

**Original Article**

## Effect of propofol or oral midazolam and thiopental sodium as induction agent for day care surgery- a comparative study

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### Abstract

**Background** Day care surgery is widely acceptable and gaining popularity for more than a decade. Early recovery and cost effectiveness is an integral part of day care surgery in developing country.

**Objective** To compare the cost effectiveness & recovery score after oral midazolam and thiopental sodium or propofol induction in day care surgery.

**Methods** A total number of sixty patients, thirty in each group of ASA grade I & II were selected. In group A patient receiving propofol 2mg/kg for induction and group B were given oral midazolam 0.25mg/kg thirty minutes before induction with thiopental sodium 2.5mg/kg. Perioperative heart rate, BP, recovery score and time to ready to go home were monitored. Average cost of induction was calculated in both groups.

**Result** Recovery scores in group A & B were  $8.8 \pm 1.75$  and  $8.01 \pm 1.03$  respectively after thirty minutes of reversal. The cost of group B (BDT  $37.88 \pm 1.37$ ) was significantly lower ( $P < 0.05$ ) than that of group A (BDT  $142.00 \pm 6.00$ ).

**Conclusion** Preoperative oral midazolam & low dose thiopental sodium induction is relatively cost effective than propofol induction in day care surgery.

**Key word:** Day care surgery, Oral midazolam, thiopental sodium, propofol.

(JBSA 2012; 25(1): 9-13)

### Introduction

Surgical day-cases are admitted for operations or investigations on a planned, non-resident basis and occupy beds for a period of time in a unit set aside the operation theatre complex and go back home on the same day, also called 'out-patient ambulatory surgical cases'. It is one of the most dramatic transformations in health care delivery in the recent past. The primary impetus for this change is the economic saving afforded by not admitting patients the night before surgery or keeping them in hospital over night after surgery. Other advantages include earlier ambulation, patients' convenience and a lessened risk of nosocomial infections<sup>2</sup>.

Prerequisites for this are agents having characteristics of rapid efficient action with quick elimination without hang-over effect and of course cost effective. None of the currently available anaesthetic agents have duration of action short enough to leave the patient with no residual effects within a few hours of surgery<sup>3</sup>. Commonly used induction agent, Thiopentone is having elimination half-life of 5 to 10 hours and up to 30% may remain in the body after 24 hours. It does not provide a clear-headed recovery in day-case anaesthesia. On the other hand, Propofol has distribution and elimination half-lives of 1 to 2 minutes and 1 to 5 hours respectively and provides rapid recovery

with minimal residual effect which is suitable for day-cases<sup>4</sup>. But high price of Propofol and also chance of contamination of vials are major hindrance to its use for day-cases in the underprivileged population<sup>2,4</sup>.

Midazolam is a potent sedative, adjuvant to hypnotics, with a flat cardio-vascular profile, readily absorbable with an onset of effects within 10 to 15 minutes after oral administration<sup>5</sup>. Even at 30 mg oral dose does not accumulate in plasma (<2ng/ml) with less chance of any adverse effects and prolonged action, thereby renders a quick and clear-headed recovery<sup>6</sup>.

This study was carried out to compare the quality of recovery from Propofol induction with thiopentone along with oral midazolam. The cost effectiveness of these induction agents were also evaluated to observe the benefit of the patient.

### Methods

This study was conducted in Department of Anaesthesia, Analgesia and Intensive Care Medicine, BSMMU, Dhaka from July to September 2005. Sixty gynaecological patients within 18 to 35 years of age, belonging to ASA (American Society of Anaesthesiologists) status I and II, scheduled for routine laparoscopic procedure on day-case basis. Patients were randomly selected by card sampling method and grouped equally into two with thirty in each group. After pre-oxygenation, Group-A received propofol 2 mg/kg for induction and Group-B were given midazolam 0.25 mg/kg orally 30 minutes before induction by thiopentone 2.5 mg/kg. Medium-acting vecuronium was used for endotracheal intubation and muscle relaxation. analgesia and maintenance were managed by fentanyl 1mgm/kg and 0.5% halothane respectively. Per-operative vital parameters were observed and recorded at 5 min interval. Recovery quality was assessed by SOCA (S-Sedation, O-Orientation, C-Comprehension, and A-Amnesia) scores and time required for fitness to go home were monitored & recorded. After completion of surgery, total cost of induction agents was calculated and recorded.

Data were collected in a pre-design 'data collection sheet'. Data were compiled and statistical analysis were done using student's 't' test with the help of SPSS version 11. Values are regarded as significant if  $p < 0.05$ .

