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A Comparison of Midazolam Coinduction with Propofol Predosing For Induction Of Anesthesia

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Abstract

Introduction: The term co-induction has been used to describe the practice of administering a small dose of sedative or another anesthetic agent10 to reduce the dose of induction agent required. The term co-induction of anesthesia has been applied to the use of two or more drugs to induce anesthesia. Currently, planned coinduction of anesthesia is practiced by anaesthesiologists exploiting drug interaction, particularly synergism. The arguments for co-induction are two-fold. First, to improve the balance of desired versus adverse effects and secondly to reduce cost. When used this way midazolam has been shown to reduce the dose of propofol required to induce anaesthesia by up to 50% without affecting recovery profile.

Aim Of Study: This study compares the midazolam co-induction and propofol predosing about 1. Dose of propofol required for induction. 2. Blood pressure variability during induction. 3. Heart rate variability during induction. For adult patients undergoing elective surgeries.

Materials And Methods: The study was done at VELS Medical college& hospital in the year 2021. All patients gave informed consent. Both the patient and observer were unaware of the group allocations. All patients were preoperatively 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 assessed for their physical status. The subjects were not premeditated and were randomly allocated to one of the three groups. Group1 received midazolam 2 mg 2min before induction. Group 2 received propofol 30 mg 2min before induction. Group 3 received 3ml of 0.9%saline 2min prior to induction of anaesthesia. This was given as a bolus over a few seconds. Patients were counseled about the method of study.

Results: 90 patients were taken up for the study. Group 1 30 patients Group 2 30 patients and Group 3 30 patients. Group1 received midazolam 2 mg 2min before induction. Group 2 received propofol 30 mg 2min before induction. Group 3 received 3ml of 0.9%saline 2min before induction of anesthesia. In this study pre-dosing of 2 mg of midazolam as a co-induction agent (Group 1) where propofol is used as induction, the agent had Lesser blood pressure variability and Lesser heart rate variability during and after induction. Midazolam co-induction is more cost-effective than control (Group3), since it requires only a single vial of propofol for induction. Pre dosing of 30 mg of propofol(Group 2) before propofol induction had Reduced dosage requirement, lesser blood pressure variability, lesser heart rate variability than group 3(control group). It is more cost-effective than the control group and midazolam co-induction. control group (Group 3) is less cost-effective than the other two groups, since it requires more than one vial of propofol for induction. It produces more hemodynamic variability which is statically significant. When compared with the other two groups.

Conclusion: Predosing of midazolam for propofol induction had less hemodynamic variability (fall in blood

pressure and heart rate during and after induction) and was more cost-effective since it requires only a single vial of propofol for induction, whereas the control group had significant hemodynamic variability, significant fall in blood pressure and heart rate .and requires more than a single vial of propofol for induction, hence it is not cost-effective. Predosing of propofol for induction with propofol had less hemodynamic variability (fall in blood pressure and heart rate) than the control group. It is more cost-effective when compared to the control group and midazolam coinduction group.

Keywords: Hemodynamic Stability, Midazolam, Propofol

Introduction

The term co-induction has been used to describe the practice of administering a small dose of sedative or another anesthetic agent to reduce the dose of induction agent required. The term co-induction of anesthesia has been applied to the use of two or more drugs to induce anesthesia. The term was introduced in 1986 to describe the unplanned induction of anesthesia by non- aesthetically trained personnel practicing sedation, unplanned anesthesia in an unsuitable environment leading to several fatalities.[1] Currently, planned co- induction of anesthesia is practiced by anaesthesiologists exploiting drug interaction, particularly synergism. The arguments for co-induction are two-fold. First, to improve the balance of desired versus adverse effects and secondly to reduce cost. [2]When used this way midazolam has been shown to reduce the dose of propofol required to induce anesthesia by up to 50% without affecting recovery profile The technique of administering two or more hypnotic drugs to facilitate induction and maintenance of general anesthesia has gained considerable popularity. One rationale for combining drugs in anesthesia is to achieve more "specific target responses while minimizing side effects and facilitating rapid and predictable recovery".[3]As yet, no single intravenous anesthetic drug can effectively and safely provide hypnosis, analgesia, and amnesia. Thus intelligent combinations of hypnotics and opioids are necessary, especially for total intravenous anesthesia (TIVA). Inescapable interactions occur, most of which are synergistic and should be evaluated for the optimal care of the patient.[5] This synergism varies considerably according to the different drugs, the different endpoints of anesthesia, and the differently combined dosage of both agents. midazolam 0.02 mg.kg-1 and thiopentone 3 mg.kg-1 was associated with a smooth and significantly faster induction, better airway control, greater hemodynamic stability and lesser incidence of untoward effects compared to midazolam 0.02 mg.kg-1 and thiopentone 2 mg.kg-1 or thiopentone 4 mg.kg-1 alone. [6]The most common disadvantages with propofol are its greater cost as compared to thiopentone is a high incidence of pain on injection (50 - 100%) and relatively more hypotension as compared to thiopentone .propofol required to produce anesthesia was reduced by 52% in the presence of midazolam. The cause of synergism was not clear but may have been interaction at CNS GABA(A) receptors.[7]The relationship between desired effects and adverse effects could be improved by skillful use of the synergism between midazolam and propofol. Co-induction of anesthesia and co-administration in long-term sedation can offer improvements in therapeutic situations compared with monotherapy.[8]

