

# Outcomes of Propofol or Thiopental Sodium and Oral Midazolam as an Induction Agent for Day Care Surgery

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## ABSTRACT

**Background:** The increasing popularity of outpatient surgery has prompted the search for new anesthetic agent that can provide safe and effective anesthesia with a rapid and smooth recovery. Day care surgical procedure is extensively accepted and has been attaining recognition for over a time. The cost effectiveness and early recovery are an essential part of day-care surgical treatment in evolving countries.

**Aim:** To compare the recovery score and cost-effectiveness after oral induction of midazolam and thiopental sodium with propofol alone in day-care surgical procedure.

**Methods:** Eighty patients were selected, 40 in each ASA grade I and II group. In A group; patients were administered propofol at dose of 2 mg / kg for induction, and in group B; 0.25 mg / kg thiopental sodium and 0.25 mg / kg midazolam orally were given 30-mins prior to induction. Perioperative heart rate, time to ready to go home, blood pressure and recovery score were observed. The average induction cost was determined in group A and B.

**Results:** After 30 minutes of reversal, the score of recovery in groups A and B were  $8.90 \pm 1.82$  and  $8.02 \pm 1.01$ , correspondingly. The group B has significantly lesser cost (PKR  $90.25 \pm 10.73$ ) in comparison to the group A (PKR  $700.0 \pm 100.0$ ) ( $p < 0.05$ ).

**Conclusions:** Preoperative induction of oral midazolam and low doses of thiopental sodium is comparatively cost effective compared to induction of propofol in day-care surgical procedure.

**Keywords:** Oral midazolam, Day care surgery, Propofol and Thiopental sodium.

## INTRODUCTION

Ambulatory surgery has become increasingly popular during the past two decades due to an

increased demand in cost saving, fewer beds Occupancy, its popularity with the patients due to

minimal separation from family and less disruption in personal life, and a rapid return to daily activities.<sup>1</sup> There is reduced risk of wound infection, deep vein thrombosis, pulmonary embolism and pneumonia.

The ideal anesthetic agent for ambulatory surgery should have a smooth and rapid induction,

fast recovery, intraoperative amnesia and analgesia and minimal side effects post operatively.<sup>1</sup>

Thiopentone is traditionally associated with rapid induction, short duration of action and minimal side

effects. However, poor psychomotor recovery and subjective feeling of tiredness and drowsiness

associated with it in the post operative period limits its usefulness in day care patients. The disadvantages, however, are cardio stimulatory effect, emergence delirium and hallucinations

postoperatively. It also has been associated with increased pulmonary resistance.

Day-care surgical cases are admitted for an operation or examination as scheduled, without the resident's stay, and occupying beds for a specified time period in a separate unit of the operating room and returning home on the similar day, also known as "day-care surgery"<sup>1-2</sup>. This is the utmost histrionic changes in the delivery of health services in the current era<sup>3-4</sup>. The main stimulus of this revolution is the cost-effectiveness resulting from not hospitalizing patients one night prior to surgical procedure or admitting them the night afterwards the operation<sup>5</sup>. Various other benefits consist of earlier mobility, reduced risk of nosocomial infections and patient comfort<sup>6</sup>. Prerequisite for this is that agents must be fast-acting, effective and of course cost-effective without any hangover effects. Not a single of the anesthetic drug is available currently which has a short action in terms of duration which has no remaining effects on patients for several hours after operation<sup>7-8</sup>. Thiopentone, a commonly used inducer, has 5-10 hours of an elimination half-life and can stay up to 30% in the body subsequently more than twenty-four hours<sup>9</sup>. It is not a better choice

for clear recovery in day-care anesthesia. Propofol, on the other side, has elimination and distribution half-lives of 1-5 hours and 1-2 minutes, correspondingly, ensuring speedy retrieval with minimal residual effects, making it suitable for day-care cases<sup>10</sup>. However, the high price of Propofol, as well as the potential for contamination of the vials, is a major obstacle to its daily use in an underprivileged population. Midazolam is a potent sedative, promotes hypnotic effects, has a flat cardiovascular profile, is easily absorbed, and begins to work 10-15 mints after oral administration<sup>11</sup>. Also, after 30 mg of an oral dose, it has no side-effect of accumulation in the plasma ( $< 2$  ng / ml), has a lower risk of side effects and has a long duration of action, thus ensuring a rapid and marked recovery<sup>12</sup>. This analysis was conducted to compare the recovery score and cost-effectiveness after oral induction of midazolam and propofol or thiopental sodium in day-care surgical procedure. These induction agent's cost-effectiveness was also assessed for the patients benefit.

