Comparison of Effective-Site Target Controlled Infusion and Manually Controlled Infusion of Propofol for Sedation during Spinal Anesthesia

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Objective: *Compare the efficacy of sedation of propofol infusion during spinal anesthesia between effective-site target controlled infusion and manually controlled infusion during spinal anesthesia.*
Material and Method: *Sixty inpatients scheduled for elective surgery undergoing spinal anesthesia were studied. The patients were allocated to one of two groups. Each group has 30 patients. The TCI group (n = 30) received propofol infusion using effective-site target controlled infusion. The initial target concentration of the effective site of propofol was 1.5 μg/ml. The MCI group (n = 30) received initial bolus 0.5 mg/kg and initial infusion rate 1.5 mg/kg/hr. The anesthesiologist adjusted to increase or decrease the infusion rate in both groups every minute in order to maintain the desired level of sedation (OAA/S score of 3 or 4). Hemodynamic, OAA/S score, the induction time, propofol dose, complications were recorded.*
Results: *The TCI group achieved the desired level of sedation (OAA/S score 3 or 4) faster than MCI group. The patients in TCI group had sedation score < 3 more than MCI group during surgery. Mean arterial pressure of TCI group were significantly lower than the MCI group at 15, 30, 45 min. Four patients in the TCI group was experienced airway obstruction. Two patients in the TCI group aspirated saliva and choked when they were sleeping. Eight patients in the TCI group and one patient in the MCI group were restless and there were intermittent patient movements.*
Conclusion: *The clinical benefit when used for sedation during spinal anesthesia of MCI was not different from TCI. There were complications in the TCI group more than the MCI group.*

Keywords: *OAA/S score, Effective-site target controlled infusion, Manually controlled infusion*

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The main uses of sedation in regional anesthesia are to reduce anxiety and improve patient comfort and cooperation[1]. Although spinal anesthesia provide anesthesia of the surgical site, the patient had unpleasant and uncomfortable result from having to remain in the same position, prolonged duration of surgery, or ambient noise in the operating room. Propofol is an agent used for sedation by anesthesiologists. The main advantage of propofol is its pharmacokinetic profile, which leads to fast induction, easy alteration of the sedation level and quick recovery[2]. Sedation with propofol can be achieved using a manually controlled infusion device. Recently target controlled infusion (TCI) device has become available for use with propofol and its has been suggested that these devices may offer advantages by more rapidly achieving and maintaining the desired level of sedation. TCI devices incorporate pharmacokinetic models to control an infusion pump thereby compensate for the distribution and elimination of intravenous drugs[3-5]. These TCI devices allow the anesthesiologist to achieve and maintain the predicted (effective site) brain concentration[6,7]. Because the cost is high, TCI devices are not commercially available in general hospitals. Manually controlled infusion devices (Syringe pump devices) are available in general hospitals. There were many studies to compare TCI devices and MCI devices used during general anesthesia but there were few studies to compare TCI devices effective site type and MCI devices for sedation during spinal anesthesia. The present study compared the efficacy of sedation of TCI devices effective site type and MCI devices by

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using an initial effective dose of propofol infusion which achieved proper sedation core for TCI devices was initial 1.5 μg/ml and for MCI devices was initial bolus 0.5 mg/kg follow with infusion rate 1.5 mg/kg/hr. The present report studied hemodynamic stability, complications of propofol infusion, and total propofol requirement for sedation during spinal anesthesia using either target controlled infusion device effective site type, or manually controlled infusion device.

Material and Method

After the present study was approved by the ethics committee of the Bangkok Metropolitan Administration, sixty inpatients scheduled for elective surgery procedure, ASA physical status 1 and 2, aged 18-80 years, undergoing spinal anesthesia for general surgery or orthopedic procedure were studied. Patients with a history of allergic reaction of propofol and/or obesity (BMI $\geq$ 30), significant central nervous system disorder, psychiatric disease, women who were pregnant, patients who had fasted less than 8 hours, hepatic, or renal disease were excluded from participation in the present study. Once informed consent had been obtained, the patients were allocated to one of two groups using a computer-generated sequence of random numbers. Each group had 30 patients.