Materials And Methods:

The study was done at VELS Medical college& hospital in the year 2021. All patients gave informed consent. Both the patient and observer were unaware of the group allocations. All patients were 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 assessed for their physical status. The subjects were not premeditated and were randomly allocated to one of the three groups. Group1 received midazolam 2 mg 2min before induction. Group 2 received propofol 30 mg 2min before induction. Group 3 received 3ml of 0.9%saline 2min before induction of anesthesia. This was given as a bolus

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over a few seconds. Patients were counseled about the method of study. Ninety ASA1 patients aged 16-50 years scheduled for elective surgery were studied. All patients were preoperatively 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 assessed for their physical status. The subjects were not premeditated and were randomly allocated to one of the three groups.Group1 received midazolam 2 mg 2min before induction Group 2 received propofol 30 mg 2min before induction. Group 3 received 3ml of 0.9%saline 2min before induction of anesthesia. This was given as a bolus over a few seconds. Patients were counseled about the method of study. Baseline measurements of Blood pressure, heart rate, and oxygen saturation were made before insertion of an 18 gauge venflon and these were repeated at 60-second intervals for the remainder of the study. Anesthesia 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 the face mask was applied firmly. Any response to the placement of the mask was noted. The study was deemed complete at this point and taken as the endpoint of induction. An induction dose of propofol was noted at this point. And further management was not influenced by the study.

Statistical Analysis

Multiple comparisons by Bonferroni t-test, Qualitative data (sex, weight age) were given in frequencies with their percentages. Quantitative data (systolic blood pressure, pulse rate, dosage)were given in mean and standard deviation. Differences between the three groups on systolic blood pressure, pulse rate were analyzed using one-way analysis of variance(ANOVA), and multiple comparisons were done by using BONFERRONI TEST. Comparison between each group pre and post-induction values were analyzed using PAIRED T TEST. Demographic data (age, sex. weight) between the groups were analyzed using the Pearson chi-square test.

Table 1: Demographic Profile

	Group 1		Group 2		Group 3	
	Midazolam		Propofol		Control	
	Mean	SD	Mean	SD	Mean	SD
Age	29.37	6.18	30.93	6.43	33.03	7.35
Wt	46.17	6.06	42.03	7.78	48.33	7.82
ASA	1.00	.00	1.00	.00	1.00	.00
SBP(baseline)	128.27	5.51	127.30	4.91	128.90	4.47
DBP	80.60	2.67	83.43	4.70	82.53	3.93
PR	88.20	6.33	86.23	6.58	89.03	4.64
SBP(pre-induction)	127.20	3.88	126.70	5.00	128.37	4.60
DBP	80.37	3.89	83.23	5.50	81.67	4.16
PR	86.70	5.09	83.53	6.77	87.63	4.54
SBP(post-induction)	118.43	3.46	114.27	4.56	115.00	4.85