## METHODS

This study was taken place in the department of anaesthesia, Lahore General Hospital for six-months duration from July 2021 to December 2021 after approval from the ethical committee. Eighty American Society of Anaesthesiologists (ASA) grades I and II patients with age range of 18 to 35 years are included for daily routine laparoscopic procedures. The patients were distributed randomly in both groups by card sampling method and each group has same number of patients. Afterwards the pre-oxygenation, A group; patients were administered propofol at dose of 2 mg / kg for induction, and in group B; midazolam at 0.25 mg / kg dose and thiopental sodium at 2.5 mg / kg orally were given 30 mints prior to induction. The vecuronium which has medium duration of action was used for muscle relaxation and endotracheal intubation. The maintenance and analgesic dose were administered at 1.5-2.5% isoflurane and 1 microgram / kg fentanyl, correspondingly. Perioperative vital signs were recorded and observed at five-minute intervals. The quality of recovery was evaluated by SOCA scores (S for Sedation, O for orientation, C for Comprehension and A for amnesia), and the time needed to go home was recorded and monitored. At the end of the operation, the induction total cost in average was determined and documented.

The pulse rate, respiratory rate, systolic and diastolic blood pressure were recorded at preinduction, just after induction, after 2,5 minutes and 10 minutes of induction. Other parameters observed were time of onset of anesthesia, amnesia, side effects like hallucinations, apnea, PONV and the hospital stay. The time of recovery from anesthesia was observed at 15 second intervals after the completion

of surgery and any complications during recovery period were noted. Time taken for obeying verbal

command on request was noted every 10 minutes after the completion of surgery, by asking the patients to open the eyes, protrude the tongue and to lift the head. The time of sitting on the bed and the time of walking in the straight line was recorded.

**Data Analysis:** The data was collected on a previously prepared "data collection sheet". The statistical analysis and data collection were performed by Student's t-test using SPSS 21.0. The value of p less 0.05 was taken as significant.

**Fitness to go home:** Person recognition, place and time orientation. 2) 30-60 minutes of stable vital signs. 3) The ability to move independently. 4) oral intake tolerability. 5) Voiding Ability. 6) No substantial bleeding or pain.

## RESULTS

Patient features are presented in Table I and there was no substantial difference between the two groups. There were 26 males and 14 females in Group A and 29 Males and 11 females in Group B.

Table-1: shows the patients features

Characteristics	Group A (n=40)	Group B (n=40)	P-value
Males/ Females	26/14	29/11	
Age in years	28.50±2.95	26.15±3.58	0.552
Body wt (kg)	64.10±5.100	60.49±3.48	0.076
Height (cm)	158.11±3.01	151.05±4.16	0.067
ASA- I	85%	92.5%	0.175
ASA- II	15%	7.5%	0.507

The patient's vital signs such as systolic and diastolic BP, heart rate were documented at various time points. There was no substantial change in vital signs among the both groups (Table II).

Table-2: shows the changes in heart rate in per, pre and post operative period

Timing	Group-A (n=40)	Group-B (n=40)	P value
Pre-operative	76±5	74±5	0.041
At induction	84±9	86±10	
At reversal	85±7	80±10	
After 5 min	80±11	79±10	
After 10 min	79±9	78±9	
After 15 min	75±7	80±8	
After 20 min	78±9	76±6	
After 25 min	78±7	76±7	
After 30 min	77±8	78±9	

The recovery results at various times are presented in Table III.

Table-3: shows the SOCA score of recovery

Timing	Group-A (n = 40)	Group-B (n=40)	P value
At reversal	6.18 ± 1.9	5.10±1.41	<0.051
At 5 mints	6.05±1.80	5.34±1.57	
After 10 min	6.92±1.94	6.01±1.15	
At 15 mints	7.30±2.47	6.49±1.89	
At 20 mints	7.49±2.95	6.67±1.89	
At 25 mints	8.89±2.15	7.24±1.15	
At 30 mints	8.90±1.82	8.02±1.01	

After 30 minutes of reversal, the score of recovery in groups A and B were 8.90 ± 1.82 and 8.02 ± 1.01, respectively. The

results were documented after five, ten, fifteen, twenty, twenty-five and thirty minutes of reversal.

Return home eligibility time was documented when the subjects met the eligibility standards to go home. The groups A has gone home time of 279 ± 42 and for B; it was 315±46 mints, correspondingly (Table IV).

Table-4: shows the Time for fitness to go home

Group	Fitness to go home (Time in minutes)	P value
Group-A (n=40)	279 ± 42	0.96
Group-B (n=40)	315±46	

The group B has significantly lesser cost (PKR 700.0±100.0) in comparison to the group A (PKR 90.25±10.73) (p <0.05). [Tab. V].

