

Original Research Article

A COMPARISON OF MIDAZOLAM CO-INDUCTION WITH PROPOFOL PREDOSING FOR INDUCTION OF ANAESTHESIA¹Dr. Senthilkumar Velayutham, ²Dr. P. Ravi, ³Dr. D. Shunmuga Priya, ⁴Dr. Arul K¹Assistant Professor, Department of Anaesthesia, Madras Medical College, Chennai²Assistant Professor, Department of Anaesthesia, Madras Medical College, Chennai³Assistant Professor, Department of Anaesthesia, Madras Medical College, Chennai⁴Professor, Department of Anaesthesia, Madras Medical College, Chennai**Corresponding Author:** Dr. Arul K

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ABSTRACT**Keywords:** Propofol, Midazolam, Co-induction**Background:** Anaesthetic technique used for any surgery in adults comprises of induction with Intravenous (IV) anaesthetic drugs. When induction agent like propofol is combined with a sedative like midazolam, synergism occurs between these two drugs causing reduction in total dose of primary drug like propofol, a technique called co-induction.**1. INTRODUCTION**

The term co-induction has been used to describe the practice of administering a small dose of sedative or another [1] anaesthetic agent to reduce the dose of induction agent required. The term was coined in 1986. Currently, has become increasingly popular.

Anesthesiologists use intentional co-induction of anaesthesia to take advantage of medication interactions, particularly synergism. Midazolam has been proven to minimize the amount of propofol required to produce anaesthesia by up to 50% without compromising the recovery profile when administered in this fashion [4].

Objectives: The aim of this study is to evaluate the midazolam co-induction and propofol pre-dosing for induction of anaesthesia with regard to dose and hemodynamic variability**2. MATERIALS AND METHODS**

The study was double blinded random controlled done at Government General Hospital, Madras Medical College, Chennai, after getting permission from the ethical committee.

Inclusion criteria:

- Patients age group 16 to 50 years
- ASA I and II patients with elective surgeries
- Patients who provides written inform consent for the study

Exclusion criteria:

- Patients age <15 years or >50 years
- Patients having any co morbid illnesses
- Patients on benzodiazepines
- Participants who do not provide consent for the study

A total of 90 patients scheduled for elective surgery meeting inclusion criteria were enrolled and studied. All patients were examined clinically and pre operatively investigated for baseline investigations like blood sugar, urea, serum creatinine, ECG in 12 leads, chest x-ray PA view and other specific investigations relevant to the disease.

All patients were counseled about the study procedure and obtained informed consent

All the subjects were randomly allocated into the three groups (30 subjects in each group).

Both the patient and observer were unaware of the group allocations.

Group 1: received midazolam 2 mg 2 min prior to induction.

Group 2: received propofol 30 mg 2 min prior to induction.

Group 3: received 3 ml of 0.9% saline 2 min prior to induction of anaesthesia

Baseline measurement of Blood pressure, heart rate and oxygen saturation were made prior to insertion of venflon and these were repeated at 60 seconds intervals for the remainder of the study. Anaesthesia was induced by infusing 1% propofol. Patients were encouraged to flex their arms to the command of the observer and the blood pressure and heart rate were recorded simultaneously if there was no response to verbal command. The propofol infusion was stopped at this point and face mask applied firmly. Any response to placement of the mask was noted. The study was deemed complete at this point and taken as the end point of induction. Induction dose of propofol was noted at this point and further management was not influenced by the study.

Statistical analysis:

Data were analysed by using SSPS version 22. All the data were expressed as means with Standard Deviation (SD). The data was analysed using test of significance based on t-test and Chi-square test. A $p < 0.05$ considered statistically significant

3. RESULTS**Table 1: Comparison of Socio-demographic characteristics between the study groups:**

Socio-demographic characteristics	Midazolam group		Propofol group		Control group		P value
	Mean	SD	Mean	SD	Mean	SD	
Age	29.37	6.18	30.93	6.43	33.03	7.35	0.11
Weight	46.17	6.06	42.03	7.78	48.33	7.82	0.01
ASA	1.00	0.00	1.00	0.00	1.00	0.00	1.00
Dosage	74.83	7.82	68.83	6.65	103.50	14.09	0.001
Gender	Frequency (%)		Frequency (%)		Frequency (%)		

Male	17	37.8%	16	35.6%	12	26.7%	0.39
Female	13	28.9%	14	31.1%	18	40%	

There was significant difference in systolic and diastolic blood pressure before and after induction between group 1 and group 2 as well as group 2 and group3 ($p<0.05$)

There was significant reduction in pulse rate between the control group as compared to other two groups ($p<0.05$)

The mean difference is significant at the 0.05 level. The dosage requirement in midazolam group, propofol pre-dosing group and control group differ significantly ($p<0.05$).

Table 1: Comparison of vital parameters before and after induction between the study groups:

Vital parameters	Midazolam group		Propofol group		Control group		P value
	Mean	SD	Mean	SD	Mean	SD	
Baseline vital parameters							
SBP	128.27	5.51	127.30	4.91	128.90	4.47	0.01
DBP	80.60	2.67	83.43	4.70	82.53	3.93	0.01
PR	88.20	6.33	86.23	6.58	89.03	4.64	0.001
Pre-induction vital parameters							
SBP	127.20	3.88	126.70	5.00	128.37	4.60	0.01
DBP	80.37	3.89	83.23	5.50	81.67	4.16	0.01
PR	86.70	5.09	83.53	6.77	87.63	4.54	0.001
Post-induction vital parameters							
SBP	118.43	3.46	114.27	4.56	115.00	4.85	0.01
DBP	75.93	3.23	73.13	3.67	72.33	3.86	0.01
PR	78.73	4.43	74.67	5.77	74.63	4.12	0.001

4. DISCUSSION

The term co-induction means the administration of a small dose of a sedative or other anaesthetic agent to reduce the dose of induction agent, improve the ratio of desired versus adverse effects and to reduce the cost of expensive drugs.

