Total Intravenous Anaesthesia with Propofol-a comparison of Target-controlled infusion (TCI) with manual controlled infusion (MCI). A randomized study

Abiodun Jasper[1], Badare Paul Efe[1], Edomwonyi Philomina Nosa[2], and Amanor-Boadu Simbo[3]

[1]Delta State University
[2]University of Benin Teaching Hospital
[3]University College Hospital Ibadan

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Abstract

Background Total Intravenous Anaesthesia (TIVA) with propofol infusion is done by manual co'ntrolled infusion (MCI) or by target-controlled infusion (TCI) devices. This is a comparative study of MCI/TCI administration. Method In this randomized controlled trial, Anaesthesia was induced with propofol 1%, using a target blood concentration of 5 Meg/ml in the TCI group or at a dose of 1.5 mg/kg at an infusion rate of 1200 ml/h in the MCI group. Subsequently, a step-down maintenance regimen (10, 8 and 6 mg/kg/h at 10-min interval) was commenced for the MCI group. Primary outcome was the time to induction of anaesthesia in both groups. Data was analysed using Statistical Package for Social Sciences (SPSS) version 20.0. Results 52 patients were recruited into the study. The duration of induction of anaesthesia in the TCI group compared to the MCI group was (94.62 ± 11.34 sec vs. 79.50 ±16.23 sec, p = 0.001). The induction dose of propofol TCI against MCI was (118.00 ± 22.33 mg vs.133.04 ± 20.58 mg, p = 0.015). Both groups were comparable in terms of total dose of propofol (I 152.92 ± 234.47 mg vs. 1014.97 ± 264.18 mg, p = 0.052), recovery time (8.45 ± 2.13 min vs. 7.86 ± 2.05 min, p = 0.314), haemodynamic parameters and incidence of adverse events. Conclusion Manual controlled infusion was comparable to target controlled infusion for the induction and maintenance of general anaesthesia using propofol; providing similar quality and ease of anaesthesia as a viable option in resource challenged settings.

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Authors

Dr. Badare Paul Efe

Department of Anaesthesia and intensive care

Delta state University Teaching Hospital

Oghara Delta State

Nigeria

*Dr Jasper Abiodun Oyinpreye

Department of Anaesthesia and intensive care

Delta state University Teaching Hospital

Oghara

Delta State

Nigeria

Professor Edomwonyi Philomina Nosa

Department of Anaesthesiology

University of Benin Teaching Hospital

Benin

Edo State

Nigeria

Professor Amanor-Boadu Simbo

Department of Anaesthesia

University College Hospital

Ibadan Oyo State

Nigeria

Running title: Seeking Comparative advantage of Manual controlled infusion over Target controlled infusion for resource challenged environment.

***Corresponding Author(ORDCID NO : 0000-0002-8975-7039)**

Email:aojasper@yahoo.com

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Method

In this randomized controlled trial, Anaesthesia was induced with propofol 1%, using a target blood concentration of 5 Meg/ml in the TCI group or at a dose of 1.5 mg/kg at an infusion rate of 1200 ml/h in the MCI group. Subsequently, a step-down maintenance regimen (10, 8 and 6 mg/kg/h at 10-min interval) was commenced for the MCI group. Primary outcome was the time to induction of anaesthesia in both groups. Data was analysed using Statistical Package for Social Sciences (SPSS) version 20.0.