On arrival in the anesthetic induction room, each patient was usual monitor. Supplement oxygen, 6 L/min, was administered via oxygen mask with sampling port for measuring expired carbon dioxide and monitor respiration. The level of intraoperative sedation was assessed using the Observer's Assessment of Alertness/Sedation (OAA/S) score by an anesthesiologist. The anesthesiologist who observed the patients were trained observers. A 20-gauge intravenous catheter was placed. A crystalloid preload was intravenous infused without premedication. Spinal anesthesia was performed at L3-4, with the patient in the lateral position. 0.5% bupivacaine was administered in a dose sufficient to provide a satisfactory sensory block for procedure and the sensory block did not exceed T10 dermatome. The sensory block level was evaluated every 1 min using a cold swab until the level was sufficient for surgery. Those patients were assigned to receive propofol infusion by two methods of intravenous drug delivery.

Group TCI (Target controlled infusion) n = 30: received propofol infusion using the Injectomat TIVA Agilia™ syringe pump (software version 4.0, Fresenius Kabi AG, Hamburg, Germany). The initial the target concentration of the effective site of propofol was 1.5 μg/ml. The target concentration at effective site was subsequently increased or decreased by 0.1 μg/ml every minute in order to maintain the desired level of sedation (OAA/S score of 3 or 4).

Group MCI (manually controlled infusion) n = 30: received propofol infusion using TOP-5200 syringe pump (Terumo, Japan). The initial bolus 0.5 mg/kg and initial infusion rate 1.5 mg/kg/hr and subsequently dose were adjusted to increase or decrease by 0.1 mg/kg/hr every minute in order to maintain the desired level of sedation (OAA/S score of 3 or 4).

The patients were observed for OAA/S score after propofol infusion. The time to start propofol infusion and the time to observe patients had OAA/S score of 4 were recorded. OAA/S score were recorded when patients have OAA/S score < 5 after propofol infusion then recorded at 15 min intervals. The anesthesiologist attempted to maintain the OAA/S score of 3 or 4 during the operation all patients. Hemodynamic and respiratory rate were recorded at 5 min intervals. Fluid and vasopressor requirement was note. Ephedrine was administered in 3 mg increments after a sustained (3-min) reduction in mean arterial pressure of 20% from baseline. Sedation was stopped if the respiratory rate was less than 8 bpm. The infusion was finally discontinued at the end of the surgical procedure, and total sedative requirement, the time until the patient was fully alert was recorded.

The data was presented as mean $\pm$ SD for laboratory values. The characteristics of the two groups were analyzed by using a two-tailed unpaired t-test. The sedation score was compared between groups using the Pearson's Chi-Square test Fisher's exact test were used for comparing the incidences of complication. Statistical significance was accepted when p was < 0.05.

Sample size was estimate based on the study of Mazzarella et al[8] as follows:

$$N = \frac{(Z_\alpha + Z_\beta)^2 \times 2P(1-P)}{(P1-P2)^2}$$

$$P = 1/2\,(P1 + P2)$$

N is sample size of each group, Z_α and Z_β are Z-value of type I and type II errors, P1 and P2 are success rate which achieved the desire level of sedation score of TCI devices and MCI devices. According to Mazzarella et al, success rate of TCI devices which achieved the desire level of sedation score was 91.2% (P1 = 0.912). In the present study, the authors expected that the success rate of MCI devices

Table 1. Demographic data and patient characteristics

	TCI (n = 30)	MCI (n = 30)	p-value
Age (yr)	46.03 ± 15.91	48.73 ± 16.23	0.518
Weight (Kg)	62.23 ± 9.72	62.63 ± 11.25	0.088
Height (cm)	163.00 ± 6.66	162.50 ± 8.86	0.534
Block level (dermatome)	9.43 ± 1.16	9.26 ± 1.52	0.270
Anesthetic time (min)	63.73 ± 30.13	72.26 ± 33.56	0.637

Table 2. OAA/S score

Time (min) Sedation score	TCI (n = 30) 5/4/3/2/1	MCI (n = 30) 5/4/3/2/1
After infusion	0/23/6/1/0	0/26/3/1/0
15 min	0/11/8/10/0	0/20/5/4/0
30 min	1/3/13/11/0	2/17/7/2/1
45 min	3/2/7/11/0	1/11/9/3/0
60 min	1/4/5/4/2	2/8/5/2/0
1.15 hr	0/5/2/2/2	1/9/3/0/0
1.30 hr	2/2/4/2/0	0/7/3/0/0
1.45 hr	1/0/5/1/0	0/6/0/0/0
2 hr	0/1/2/1/2	1/3/1/0/0