Present study found that there was significant reduction in systolic and diastolic blood pressure between group1 and group 2 as well as group 1 and group 3 ($p<0.05$), this study also reported significant fall in MAP in control group immediately after induction.

The Pulse Rate (PR) changes were also recorded in current study, significant fall of PR after

induction of anaesthesia was found in all the group ($P < 0.05$), in agreement with the Aparanji K, et al [15]. This observation is contrary to the observations reported by Major E, et al [16] who observed significant increase in PR at post induction as well as post intubation in midazolam co-induction group as compared to the baseline values and post-induction/post intubation values in propofol alone group.

In our study, we found that both the co-induction agents were effective in reducing the dose of propofol considerably. However, the dose of propofol required for induction was significantly less when propofol was used as co-induction agent (auto coinduction) as compared to induction dose requirement of propofol when midazolam was used as co-induction agent. Our observations comparable with the other studies like: Shrivastava et al [17] and Saha K, et al [18].

Present study found that Pre dosing with propofol is as effective as midazolam in reducing the dose of propofol to induce anaesthesia [19].

5. CONCLUSION

Predosing of midazolam for propofol induction had less hemodynamic variability (fall in blood pressure and heart rate during and after induction) and more cost effective since it requires only single vial of propofol for induction, whereas control group had significant hemodynamic variability and requires more than a single vial of propofol for induction, hence Midazolam–propofol co-induction appears to be a safe and effective alternative induction method.

6. REFERENCES

1. Co-induction of anaesthesia: the rationale. *Eur J Anaesthesiol Suppl.* 1995 Nov; 12:5-11. Review. 452-7.
2. Whitwam JG. Co-induction of anaesthesia: day-case surgery. *European Journal of Anaesthesiology. Supplement.* 1995; 12:25-34.
3. Sanchez A, Belda E, Escobar M, Agut A, Soler M, Laredo FG. Effects of altering the sequence of midazolam and propofol during co-induction of anaesthesia. *Veterinary Anaesthesia and Analgesia.* 2013; 40(4):359-66.
4. Lader M. Benzodiazepine harm: how can it be reduced?. *British journal of clinical pharmacology.* 2014; 77(2):295-301.
5. Galvez-Escalera I, Thorpe CM. The effect of coinduction with midazolam on propofol injection pain. *European Journal of Anaesthesiology.* 2004; 21(7):579-81.
6. Anil kumar A, Sanikop CS, Kotvr PF. Effect of priming principle on induction dose requirement of propofol-A randomized control trial. *IJA.* 2006; 50(4):283-287
7. Amatya A,1 Marhatta MN, A Comparison of Midazolam Co-induction with Propofol Priming in Propofol Induced Anesthesia *J Nepal Health Res Counc.* 2014; 12(26):44-8
8. Durga K, Shweta K, Madhumita M. Haemodynamic effects and recovery profile with midazolam and propofol as coinduction agents for day care surgery. *Journal of Evolution of Medical and Dental Sciences.* 2018; 7(32):3565-9.

9. Cressey DM, Claydon P, Bhaskaran NC, et al. Effect of midazolam pretreatment on induction dose requirement of propofol in combination with fentanyl in younger and older adults. *Anaesthesia* 2001; 56(2):108-113.
10. Saha K, Saigopal M, Sundar R, et al. Comparative evaluation of propofol-ketamine and propofolfentanyl in minor surgery. *Indian J Anaesth* 2001;45(2):100-103
11. L. Anderson and H. Robb, A comparison of midazolam co-induction with propofol pre-dosing for induction of anaesthesia, *Anaesthesia*, 1998, 53, 1117–1129
12. Roopam Katria, Ajay Singhal, Sukirti Prakash, Ishwan Singh. A comparative study of efficacy of propofol auto co-induction versus midazolam propofol co-induction using priming principle. *IJAnaesth*. 2010; 54(6):558-561
13. Sanket H Mehta, Pinalben G Dabhi, Golwala MP, Upadhyay MR. Effect of priming Principle on the induction dose Requirement of Propofol. *Int J Res Med*. 2015; 4(1):69-73
14. Aparanji K, Radhasundari M, Gopalakrishna K. Induction of propofol with coinduction of propofol, midazolam versus propofol auto coinduction- A comparative study. *J. Evid. Based Med. Healthc*. 2017; 4(93), 56705674. DOI: 10.18410/jebmh/2017/1138
15. Major E, Verniquet AJW, Waddell JM, et al. A study of three doses of ICI 35 868 for induction and maintenance of anaesthesia. *Br J Anaesth* 1981; 53:267-272.
16. Srivastava U, Sharma N, Kumar A, et al. Small dose propofol or Ketamine as an alternative to midazolam coinduction to propofol. *IndianjournalAnaesthesia*2006;50(2):112-114