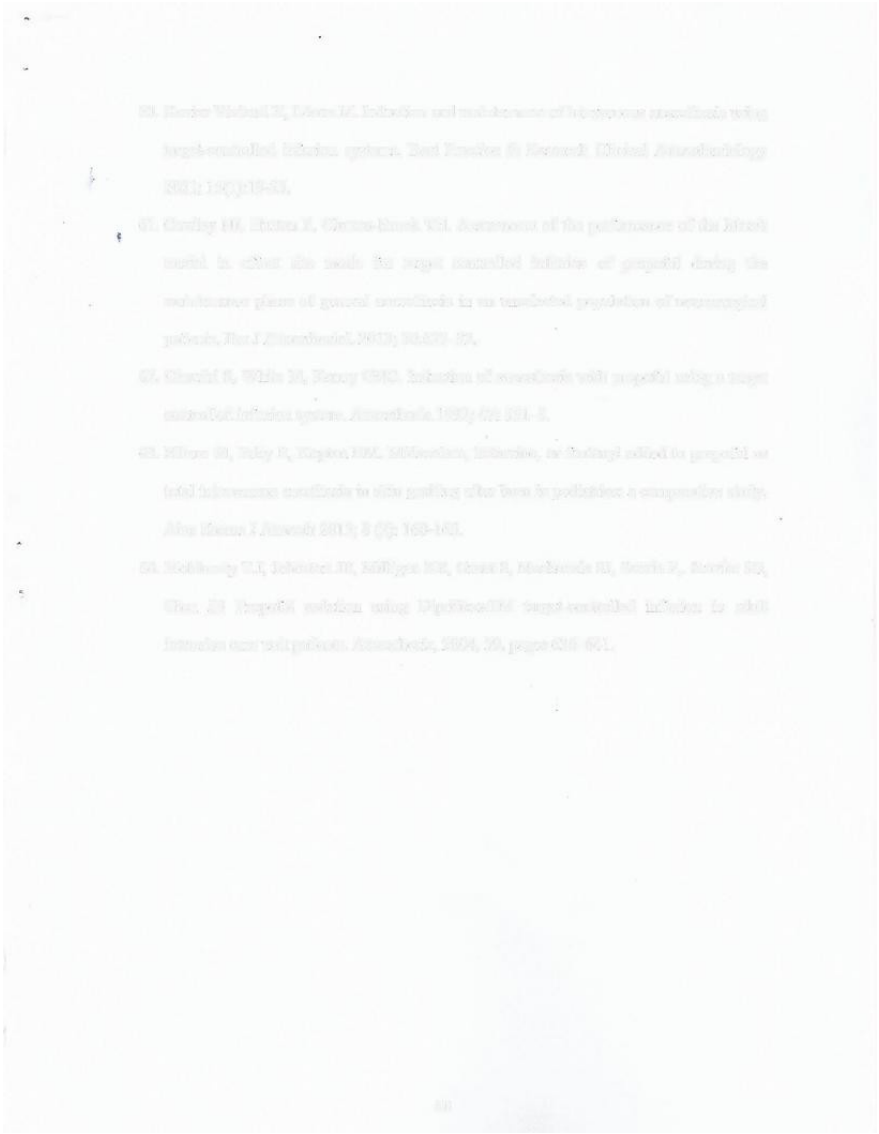
Results

A total of 52 patients completed the study. The duration of induction of anaesthesia in the TCI group compared to the MCI group was (94.62 $\pm$ 11.34 sec vs. 79.50 $\pm$16.23 sec, p = 0.001). The induction dose

of propofol TCI against MCI was (118.00 ± 22.33 mg vs.133.04 ± 20.58 mg, p = 0.015). Both groups were comparable in terms of total dose of propofol (I 152.92 ± 234.47 mg vs. 1014.97 ± 264.18 mg, p = 0.052), recovery time (8.45 ± 2.13 min vs. 7.86 ± 2.05 min, p = 0.314), haemodynamic parameters and incidence of adverse events.

Conclusion

Manual controlled infusion was comparable to target controlled infusion for the induction and maintenance of general anaesthesia using propofol; providing similar quality and ease of anaesthesia as a viable option in resource challenged settings.