Table 3. Incidence of intraoperative complication

	TCI (n = 30)	MCI (n = 30)	p-value
Coughing or choking	2	0	0.15
Intermittent movements	8	1	0.01*
Airway obstruction	4	0	0.03*
Pain at infusion site	0	1	0.31

should be within 30% of the success rate of TCI devices (P2 = 0.6). When the authors considered α = 0.05 and β = 0.20 (Z_α = 1.96 and Z_β = 0.84), the authors obtained P = 0.756 and N = 29.71. The sample size of each group required 30 patients

Results

The two groups did not differ with respect to age, weight, height, and baseline mean arterial pressure. There were no significant differences between the groups regarding final analgesic level achieved and duration of surgery (Table 1). The peak level of sensory block was not above T10 in all patients. Sedation scores were practically identical for both groups, with a constant degree of sedation being maintained over time. The TCI group achieved the desired level of sedation (OAA/S score 4) faster than the MCI group (4.83 ± 3.15 min vs. 6.70 ± 3.09 min, p < 0.02). The number of patients in TCI group had sedation score < 3 more than the MCI group during surgery at 15, 30, 45 min (Table 2). Mean arterial pressure of the TCI group was significantly lower than the MCI group at 15, 30, 45 min (Fig. 1). The incidences of complications were comparable (Table 3). Four patients in the TCI group experienced airway obstruction. This was corrected by decreasing the target concentration of effective site and maintaining their airway with an oxygen mask for a few minutes then they came back to spontaneous respiration. Two patients in the TCI group aspirated saliva and choked when they were sleeping. Eight patients in the TCI group and one patient in the MCI group had intermittent patient movements but not interfering with the operation. They corrected by increasing the dose of propofol infusion to achieve the desire level of sedation and complete the surgery. The mean total propofol dose of TCI much more than MCI (242.58 ± 116.01 mg vs. 150.84 ± 76.52 mg, p < 0.001).

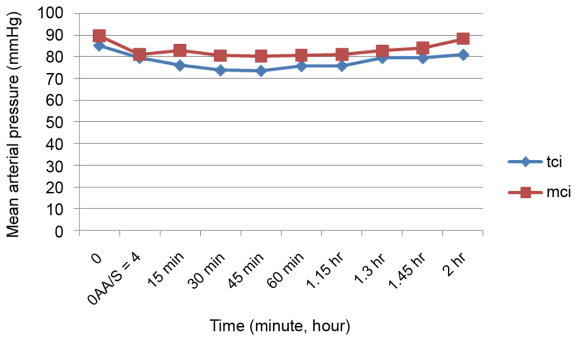

Fig. 1 Mean arterial pressure value (mean ± SD) recorded during the intraoperative course after propofol infusion, at the time to OAA/S < 5 and 15-min intervals for each of the two groups. Symbols represent the TCI group (◆) and the MCI group (■). The mean arterial pressure of the TCI group was significantly lower than the MCI group at 15 min, 30 min and 45 min

Discussion

The TCI system has been described by Schwilden et al[3]. They showed that it was possible to attain the desired plasma concentration of intravenous anesthetic drugs by using a computer-controlled pump programmed with published pharmacokinetics of drugs. The TCI pump was developed to calculate the infusion rate from setting concentration of effective site (brain) by using microprocessor programmed with pharmacokinetic data. The TCI devices have been used for propofol infusion to maintain anesthetic level during surgery. The authors performed a systemic review using the Cochrane Library to evaluate administration technique for intravenous propofol infusion during general anesthesia have reported that TCI offer advantages over MCI with faster sleep. However, the mean total propofol dose of TCI is much more than MCI[9]. There were previous studies evaluating the sedation efficacy in the TCI group and MCI group. Christopher N et al[10] compared the infusion technique for sedation in breast biopsy between MCI, TCI and intermittent bolus. They reported that the quality of sedation, operating condition, and clinical recovery profiles were similar in all three groups. Adrian F et al[11] reported that optimum target concentration of propofol infusion range was 1.4 ± 0.4 μg/ml to achieve the desire sedation (OAA/S score 4) for oral surgery. Ka Young Rhee et al[12] compared the efficacy sedation of TCI between propofol-midazolam combination and propofol alone during spinal anesthesia, they found that the effective site concentration of propofol infusion alone to achieve the target sedation was 1.5 ± 0.4 μg/ml.