Table-5: shows the induction agents cost

Group	Induction agents cost in PKR	P value
Group-A (n=40)	700.0±100.0	0.029
Group-B (n=40)	90.25±10.73	

## DISCUSSION

Proper selection, planning and trouble-free anesthesia recovery are the trademarks of successful Day-care surgical treatment. Various surgeries performed as day-care surgery has 1/5<sup>th</sup> cost of the total expenses for planned surgery<sup>13-14</sup>. They are inexpensive when patient safely discharged early. This analysis aimed to discover a cost-effective induction drug, an alternative to propofol that is preferred drug but quite costly in day-cases surgeries<sup>15-16</sup>. Concomitant 0.25 mg / kg oral midazolam induction and conventional intravenous thiopental at a compact dosage of 2.5 mg / kg resulted in recovery almost similar to that of propofol<sup>17-18</sup>. The differences in recovery and physical readiness to return home were almost similar in the two groups<sup>19</sup>.

Richard Johnson et al<sup>19</sup> also reported faster recovery with propofol as compared to thiopentone group. They observed remarkable clear headedness of the patients recovered from propofol. Redistribution is the principal mechanism for early awakening after a single dose of induction agents used. According to Kalman et al there was no difference in the results of early or late recovery tests but patients receiving propofol experienced fewer post operative symptoms and were more cheerful. Propofol compared to thiopentone and Ketamine was associated with a short time discharge from the recovery room. Collum et al<sup>19</sup> compared four intravenous agents, thiopentone, propofol, etomidate, methohexitone and found least pain at the site of injection with thiopentone. Collum noted mild, transient excitatory movements with propofol as compared to methohexitone, etomidate and thiopentone.

Moreover, perioperative parameters, such as alterations of systolic and diastolic pressure, heart rate were similar between the groups. One study found that afterwards taking midazolam at 10 mg dose; recovery was achieved within 15 minutes depending on time and site orientation<sup>20-21</sup>. The pharmacokinetics of midazolam are very similar following oral and intravenous administration to healthy volunteers. When patients are induced with thiopental, recovery varies between 1½ and 2½ times longer with midazolam<sup>22-23</sup>. Therefore, to evade this postponement, low doses of thiopental were given and small supplemented doses of volatile substances were directed to sustain an acceptable penetration of anesthesia<sup>24</sup>. The adding of strong opioids usually prolongs recovery but does not delay recovery when fentanyl is administered up to 1.5 µg / kg just prior to induction. In all under-developing states as Pakistan, cost effectiveness includes effective consumer appraisal of healthcare<sup>25</sup>. In this study, the cost of propofol was PKR-700.0±100.0 / ampule/ patient in Group-A and one ampoule has propofol at 200 mg strength, though the normal requirement for induction is 142 ± 14 mg; Any remaining

medication should be discarded as there is a greater risk of contamination. Consequently, the actual cost per case increases due to system loss. However, in group B, PKR 90.25±10.73 was the average cost of induction agents. Also, thiopentone attains stability for 24 to 36 hours after mixing, allowing many patients to direct multiple-doses vials and thus appears more economical.

## CONCLUSION

We conclude that the induction with intravenous thiopental sodium and oral of midazolam in day-care surgery is vastly cost effective in comparison to propofol given alone, with no significant changes in hemodynamics, recovery, and go home time.