Key words: Propofol, Target controlled infusion, Manual controlled

Infusion, Total intravenous anaesthesia, Resource Challenged environment

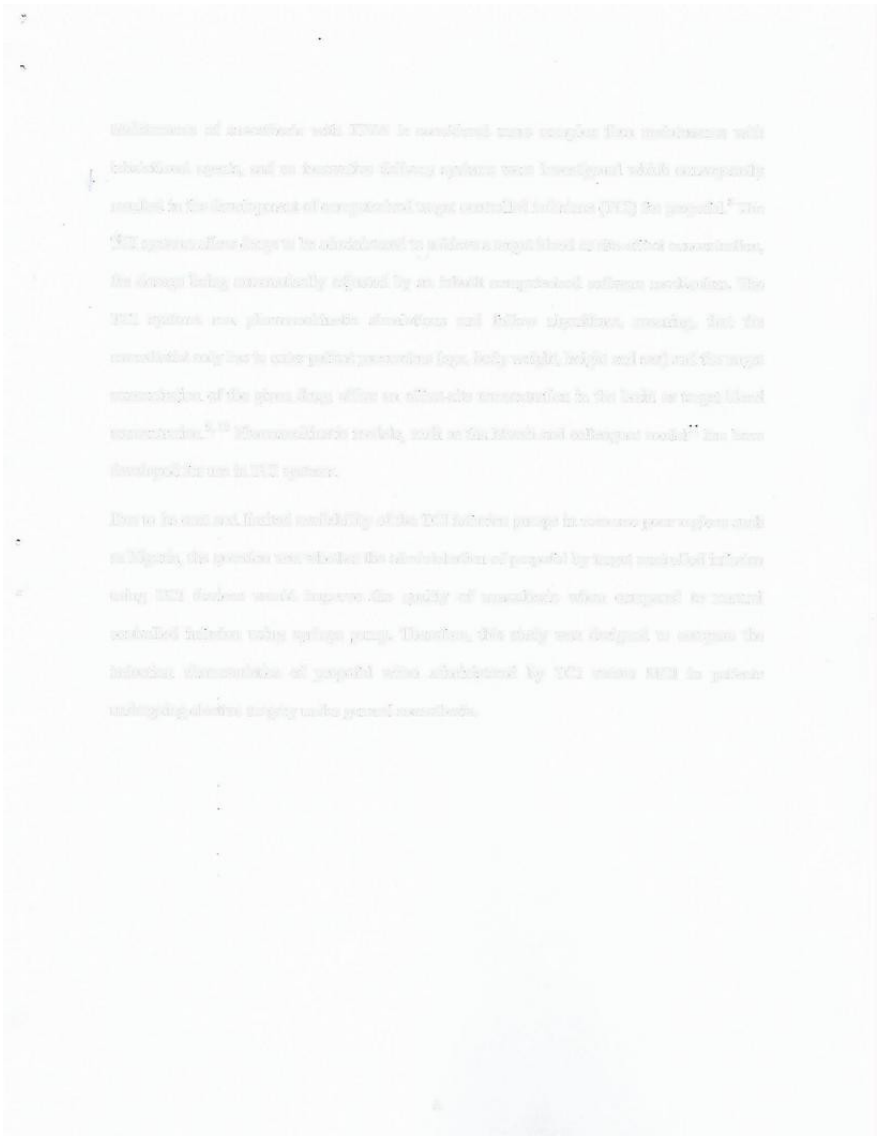
Introduction

Total intravenous Anaesthesia (TIVA) is an anaesthetic procedure which involves use of intravenous drugs to anaesthetize patients without the use of inhalational agents. (1)

Goals of TIVA is to allow smooth induction, reliable and titratable maintenance of anaesthesia and rapid emergence from the effects of infused drug as soon as the infusion is terminated. It also reduces theatre pollution. (2) The advantages of TIVA using propofol include rapid and smooth induction without significant haemodynamic alterations, good maintenance of anaesthesia, less incidence of postoperative nausea and vomiting (PONV), faster and better recovery profile resulting in higher patient satisfaction. (3) As a consequence of these favourable indices, Propofol remains widely used for gynecological, neurosurgical, and day-case anaesthesia. TIVA is particularly mandatory when anaesthetizing patients with malignant hyperthermia (4).

The need for Considerable experience, relatively higher cost and increased incidence of awareness under anaesthesia are some of its setbacks. (3) Propofol can be used in different combinations with remifentanil, fentanyl, midazolam or sufentanil. (3)

Propofol administration during TIVA may be achieved by intermittent boluses, manual infusion, or controlled infusion techniques (manual controlled infusion [MCI] using syringe pumps or target controlled infusion [TCI] using TCI devices) which are relatively more expensive. Because of its favourable pharmacokinetic profile, controlled infusions at induction and maintenance of general anaesthesia, Propofol allows easy titration of anaesthetic depth and rapid recovery from anaesthesia.(5) Roberts et al,(5) postulated an MCI regimen where anaesthesia may be induced with a bolus of 1% propofol at infusion rate of 1200 ml/h or 600 ml/h until loss of verbal contact, while maintenance involves stepping down at I0-min intervals from 10 *mg/kg/h* to 8 mg/kg/h; and thereafter to 6mg/kg/hr. or an infusion at a fixed rate of 6mg/kg/hr.(4,5,6)



Maintenance of anaesthesia with TIVA is considered more complex than maintenance with inhalational agents, and so innovative delivery systems were investigated which consequently resulted in the development of computerized target-controlled infusions (TCI) for propofol. (7) The system allows drugs to be administered to achieve a target blood or site-effect concentration, with dosages automatically adjusted by an inbuilt computerized software mechanism. It runs pharmacokinetic simulations and follow algorithms, where the anaesthetist only enters patient parameters (age, body weight, height, and sex) and the target concentration of the given drug: either an effect-site concentration in the brain or target blood concentration. (8,9)

Pharmacokinetic models, such as the. Marsh and colleagues' model (10) have been developed for use in TCI systems. Due to its cost and limited availability of the TCI infusion pumps in resource poor regions such as Nigeria, the question was whether the administration of propofol by target-controlled infusion using TCI devices improves the quality of anaesthesia significantly, compared to manual controlled infusion using syringe pump-hence the need for this study.

METHOD

This prospective randomized double-blind study was carried out at a tertiary health facility located in Delta State, Nigeria. Ethical approval was obtained from the Hospital Ethics and Research Committee and written informed consent was obtained from the patients according to the Helsinki guidelines and declaration.

The purpose was to evaluate the comparison of MCI and TCI in providing effective induction and maintenance profile in patients undergoing general anaesthesia. Each eligible patient was randomly allocated to either the TCI group (T) or the MCI (M) group using a computer-generated random number table (Stat Trek's Random Number Generator: stattrek.com). computer-generated codes placed in sealed envelopes in a box from which each patient picked slips an envelope. The number picked by the patient determined his/her appropriate group.