Henry P Frizzele et al[13] studied the efficacy sedation of MCI technique during spinal anesthesia between propofol-ketamine combination and propofol alone. There were no differences between the intra-oprative sedation score between propofol-ketamine combination and propofol alone. The dose of propofol infusion of propofol alone group was initial bolus of propofol 0.5 mg/kg and then followed with infusion rate 1.5 mg/kg/hr, they found that the dose had little respiratory effect and achieved the desire sedation score. The authors used the dose of propofol infusion following previous studies and adjusting the dose by increased or decreased dose in both groups for attempting to maintain the desired level of sedation (OAA/S score of 3 or 4), because of the considerable interpatients pharmacokinetic variability. The monitor of sedation score the authors used only the Observer's Assessment of Alertness/Sedation (OAA/S) score. The authors did not use BIS (Bispectral index), because the recent study of D. H□hener et al[14] found that BIS does not seen to be reliable for monitor sedation with light sedation in spinal anesthesia. However, the authors are unaware of any published studies comparing the TCI technique effective site type and MCI technique to sedate patients for spinal anesthesia.

In the present study, the authors found that the TCI group had a lower induction time than the MCI group. The sedation score after infusion had no significant differences between the groups. The patients in the TCI group had sedation score < 3 more than MCI group during surgery at 15, 30, 45 min after infusion (Table 2). These data are similar to the results reported by Christopher N. et al[10]. The Many patients in the TCI group had OAA/S score < 3 than the MCI group during surgery. This problem was following bolus injection of TCI, plasma propofol level increased rapidly and distributed to a high rich vessel organ (brain). TCI device adjusted the infusion rate to achieve the concentration of effective site at brain and maintained it during the operation. TCI needed time 10-15 min for plasma/effective site (brain) equilibration. In the setting of regional anesthesia, the patients had no pain. Only light sedation was required. The patients who had the sedation score < 3 may be at risk for airway obstruction.

In the present study, four patients in the TCI group had airway obstruction when their sedation score was < 3[15,16]. They corrected by decreasing the target concentration of effective site and maintaining their airway with an oxygen mask for a few minute then they came back to spontaneous respiration. Two patients in the TCI group aspirated saliva and choked when they were sleeping. It was described by fast sedation, which may compressed gag reflex and affect swallowing. Park JY et al[17] studied target-controlled propofol infusion for sedation in patients undergoing transrectal ultrasound-guided prostate biopsy. They found that the incidence of hypoxia increased as the level of sedation was decreased. In contrast, when starting sedation by MCI, the anesthesiologist selected and adjusted the infusion rate to achieve the desire level sedation (OAA/S of 3 or 4). Following initial small bolus injection, the plasma propofol level was slowly increased and distributed to high rich vessel organ (brain). When the concentration of propofol at the brain increased, the plasma concentration was decreased from rapid

clearance of propofol. The propofol infusion could maintain the plasma propofol level[18]. No patient in the MCI group had airway obstruction. The sedation score (OAA/S score) of the MCI group were stable at the desired level sedation score (OAA/S score 3 or 4) after starting infusion and during operation.

Mean arterial blood pressure of the two groups were not different from baseline at induction time and achieved sedation score. During surgery mean arterial blood pressure of the TCI group were significantly lower than the MCI group at 15, 30, and 45 min (Fig. 1). The results were similar to the study of Wakeling et al[19]. They found no adverse cardiovascular consequences during peak drug effect and the peak cardiovascular depression occurred after 10 min. They found the maximal decrease of mean arterial blood pressure in TCI effective site group average 23%. In the present study, mean arterial pressure of both groups were not reduced 20% from baseline. When mean arterial pressure decreased, they corrected by decreasing setting target infusion both in groups then they came back to baseline of mean arterial blood pressure.

In conclusion, the present study suggests the clinical benefit of MCI was not different from TCI. MCI may be safer than TCI when used for sedation in spinal anesthesia. However, the use of TCI device or MCI device required decision by the anesthesiologists up to their experience. Further studies are necessary to assess the cost-effectiveness of using new infusion technique for maintenance of propofol sedation during spinal anesthesia.