## REFERENCES

- Konwar C. A Clinical Comparative Study of Propofol, Thiopentone Sodium and Midazolam as Anaesthetic Inducing Agents. *Journal of Evolution of Medical and Dental Sciences*. 2020 Sep 14;9(37):2680-6.
- Saleem S, Ch WI, Naaman K. An interventional comparative study of haemodynamic effects of induction doses of propofol/thiopentone and propofol-ketamine combinations. *Anaesthesia, Pain & Intensive Care*. 2019 Feb 5;82-7.
- Ahthana V, Agrawal S, Sharm JP. Comparative Evaluation of Intravenous Propofol, Thiopentone Sodium and Ketamine for Short Surgical Procedures. *Anaesthesia, Pain & Intensive Care*. 2019 Jun 26.
- Garba SU, Mohammed AD. The effects of midazolam pretreatment on the induction dose of propofol in Nigerian Adults. *Nigerian Journal of Basic and Clinical Sciences*. 2017 Jan 1;14(1):34.
- Younes MM, Mahareak AA, Badr OI. The use of minidose muscle relaxant to facilitate insertion of a laryngeal mask airway. *The Scientific Journal of Al-Azhar Medical Faculty, Girls*. 2019 Jan 1;3(1):220.
- Liu X, Rabin PL, Yuan Y, Kumar A, Vasallo III P, Wong J, Mitscher GA, Everett IV TH, Chen PS. Effects of anesthetic and sedative agents on sympathetic nerve activity. *Heart rhythm*. 2019 Dec 1;16(12):1875-82.
- Subhashini M. A Comparative Study between the Effects of Propofol and Etomidate in Adults Undergoing Surgeries under General Anaesthesia (Doctoral dissertation, Kilpauk Medical College, Chennai).
- Aswathappa PG, Vijayalakshmi BC, Shashikala TK. A prospective comparative study to know the haemodynamic response of thiopentone, propofol and etomidate on laryngoscopy and intubation in adult patients posted for elective surgeries under general anaesthesia. *Indian Journal of Clinical Anaesthesia*. 2020;7(2):290-4.
- Cho EA, Cha YB, Shim JG, Ahn JH, Lee SH, Ryu KH. Comparison of single minimum dose administration of dexmedetomidine and midazolam for prevention of emergence delirium in children: a randomized controlled trial. *Journal of anesthesia*. 2020 Feb;34(1):59-65.
- Kaniyil S, Krishnadas A, Parathy AK, Ramadas KT. Financial implications of intravenous anesthetic drug wastage in operation room. *Anesthesia, Essays and Researches*. 2017 Apr;11(2):304.
- Bakeer AH, Abdallah NM. Attenuation of the hemodynamic response to tracheal intubation with gabapentin and oral midazolam. *Anaesthesia, Pain & Intensive Care*. 2019 Jul 3;23(1).
- Sahajanandan R. Comparative evaluation of the effects of Etomidate versus midazolam on hemodynamic stability during induction in patients with impaired left ventricular function undergoing cardiac surgery (Doctoral dissertation, Christian Medical College, Vellore).
- Momin AG, Jha RK, Bhade MA. Comparative study of etomidate and fentanyl citrate with propofol (1%) and fentanyl citrate for total intravenous anaesthesia in short surgical procedures. *Indian Journal of Clinical Anaesthesia*. 2020;7(2):348-54.
- Ali ZT. A comparative study between propofol vs. thiopentone plus Lidocaine effects on hemodynamic changes during laryngeal mask airway (LMA) insertion in urological surgery in Baghdad hospital. *Al-Kufa University Journal for Biology*. 2018 Oct 1;10(2).
- Malini P. A Comparative study of Oral Midazolam and Oral Melatonin for Premedication in Paediatric Anaesthesia (Doctoral dissertation, Stanley Medical College, Chennai).
- Dwivedi MB, Puri A, Dwivedi S, Deol H. Role of opioids as coinduction agent with propofol and their effect on apnea time, recovery time, and sedation score. *International Journal of Critical Illness and Injury Science*. 2018 Jan;8(1):4.
- Farrukh R, Awan WS, Khan AH, Rana AR, Jilani AA, Mahmood K. Comparison of dexmedetomidine and propofol for hemodynamic and recovery characteristics in dilatation and curettage. *The Professional Medical Journal*. 2020 Jun 10;27(06):1244-8.
- Tola EN. The effect of anesthetic agents for oocyte pick-up on in vitro fertilization outcome: A retrospective study in a tertiary center. *Taiwanese Journal of Obstetrics and Gynecology*. 2019 Sep 1;58(5):673-9.
- Aswathy BS. A Comparative study of oral clonidine and oral midazolam as premedication in paediatric (4-12yrs) group undergoing tonsillectomy (Doctoral dissertation, Tirunelveli Medical College, Tirunelveli).
- Kaye AD, Fox CJ, Padnos IW, Ehrhardt KP, Diaz JH, Cornett EM, Chandler D, Sen S, Patil S. Pharmacologic considerations of anesthetic agents in pediatric patients: a comprehensive review. *Anesthesiology Clinics*. 2017 Jun 1;35(2):e73-94.
- Sweta DS. Complications of Sevoflurane-Fentanyl Versus Propofol-Fentanyl Based Anesthesia in Pediatric Cleft Lip And Palate Surgery. *Journal of Advanced Medical and Dental Sciences Research*. 2019 Dec;7(12).
- Vadigeri P. A Prospective Randomised Comparative Study Of Efficacy And Safety Of Combination Of Inj. Dexmedetomidine-Propofol And Inj. Fentanyl-Propofol For The Insertion Conditions Of Proseal Laryngeal Mask Airway (Doctoral dissertation, BLDE (Deemed to be University)).
- Ghazal EA, Vadi MG, Mason LJ, Coté CJ. Preoperative evaluation, premedication, and induction of anesthesia. In: *A practice of anesthesia for infants and children* 2019 Jan 1 (pp. 35-68). Elsevier.
- Farrell NM, Killius K, Kue R, Langlois BK, Nelson KP, Golenia P. A comparison of etomidate, ketamine, and methohexital in emergency department rapid sequence intubation. *The Journal of Emergency Medicine*. 2020 Oct 1;59(4):508-14.
- Beck R, Brizzi A, Cinnella G, Raimondo P, Kuczkowski KM. Anesthesia and analgesia for women undergoing oocyte retrieval. In: *Pick up and oocyte management 2020* (pp. 99-119). Springer, Cham.