These were Patients with age (18 to 60 years), weighing (45 to 110 kg) , (ASA) class I or II and Elective surgical, non-obstetric, procedures under general anaesthesia lasting between 60-12 minutes.

Those with neurological or cardiovascular disorder, history of drug abuse, allergy to egg lecithin or soybean oil were excluded. Others were Patients taking sedatives or analgesics (within 24-hour) preceding surgery, Prolonged surgeries (more than 120minutes), difficult airways such as short neck, restricted mouth opening, large neck tumors, Mallam Patti 3 and 4.and those weighing <45 kg or> 110 kg.

From a previous study, the duration of induction of anaesthesia with propofol in patients who received MCI at an infusion rate of 600mls per hour was 75± 18.8secs.(11);It was assumed that the time of induction of anaesthesia would be reduced to 60secs when the infusion rate is set at 1200ml/hr. Therefore, the effect size was (75-60) sec=15secs(12)

Sample size of 50 was calculated with twenty-five patients required per group through power analysis. By adding an assumed 10% attrition rate which was 5, it gave a total sample size of 55. Therefore 56 patients at 28 per group were recruited for this study.

Study protocol

After Pre-anaesthetic evaluation, ASA status, full blood count (FBC), electrolytes, urea and creatinine were done for each patient. Blood was also grouped with 2 units of compatible blood crossmatched. Routine 8hr fasting guideline was observed. Intravenous cannulation was done after equipment and drug checks and baseline vital signs taken.

The researcher, having randomized the patient into the T or M group, anaesthetized the patients according to the allocated study protocol. The INJECTOMAT TIVA AGILIA (Fresenius Kabir, France), being a system capable of delivering propofol by both manual controlled infusion or target controlled infusion, was used for both the MCI and the TCI Groups, thus, blinding the patient. The infusion machine was covered with opaque cloth by the researcher. A second anaesthetist who collected the data, was not present during randomization and induction of anaesthesia, and was also unaware of which infusion system was running, and thus, was completely blinded to the study protocol. In the T group, anaesthesia was induced using the TCI Marsh and Schneider model of the Injectomat infusion machine by targeting a propofol blood concentration of 5 mcg/ml(6,13) at a rate of 1200 ml/h, until loss of verbal contact was achieved,(12,11,14) which ended the induction period. Further changes in the target concentration were then made by the researcher as dictated by clinical signs For the M group, anaesthesia was induced with a bolus of propofol using the MCI mode of the Injectomat infusion machine at an initial propofol dose of 1.5 mg/kg, with the same rate limitation (1200 ml/h). (13) The propofol infusion was continued until loss of verbal contact was attained. To determine loss of verbal contact, patients were asked to count out aloud during induction until loss of vocalization, and the time to achieve loss of verbal contact was taken as induction time.(11) Subsequently, a propofol maintenance infusion was commenced for the MCI group at IO mg/kg/h, being reduced to 8 and 6 mg/kg/h at I0-min intervals according to a standard regimen. (7,11) Further boluses or alterations in the propofol infusions were dictated by clinical signs as in the TCI group. Thecriteria for inadequate anaesthesia described by Ausems et.al (15) was used:

1 for an increase in systolic blood pressure to more than 15 mmhg above the baseline for that patient :2 -

heart rate more than 90 beats/min in the absence of hypovolaemia:3 - other autonomic signs such as sweating or flushing:4 - somatic responses such as movements or swallowing. Signs of an excessive level of anaesthesia were taken to be 1 - mean arterial pressure less than 60 mmhg and 2 - heart rate less than 50 beats/min.

After the patient had lost consciousness, atracurium at 0.5 mg/kg was administered to facilitate laryngoscopy and tracheal intubation, while anaesthesia was maintained using propofol. Fentanyl 1mcg/kg IV and Diclofenac 1mg/kg IM were administered for analgesia. Intraoperatively, vital signs (Electrocardiography, Pulse Rate, Sp02, Respiratory rate, End-tidal carbon-dioxide(etC02) were monitored continuously while noninvasive arterial blood pressure was monitored at 5 minutes intervals throughout the surgery. Maintenance fluid with 0.9% saline was administered, while blood loss and urine output were recorded. Hypotension (defined as blood pressure drop of $>$ 20% of baseline) was treated with rapid administration of 0.9% saline intravenous fluid and aliquots of IV ephedrine 3mg when indicated.