Potential conflicts of interest

None.

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Appendix. Observer's Assessment of Alertness/Sedation Score

Reponsiveness	Speech	Facial express	Eye	Composite score level
Responds readily to name spoken in normal tone	Normal	Normal	Clear, no ptosis	5
Lethargic response to name spoken in normal tone	Mild slowing or thickening	Mild relaxation	Glazed or mild ptosis (less than half the eye)	4
Responds only after name is called loudly and/or repeatedly	Slurring or prominent slowing	Marked relaxation	Glazed and marked ptosis (half the eye or more)	3
Responds only after mild prodding or shaking	Few recognizable words			2
Does not respond to mild prodding or shaking				1

การเปรียบเทียบประสิทธิภาพการทำให้ผู้ป่วยที่ได้รับ spinal anesthesia สงบโดยการให้ยา propofol infusion ด้วยวิธี target controlled infusion ชนิด effective site กับการให้ยา propofol infusion ด้วยวิธี manually controlled infusion

สุรจักร เหล่าสุวรรณ, สุกัญญา พงศ์ฤกษ์ดี, รุศนา ทหราวานิช

วัตถุประสงค์: เพื่อเปรียบเทียบประสิทธิภาพการ ทำให้ผู้ป่วยที่ได้รับ spinal anesthesia สงบโดยการให้ยา propofol infusion ด้วยวิธี target controlled infusion ชนิด effective site (TCI) กับการให้ยา propofol infusion ด้วยวิธี manually controlled infusion (MCI)

วัสดุและวิธีการ: ทำการศึกษาผู้ป่วย 60 คน ที่มารับการผ่าตัดไม่เร่งด่วนและได้รับการระงับความรู้สึกแบบ spinal anesthesia แบ่งผู้ป่วยเป็น 2 กลุ่ม ๆ ละ 30 คน กลุ่ม TCI ได้รับ propofol infusion ด้วยเครื่อง effective-site target controlled infusion โดยการตั้ง effective site ตั้งต้นที่ 1.5 μg/ml กลุ่ม MCI ได้รับ propfol infusion ด้วยเครื่อง syringe pump โดยการตั้งเครื่องให้ยาครั้งแรก 0.5 mg/kg. และ infusion rate 1.5 mg/kg/hr. ทั้งสองกลุ่มวิสัญญีแพทย์สามารถปรับเครื่องทุก 1 นาทีระหว่างทำผ่าตัดเพื่อรักษา OAA/S score ให้เท่ากับ 3 หรือ 4 ทำการบันทึกสัญญาณชีพ บันทึกเวลาที่เริ่มให้ยา และเวลาที่ผู้ป่วยเริ่มมี OAA/S score เท่ากับ 4 บันทึก OAA/S score ระหว่างผ่าตัด ขนาดยา propofol ที่ใช้และภาวะแทรกซ้อนที่เกิดขึ้น

ผลการศึกษา: กลุ่ม TCI ผู้ป่วยมี OAA/S score น้อยกว่า 5 เร็วกว่ากลุ่ม MCI หลังให้ propofol infusion ระหว่างผ่าตัดพบผู้ป่วยในกลุ่ม TCI มีOAA/S score น้อยกว่า 3 มากกว่ากลุ่ม MCI ค่า mean arterial pressure ระหว่างผ่าตัดกลุ่ม TCI ต่ำกว่ากลุ่ม MCI อย่างมีนัยสำคัญที่เวลา 15, 30, 45 นาที ผู้ป่วย 4 รายในกลุ่ม TCI มีปัญหา airway obstruction ระหว่างผ่าตัด ผู้ป่วย 2 รายในกลุ่ม TCI มีการสำลักน้ำลาย และไอระหว่างผ่าตัด พบผู้ป่วย 8 รายในกลุ่ม TCI และผู้ป่วย 1 รายในกลุ่ม MCI ขยับแขนขาและไม่สามารถอยู่นิ่งได้ระหว่างผ่าตัด

สรุป: ประสิทธิภาพการ ทำให้ผู้ป่วย spinal anesthesia สงบระหว่างกลุ่มที่ใช้ MCI ไม่แตกต่างจากกลุ่มที่ใช้ TCI และพบว่าเกิดภาวะแทรกซ้อนในกลุ่ม MCI น้อยกว่า