### SOCA Score<sup>7</sup>

<b>Sedation:</b>	
Awake and alert or tense	4
Awake and not alert or tense	3
Drowsy	2
Sleepy or asleep but rousable	1
Asleep and not rousable	0
<b>Orientation:</b>	
Full orientation	2
Partial disorientation	1
Total disorientation	0
<b>Comprehension:</b>	
Execution of order	2
Execution of order only by initiation	1
No execution of order	0
<b>Amnesia:</b>	
No amnesia	3
Slight amnesia	2
Moderate amnesia	1
Severe amnesia	0

\* 10 out of 11 must be scored before discharge under normal circumstances.

### Fitness to go home<sup>8</sup>

- 1) Orientation to person, place and time.
- 2) Stable vital signs for 30-60 minutes.
- 3) Ability to ambulate unassisted.
- 4) Ability to tolerate oral fluids.
- 5) Ability to void.
- 6) Absence of significant pain or bleeding.

### Results:

Patient's characteristics are shown in table-I and there were no significant differences among both groups.

Patient's vital parameters like heart rate, systolic and diastolic blood pressure were recorded at various timing. There was not much variation regarding those vital parameters among both groups (Table II and Figure 1).

Recovery score at different timing is shown in Table-III. Immediately after reversal recovery score for group A and group B were  $5.98 \pm 2.00$  and  $5.26 \pm 1.84$  respectively. Score were recorded after 5, 10, 15, 20, 25 and 30 minutes of reversal. Thirty minutes after reversal this score was  $8.86 \pm 1.75$  and  $8.01 \pm 1.03$  for group A and group B respectively.

Time for fitness to go home was recorded when patients were fulfilled the criteria for fitness to go home. It was  $281 \pm 44$  and  $321 \pm 53$  minutes for group A and group B respectively (Table-IV).

Cost of induction agents was relatively higher in group A ( $142.00 \pm 6.00$ ) than that of in group B ( $37.88 \pm 1.37$ ) [Table-V].

**Table I** Patients characteristics like age, body weight, height and ASA grading.

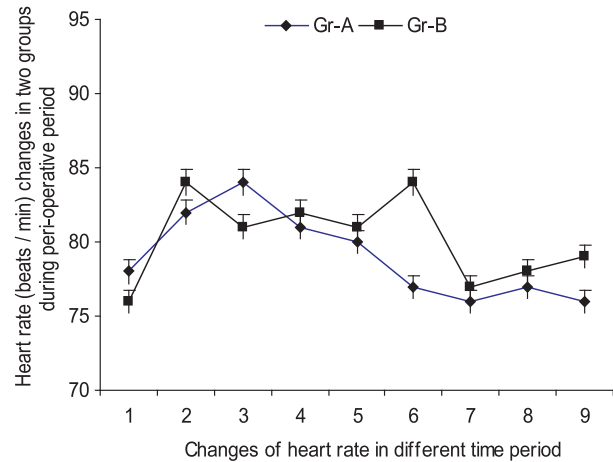
Characteristics	Group A (n=30)	Group B (n=30)	P value
Age (years)	$27.20 \pm 3.14$	$25.95 \pm 3.80$	0.546 <sup>NS</sup>
Body wt (kg)	$63.80 \pm 4.37$	$61.50 \pm 3.46$	0.071 <sup>NS</sup>
Height (cm)	$156.25 \pm 3.49$	$152.65 \pm 4.04$	0.063 <sup>NS</sup>
ASA-I	86.66%	93.33%	0.181 <sup>NS</sup>
ASA-II	13.34%	6.67%	0.512 <sup>NS</sup>

Values are expressed as mean  $\pm$  SD. NS: not significant  $p > 0.05$  (among two groups) for age, body weight, height, ASA grade-I & II; Student's 't' test was done to find out the difference between groups.

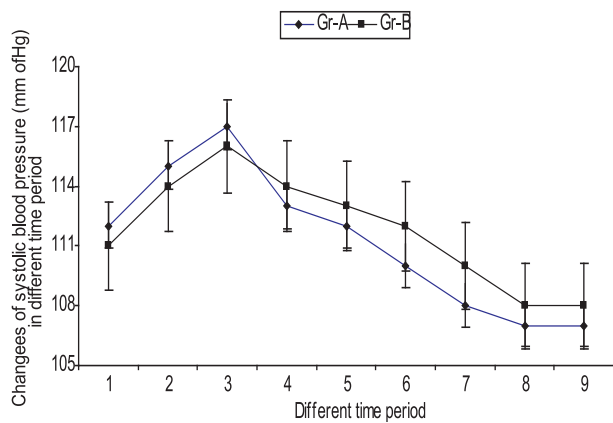
**Table II** Heart rate changes in both groups in pre, per and post operative period.