At the end of surgery, reversal agents (glycopyrrolate 0.01 mg/kg IV and neostigmine 0.04 mg/kg IV) were given and propofol infusion was stopped. The times to verbal response (response to name calling), eye opening (spontaneous or to command) endotracheal extubation and alertness (mobile phone number, date of birth or house address) were noted and recorded. Thereafter, oxygen was given with a face mask for about 10 minutes. Patients were transferred to PACU when fully oriented, hemodynamically stable and maintaining adequate saturation in room air. Postoperatively, vital signs, shivering score, pain score, level of sedation and PONV were assessed every 15 min in PACU and recorded. Postoperative analgesia was achieved with pentazocine 30 mg 4 hourly and paracetamol I g 8 hourly intravenously. Patients were observed in PACU and subsequently discharged to the ward when they achieved an Aldrete score of 9. (16) The time to discharge from the recovery ward was recorded.

Measurement

The induction time; was defined as the time (sec) from the start of propofol administration until loss of verbal contact. Recovery time; was defined as the time (min) from discontinuation of propofol infusion to eye-opening.

Discharge time: was defined as time from admission at PACU to time of achieving an Aldrete score of 9.(16)

The induction volume was defined as the volume (ml) of propofol administered from the start of propofol administration until loss of verbal response to command.

The induction dose was defined as the amount (mg) of propofol administered from the start of Propofol administration until loss of verbal response to command.

The total volume (ml) of propofol infused and the number of changes in target concentration or infusion rate were noted.

Target concentrations or infusion rates throughout anaesthesia were recorded. Adequacy of anaesthesia was based on the absence of haemodynamic changes (heart rate and arterial blood pressure within 20% of baseline values), and somatic (movement, grimacing) and autonomic (lacrimation, sweating) responses.(6) The quality of maintenance of anaesthesia was assessed by the anaesthetist as "good" (uncomplicated maintenance), "adequate" (minor problems but easily managed) or "poor" (significant problems).(12) The ease of control of anaesthesia was assessed by the number of adjustments to be: Good= 4 number of adjustments, Adequate= 5-7 number of adjustments and Poor $>$7 number of adjustments. Awareness was assessed using the modified Brice questionnaire. (17)

The safety of TCI vs. MCI was assessed by recording haemodynamic and respiratory parameters, movement during surgery and other adverse events.

Data analysis

Data entry and analysis were done using Statistical Package for the Social Sciences (SPSS) version 20.0 (IBM). Primary outcome variable was induction time. Secondary outcome variables were induction dose,

recovery time and quality of maintenance of anaesthesia. Others were ease of control of anaesthesia, target concentrations and infusion rates, numbers of boluses given and haemodynamic variability. Parametric data were compared using unpaired Student's t-test. Non-parametric data were compared using Mann-Whitney U test, while categorical data were compared using Chi-square test and Fisher's exact test. Results were presented as mean (SD), median, counts and proportions; P <0.05 was considered statistically significant.

Results

A total of 56 patients were enrolled for the study, however, only 52 completed the study. Four patients were excluded from the study, two because of prolonged surgery over 2 hours and another 2 because of unexpectedly short duration of surgery lasting less than an hour.

Table I shows patients demographic characteristics. The patients were comparable in both groups in terms of age (p = 0.644), weight (p = 0.726), height (p = 0.541), BMI (p = 0.918), ASA (p = 0.388) and sex (p = 0.500). Table II reveals the surgical procedures scheduled for both groups. The major procedure carried out was ORIF (23.2%). Other significant procedures performed included herniorrhaphy, hemorrhoidectomy, myomectomy, mastectomy, and thyroidectomy.

The patient baseline parameters are shown in Table III. No statistically significant differences were observed in terms of PR (p = 0.634), SBP (p = 0.378), DBP (p = 0.151), MAP (p = 0.113), RR (p = 0.4 72), SP02 (p = 0.345) and temperature (p = 0.059).

Table IV shows intraoperative characteristics of the patients in both groups. The duration of induction of anaesthesia was longer for TCI than for MCI (94.62 ± 11.34 sec vs. 79.50 ± 16.23 sec) and the difference was highly significant (p = 0.001). The induction dose of propofol was lower with TCI than with MCI (118.00 ± 22.33 mg vs.133.04 ± 20.58 mg) and the difference between the 2 groups statistically significant (p = 0.015). While the total dose of propofol used was higher for the TCI group than the MCI group, (1152.92 ± 234.47 mg vs. 1014.97 ± 264.18 mg,), no significant difference was observed between the 2 groups (p = 0.052. Fewer adjustments were needed for the TCI compared to the MCI (4 vs. 7), and the difference observed was highly significant (p=0.00 **I).**

Intraoperative maintenance parameters are shown in Table V. Duration of surgery, duration of Anaesthesia and recovery time were similar between the two groups (p = 0.829, 0.592 and 0.314, respectively). Moreover, mean doses of fentanyl, atracurium and diclofenac injections were comparable (P = 0. 760, 0.403 and 0.465, respectively). Intravenous fluid maintenance and estimated blood loss were not significantly different between the 2 groups (p = 0.504 and 0.303 respectively). Table VI displayed the haemodynamic parameters at baseline and at end of surgery in the 2 groups. The SBP, DBP and MAP were Significantly lower at the end of surgery compared to baseline, but the fall in PR did not attain statistical significance for both the TCI and MCI groups.

