] Mu J, Jiang T, Xu XB, Yuen VM, Irwin MG. Comparison of target-controlled infusion and manual infusion for propofol anaesthesia in children. British Journal of Anaesthesia 2018; 120:1049–55. https://doi.org/10.1016/j.bja.2017.11.102.

[9] Passot S, Servin F, Allary R, Pascal J, Prades J-M, Auboyer C, et al. Target-controlled versus manually-controlled infusion of propofol for direct laryngoscopy and bronchoscopy. Anesth Analg 2002; 94:1212–6. https://doi.org/10.1097/00000539-200205000-00030.

[10] 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; 45:907–14. https://doi.org/10.1055/s-0033-1344645.

[11] Jasper A, Efe BP, Nosa EP, Simbo AB. Total Intravenous Anaesthesia with Propofol-a comparison of Target-controlled infusion (TCI) with manual controlled infusion (MCI). A randomized study. Authorea Preprints.

2022. https://doi.org/10.22541/au.165936244.49446058/v1.

[12] Kateliya R, Madhukant, Dubey M, Chandra S, Sahay N. Comparison of recovery profiles in target-controlled infusions (TCI) versus manually controlled infusions for total intravenous anesthesia (TIVA) in laparoscopic surgeries. A randomized controlled trial. J Anaesthesiol Clin Pharmacol 2023; 39:258–63. https://doi.org/10.4103/joacp.joacp_396_21.

[13] Breslin DS, Mirakhur RK, Reid JE, Kyle A. Manual versus target-controlled infusions of propofol. Anaesthesia 2004; 59:1059–63. https://doi.org/10.1111/j.1365-2044.2004.03870.x

[14] Servin FS. TCI compared with manually controlled infusion of propofol: a multicentre study. Anaesthesia 1998;53 Suppl 1:82–6. https://doi.org/10.1111/j.13652044.1998.53s107.x.

[15] Niewiadomski S, Chwojnicki K, Owczuk R. Is target-controlled infusion better than manual-controlled infusion during TIVA for elective neurosurgery? Results of a single-centre pilot study. Neurol Neurochir Pol 2024; 58:331–7. https://doi.org/10.5603/pjnns.99294.

[16] 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; 12:5280. https://doi.org/10.3390/jcm12165280.