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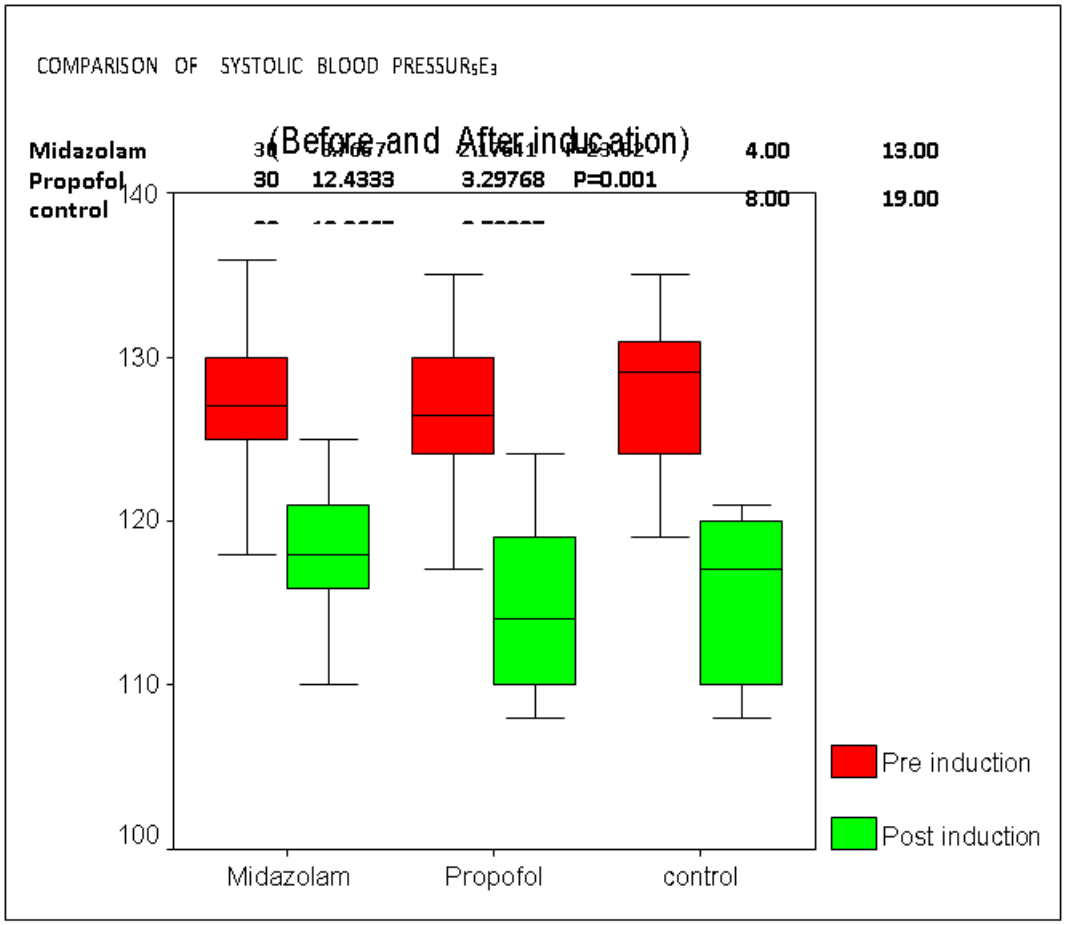
DBP	**75.93**	**3.23**	**73.13**	**3.67**	**72.33**	**3.86**
PR	**78.73**	**4.43**	**74.67**	**5.77**	**74.63**	**4.12**
Dosage	**74.83**	**7.82**	**68.83**	**6.65**	**103.50**	**14.09**

Table :1 Sex wise there are no significant differences between the three groups. The male and female ratio is equal in all three groups(x2=1.86 p=0.39)



Graph :1 There was a significant difference in systolic blood pressure before and after induction between group 1 and group 2as well as group 2 and group3 (p=0.001)