Figure 1 and 2 showed the trend of haemodynamic parameters, respiratory rate, and oxygen saturation. The SBP, DBP and MAP were comparable at 0, 5, 30, 60 and end of surgery between the two groups. The PR, RR and Sp02 were also comparable between the 2 groups throughout the duration of surgery.

Table VII showed the complications observed intraoperatively. More complications were observed with TCI than with MCI (56.7% v. 43.3%). However, the difference was not statistically significant (p = 0.541). Among the TCI and MCI groups, apnea (69.2% vs. 46.2%), tachycardia (61.5% vs. 53.8%) and hypotension (50% vs. 34.6%) were the commonest complications observed respectively. Bradycardia was found in 34.6% vs. 19.2% of the TCI and MCI groups, with no significant difference observed (0.087). While the values tended to be higher in the TCI groups compared to the MCI groups, the differences were not statistically significant. The incidence of other complications such as hypertension, bradycardia and respiratory depression were low and comparable between the two groups. No incidence of awareness or delayed recovery was observed among the patients in the two groups.

The quality of anaesthesia and the ease of anaesthesia are shown in Figures 3 and 4. The quality of anaesthesia was adjudged to be good (57% vs 57%), adequate (42.3% vs. 38.5%), or poor (0% vs. 3.8%) with both TCI

and MCI, and the difference was comparable between the two groups (p = 0.592). The result showed that it was easier to control anaesthesia with TCI than with MCI (good - 76.9% vs. 57.7%, poor - 0% vs. 7.7% respectively). However, the differences observed were not clinically significant (p = 0.191)

DISCUSSION

Induction Time

Induction time in a previous study(index)(11) indicates that the mean propofol induction dose was lower in the TCI group compared to the MCI group (118.60 ± 22.33 mg vs. 133.04 ± 20.58 mg), and the difference was statistically significant (p = 0.015). Longer induction times, with lower induction doses, are consistently reported with TCI compared with MCI when induction target concentrations are 4-6 μg/ml.(14,18,19) This is similar to the findings reported by Hunt-Smith et al.(12) Passot et al.(20) and Gale et al.(18) Nevertheless, Russel et al.(11) found propofol induction dose to be higher in the TCI group compared to the MCI group and the difference was statistically significant (201 ± 42.5 mg vs. 160 ± 23.5 mg, p <0.05). The authors used a higher targetconcentration (6 mcg/ml vs. 5 mcg/ml) and lower manual infusion rate (600 ml/hr vs. 1200ml/hr) compared to the index study. Studies have shown that the higher target concentration will lead to higher dose of propofol, while the lower manual infusion rate will lead to lower dose of propofol.

Nevertheless, Chiang et al. (13) found no significance in propofol induction dose between the 2 groups, though the dose was higher in the MCI group compared to the TCI group (p =0.119). The authors used a lower propofol target concentration compared to the index study (4 mcg/ml vs. 5 mcg/ml) against a manual infusion dose of 1.5 mg/kg. The lower target concentration used by Chiang et al. (13) may account for why they did not observe any significant difference between the 2 groups in their study in contrast to the index study.

In this study the mean total propofol consumption was higher in the TCI group compared to the MCI group (1152.92 ± 234.47 mg vs. 101 1 . 97 ± 234.18 mg), although the difference was not statistically significant (P = 0.052). This higher total dose recorded by the TCI group was achieved despite the initial lower induction dose used in the group. Computer simulations suggest that more propofol is used with TCI because the target blood concentration during maintenance always remained higher than in MCI group. (14) Studies done by Passot et al. (20) Gale et al. (32) and Rehberg et al. (21) also reported similar findings.