Timing	Group-A (n=30)	Group-B (n=30)	P value
Pre-operative	$78 \pm 4$	$76 \pm 6$	0.039
At induction	$82 \pm 8$	$84 \pm 9$	
At reversal	$84 \pm 8$	$81 \pm 13$	
After 5 min	$81 \pm 12$	$82 \pm 9$	
After 10 min	$80 \pm 8$	$81 \pm 8$	
After 15 min	$77 \pm 5$	$84 \pm 7$	
After 20 min	$76 \pm 6$	$77 \pm 8$	
After 25 min	$77 \pm 7$	$78 \pm 6$	
After 30 min	$76 \pm 6$	$79 \pm 8$	

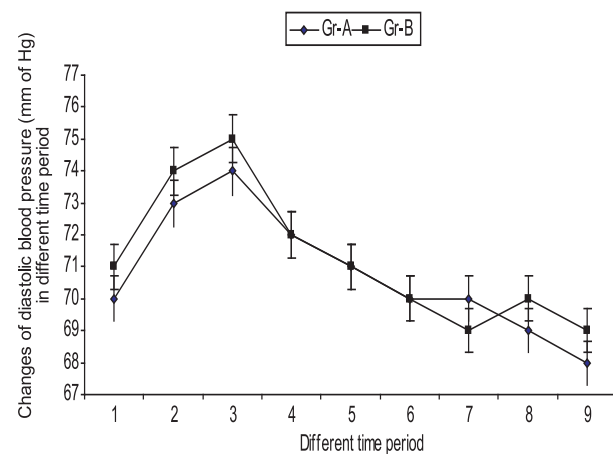
Values are expressed as mean  $\pm$  SD. Sig: Significant  $p < 0.05$  (among two groups) for heart rate changes in both groups in pre, per and post operative period; Student's 't' test was done to find out the difference between groups.



**Fig 1** Heart rate changes in both groups in pre, per and post operative period.



**Fig 2** Systolic blood pressure variations between two groups in different time period.



**Fig 3** Diastolic blood pressure variations between two groups in different time period.

**Table III** Recovery score (SOCA) in both group.

Timing	Group-A (n = 30)	Group-B (n=30)	P value
At reversal	5.98 ± 2.0	5.26±1.84	<0.047 <sup>S</sup>
After 5 min	6.00±1.79	5.66±1.62	
After 10 min	7.02±1.72	6.10±1.08	
After 15 min	7.26±2.01	6.46±1.24	
After 20 min	7.78±2.82	6.86±1.27	
After 25 min	8.10±2.25	7.08±1.24	
After 30 min	8.86±1.75	8.01±1.03	

Values are expressed as mean ± SD. Sig: Significant  $p < 0.05$  (among two groups) for recovery score (SOCA) in both group; Student's 't' test was done to find out the difference between groups.

**Table-IV** Time for fitness to go home in both groups.

Group	Fitness to go home (time in minutes)	P value
Group-A (n=30)	281 ± 44	0.98 <sup>NS</sup>
Group-B (n=30)	321±53	

Values are expressed as mean ± SD. NS: not significant  $p > 0.05$  (among two groups) for fitness to go home; Student's 't' test was done to find out the difference between groups.

**Table V** Cost of induction agents in both group.

Group	Cost of induction agents in Taka	P value
Group-A (n=30)	142.00±6.00	0.027 <sup>s</sup>
Group-B (n=30)	37.88±1.37	

Values are expressed as mean ± SD. Sig: significant  $p < 0.05$  (among two groups) for cost of induction agents; analysis was done by Student's 't' test.

## Discussion

Proper selection, planning & uneventful clear-headed anaesthetic recovery are the hallmarks of

fruitful day-case surgery. Many operations are performed at one-fifth cost of inpatient surgery if carried out on a day-case basis<sup>9</sup>. These are economical when they come-out safely with an early discharge. This study was to find-out a cost-effective recipe of induction agent, alternative to propofol which is the choice in day-cases but quite expensive. Co-induction with oral midazolam (0.25 mg/kg) and a reduced dose (2.5 mg/kg) of conventional intravenous thiopentone revealed the recovery status nearly closed to that of propofol. The variation in recovery scores (Table-III) and time for fitness to go home (Table-IV) between the two groups were almost similar. Moreover, the peri-operative parameters like heart rate, systolic and diastolic blood pressure (Table-II and Figure-1) deviations between the groups were also similar.