Propofol infusion rate

However, Breslin et al., Mu et al. (22) and Liu et al. (23) recorded a statistically significant difference in total propofol consumption between the TCI and MCI groups (p = 0.00 I, 0.03 and 0.000 I respectively). Breslin et al. used a lower propofol dose for manual infusion unlike the index study (1 mg/kg vs. 1.5 mg/kg) to compare with the same propofol target concentration of 5 mcg/ml. The smaller dose used for MCI by Breslin et al. (6) could explain why they found a significant difference. On the other hand, Mu et al. (22) used a paediatric model for propofol infusion (Paedfusor) unlike the index study where the Marsh model for adults was used. A high target concentration of propofol at induction is required when the Paedfusor plasma target TCI system was used.(22) Due to altered pharmacokinetics of intravenous drugs in children because of increased central compartment size and volume of distribution, larger induction bolus doses (e.g, propofol 3 to 5 mg/kg in children versus 1.5 to 2Mg/kg in adults) and higher initial infusion rates are required.(24) This may have resulted in a significantly higher total propofol consumption in the Mu et al.(22) study in the TCI group compared to the MCI group. Meanwhile Mu et al. (22) study used BIS as a monitor of both Analgesia and depth of hypnosis which we did not use. Moreover, BIS monitoring assesses only the hypnotic component of anaesthesia and not the analgesic component. (25) The difference in methodology may have led to the disparity in outcome measures observed. In contrast, Laso et al. (26), Chiang et al (13) Struys et al (14) and Yeganeh et al. reported higher total propofol consumption with manual infusion compared to target infusion. While Laso et al. (26), Struys et al (14) and Chiang et al. (13) found no significant difference between the 2 groups, Yeganeh et al (27).so found a highly significant difference between the 2 groups. In Struys et al. (14) study, Propofol maintenance was kept at a fixed infusion rate of 10 mg/kg/h unlike the index study where a step-down regime by Robert et al(5) was used. Moreover, in the study done by Laso et

al.(26)

Opioid inclusion

And Yeganeh et al. (27) the combination of propofol and remifentanil was used for induction. Opioids are known to reduce the dose of propofol needed for induction and maintenance of anaesthesia. Pharmacodynamic synergism has been shown between propofol and opioids, such that the higher the opioid plasma concentration, the lower the plasma propofol concentration required for the same effect. It is also known that optimal propofol concentration is dependent on the opioid chosen and the length of infusion duration. (3,28) This may have accounted for the lower dose of propofol used by the authors unlike the index study where only propofol was used for induction anaesthesia.

Infusion adjustment

The number of adjustments for propofol infusion was significantly lower in the target infusion group compared to the manual infusion group (4 vs 7, $p = 0.001$). Lin et al.(29) reported similar findings. This finding supports existing literatures that maintenance of anaesthesia was easier with the TCI than with the MCI because the use of an infusion pump reduced the number of times the anaesthetist had to intervene.(19,30,31) The less adjustments needed for TCI was probably due to the ability of the module to regulate its infusion rate automatically to maintain the set

Target concentration. This is one of the advantages of TCI over MCI. This resulted in smoother maintenance of anaesthesia, fewer haemodynamic perturbation and better quality of anaesthesia compared to MCI. In initial reports TCI has been demonstrated to provide easily controlled induction with excellent haemodynamic and respiratory stability. Furthermore, this advantage of TCI results in better ease of use and explains its preference by anaesthetists over MCI. (12,18,31)

In contrast, Newson et al. (30) had comparable number of adjustments between the TCI and the MCI groups (4 vs 4, $p = 0.72$). The TCI delivery system has been reported to be "easier to use" and anaesthesiologists were alleged to "feel more confident variable-rate infusion pump was used. This may possibly lead some practitioners to "set and forget" the target, resulting in a reduced effort by the operator to seek each patient's minimum sedative threshold (12,32). Moreover, Mu et al. (22) reported higher adjustments with TCI than with MCI, which is contrary to the finding in the index study. In the case of Mu et al. (22) investigator bias may be responsible for the higher rate of the TCI adjustments, especially because of more information derivable from the TCI machine. However, fewer interventions and less movement during anaesthesia may account for the conclusion from previous investigators that TCI is easier to use and provide better quality of anaesthesia than MCI.(19,31,33)

Time to Recovery

In the MCI group, the present study recorded a recovery time of 7.86 ± 2.05 min. This is comparable to 8.75 ± 2.81 min and 6.21 ± 3.48 min reported by Yeganeh et al. (27) and Russell et al. in their respective studies. However, Breslin et al. (6) and Hunt-Smith et al. recorded significantly longer recovery time with MCI compared to the index study (9.5 ± 5 min, 11 ± 7 and 15 ± 9.6 min vs. 7.86 ± 2.05). In the Hunt-Smith et al.(12) Study,the dose of adjuvant drugs that Were given (sedatives, analgesics, and muscle relaxants), and the stoppage of propofol infusion at the end of surgery was at the discretion of the anaesthetists. This unstandardized management may account for the longer recovery time observed by the authors compared to the index study.

On the other hand, Breslin et al.(6) administered i.v morphine 0.1 mg/kg 15 min before the end of surgery, and this is known to prolong recovery from anaesthesia.(34,35) In contrast, Struys et al.(14) a shorter recovery time from anaesthesia compared to the index study (12).28 ± 1.8 vs.7.86 ± 2.05 min), even when the total dose of propofol consumption with MCI was more than in the index study (1.028.79 mg vs. 1014.97 mg). The reason for this is not immediately apparent, however, the large inter-individual pharmacokinetic and pharmacodynamic variability may be responsible.