One study showed that after receiving 10 mg of i.v. midazolam the recovery in relation to orientation of time and place occurs within 15 minutes. Pharmacokinetics of midazolam after both i.v. and oral administration to healthy volunteers are broadly similar<sup>10</sup>. When patients are induced with thiopentone, awakening ranges from 1½ to 2½ times prolonged with midazolam<sup>11</sup>. So, to avoid that delay, a reduced dose of thiopentone was used and supplemented with low-dose volatile to maintain adequate depth of anaesthesia. The addition of potent opioids tends to prolong the recovery, but fentanyl up to 1.5 µgm/kg does not delay emergence when given immediately before induction<sup>12</sup>.

In all the poor countries like ours, cost-effectiveness is an influential consideration related to the health-care consumers along with other aspects. In this study, it is found that the expense for propofol is Tk-142.00±6.00/= per patient. One ampoule costing Tk-260/= contains 200 mg of propofol while the average requirement is 140±12 mg for induction; rest of the drug has to discard for its higher risk of contamination<sup>13</sup>. So, actual expenditure per case goes high due to system loss. On the other hand, in group-B, the average cost of induction agents is Tk-37.88±1.37/ per case, i.e. 26.66% of that of group-A (Table-V). Moreover, thiopentone remains stable for 24-36 hours after mixing and is permitted to use in several patients from multi-dose vials<sup>14</sup> and thereby seems more economic. Tab midazolam (7.5 mg) charges simply Tk-10/= and most of the patients require 15 mg

which costs Tk-20/= only. So, the cost of these co-induction agents is significantly less than that of injection propofol.

Under the condition of present study, we could conclude that oral midazolam and intravenous thiopental sodium induction in day care surgery is highly cost effective than propofol alone induction agent without any significant changes in hemodynamics, recovery scores as well as time to ready to go home.

### References

1. Penketh R, Griffiths A. A prospective observational study of the safety and acceptability of vaginal hysterectomy performed in a 24-hour day case surgery setting. *Brit J Obs & Gyn.* 2007; 114(4): 430-6
2. Ackerman S. *Outpatient Anaesthesia.* 3<sup>rd</sup> edn. Lange Medical Books, 2002, 882-888.
3. Cooper G. *Recovery Rounds.* Empirical Chemical Industries PLC, England, 1986; 19:3-7
4. Reves JG, Fragen RJ, Vinik HR. Midazolam: Pharmacology and uses. *Anesthesiology.* 1985; 62:310-324
5. Elder JS, Longenecker R. Pre-medication with oral midazolam for voiding cysto-urothrography in children: Safety and efficacy. *Am JR* 1995; 164: 1229-1232
6. Bornemann LD. Dose dependent pharmacokinetics of midazolam. *Eur J Clin Pharmacol.* 1985; 29: 91-95
7. Alon F, Baitfella L, Hossli G. Double blind study of reversal of midazolam supplemented general Anaesthesia. *Br J Anaesthesia,* 1987; 59: 455
8. Gatt M, Reddy BS, Mainprize KS. Day-case stoma surgery: is it feasible? *Surgeon.* 2007; 5(3):143-7
9. Feeley TW. *The Recovery Room,* Miller RD, Anaesthesia, 2<sup>nd</sup> edn. Churchill-Livingstone, New York 1986; 3:1925-1935
10. Pentikainen PJ, Valisalmi L. Pharmacokinetics of midazolam following IV & oral administration in patient with chronic liver disease & in healthy subjects. *J Clin pharmacol* 1989; 29: 272-277
11. Wood M, Wood M, Wood AJJ. *Drugs and Anaesthesia,* 2<sup>nd</sup> edn Williams and Wilkins 1990; 179-223
12. Vinik HR. Intravenous anaesthetic drug interaction: Practical applications. *Eur J Anaesth* 1995; 6: 9-13
13. Chen H, Zhang Z. A novel, lipid-free nanodispersion formulation of propofol and its characterization. *Pharm Res.* 2005; 22(3): 356-61
14. Sklar GS, Sonn DD, Watson WA. Thiopental-sparing properties of butorphanol/diazepam for induction of anesthesia in ambulatory gynecologic surgery. *DICP.* 1989; 23(9):659-62