Haemodynamic stability

Haemodynamic parameters (BP, DBP, MAP) were significantly lower at the end of surgery compared to base line for both TCI and MCI groups. Though, the PR was lower at the end of surgery compared to baseline for both TCI and MCI, the differences were not significant. Moreover, while the SBP, DBP and MAP were slightly lower in the TCI group compared to the MCI group at 0, 5, 30,60 min and end of surgery, none of these differences attained statistical significance (p >0/05). In contrast, the PR was higher in the MCI group compared to the TCI group both at baseline and at the end of Surgery with no significant difference (p >0.05). Lower dose of propofol in the MCI group may be the cause of higher pulse rate due to less cardiovascular depressant effect. Giving higher concentrations of propofol may decrease awareness but cause haemodynamic side effects. (26,36). The stable haemodynamics is consistent with Previous reports of other studies. (6,1219,) Chaudri et al. (37) recorded a decrease in systolic and diastolic blood pressures of 10-12% during induction with TCI devices; representing an improvement compared with induction using fixed bolus doses (e.g. 2 mg/kg). In initial reports, TCI has been demonstrated to provide easily controlled induction with excellent haemodynamic and Respiratory stability. Careful control of the blood concentration of propofol can lead to a better control of haemodynamic and respiratory side-effects. (11,19,37) There were no episodes of intraoperative awareness with either of the techniques. Other studies reported similar outcome. The advantage of using TCI or MCI technique over bolus technique is the lack of intraoperative awareness or delayed recovery.

Tachycardia

Tachycardia was a common finding in both groups in this study, though the incidence is comparable. This is in keeping with reports in existing literature. (20,38) However, lower incidence of tachycardia was found in the Taylor et al.(38) The occurrence of tachycardia may be due to reflex sympathetic stimulation from hypotension experienced by the patients following propofol administration. Low incidences of hypertension, bradycardia and respiratory depression occurred among the patients in both groups.

Respiratory stability

In this study, there was a some incidence of apnea in the TCI group compared to the MCI group 69.2% vs. 46.2%, though the difference was comparable (p = 0.080). This is even though propofol induction dose was lower in the TCI group compared to the MCI group (118 mg vs 133 mg). This is in keeping with the findings in the literatures.(11,12) Nevertheless, Passot et al.(20) and Struys et al(20)recorded significantly lower apneic episodes with TCI than with MCI. The incidence of apnea following propofol induction is reported to depend on the dose and rate of administration. Computer simulations suggest that the high propofol concentration seen in the manually controlled infusion groups during induction was responsible for the high incidence of apnoea. The higher the induction dose of propofol, the higher the incidence and duration of apnoea.

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Quality of Anaesthesia

The quality of anaesthesia in the index study was comparable between the 2 groups (good - 57% vs. 67%). Moreover, it was easier to control anaesthesia with TCI than with MCI (good - 76.9 vs 57.7%). However, the difference in quality and ease of control of anaesthesia were not Significant among the 2 groups in the index study (p-value = 0.191 and 0.592 respectively). The superiority of the TCI was evident from the fewer adjustments (4 vs. 7) needed to maintain adequate depth of anaesthesia compared to MCI. This is supported by reports from other studies(12). McMurray et al (39) reported that the ease of control of sedation was Good, adequate, or poor in 79.5%, 16.4% and 4.1% patients respectively when using the TCI technique. In the study by Hunt-Smith et al (12), the ease of control of anaesthesia was reported as "good" in 96% of the TCI group and 86% of the MCI group. Nonetheless, from the present clinical evaluation it can be concluded that target-controlled infusion of propofol provides better ease and safe management of intraoperative anaesthesia, allowing fast and predictable changes in the depth of anaesthesia minimizing the risks of drug-related hemodynamic and respiratory side effects due to the minimal risk for propofol

overdosing.

Recommendations and Limitations

When the need for TIVA arises, MCI may be used where TCI equipment is unavailable with empirical cost benefits that need to be confirmed by further research. It would have been desirable also to have BIS Index measurement to objectively monitor the depth of anaesthesia facilities to measure blood concentrations of propofol or triglycerides (bye products of propofol).

Conclusion

MCI is comparable to TCI when propofol is administered during TIVA, though it falls behind TCI in terms of ease of use. Interestingly, MCI provides better haemodynamic stability and fewer complications compared to TCI. It is also remarkable **in** preventing awareness under general anaesthesia. It is less expensive to acquire and easier to deploy. Therefore, MCI remains a good option for induction and maintenance of general anaesthesia in the absence of TCI, in resource -restricted environments.

Conflict of interest- Nil

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