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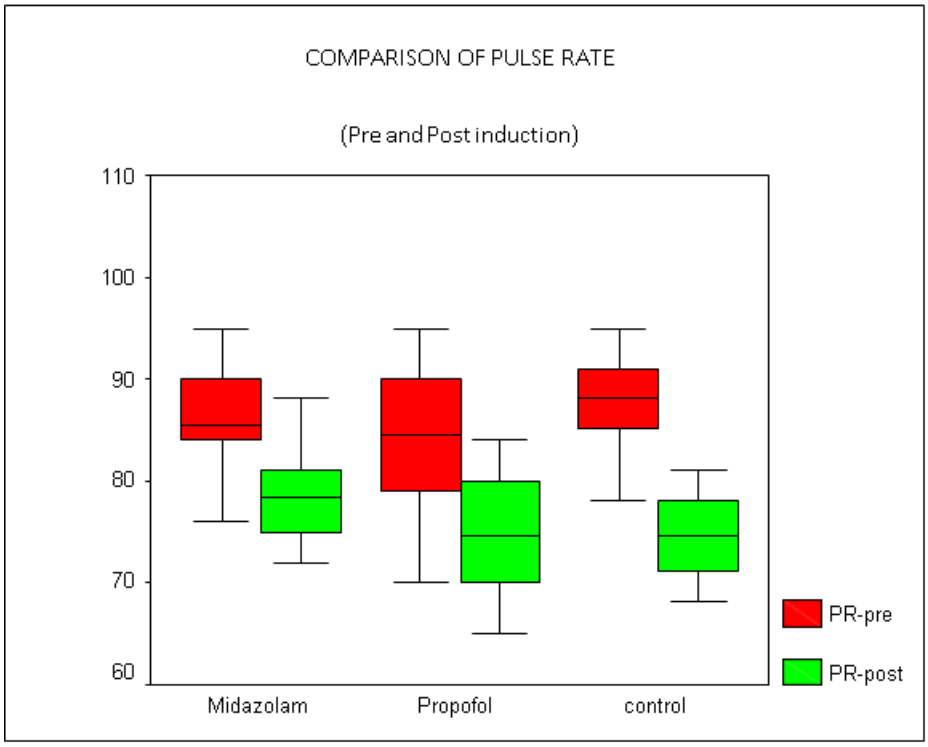
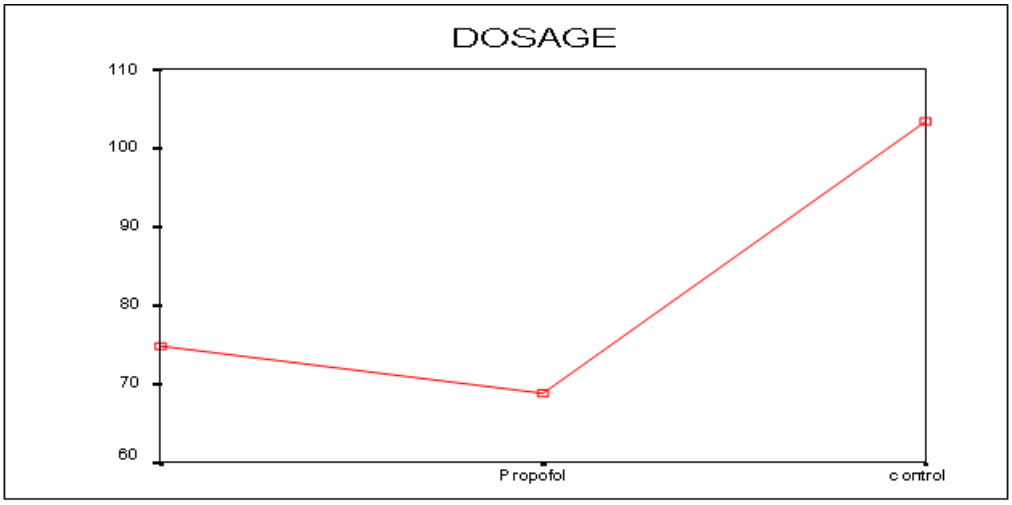
GRAPH:2 PULSE RATE



Graph:2 There was a significant reduction in pulse rate between the control group and the other two groups(f=20.47,p=0.001)

GRAPH :3 MULTIPLE COMPARISON



Graph :3 The mean difference is significant at the .05 level. The dosage requirement in midazolam group(1) was (mean=74.83 mgs),propofol predosing group(2) was (mean=68.83 mgs) and control group3 was (mean=103.50 mgs) which was significant(p=0.001).

Discussion

We have shown that predosing with 30 mg of propofol is as effective in reducing the induction dose of propofol as coinduction with 2 mg of midazolam when loss of verbal contact is taken as the end point. In our study, the induction dosage was reduced by

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36% in group 1(midazolam group) and 32% in group2 (propofol predosing group). The combination having 1.35 times the potency of individual agents[9] Interactions between IV propofol and midazolam for induction of anesthesia in 200 unpremeditated female patients undergoing elective gynecological surgery using endpoints of hypnosis (loss of response to verbal command) and anesthesia (loss of response to 5-s transcutaneous tetanic stimulus) and found that synergistic interaction was found. The combination has 1.44 times the potency of the individual agents. The dose of propofol required to produce anesthesia was reduced by 52% in the presence of midazolam In our study, the induction dosage was reduced by 36% in group 1(midazolam group) and 32% in group2 (propofol predosing group).[10]The combination having 1.35 times the potency of individual agents A double-blind study of 90 ASA 1 and 2 women undergoing elective surgery revealed the ED 50 in the propofol group was 1.56 mg/kg and that of the midazolam group was 0.24 mg/kg. In the midazolam propofol group, the ED 50 of midazolam was reduced by approximately a quarter 0.068 mg/kg.[11].In our study, the induction dosage was reduced by 36% in group 1(midazolam group) and 32% in group2 (propofol predosing group). The combination having 1.35 times the potency of individual agents In our study the induction dosage was reduced by 36% in group 1(midazolam group) and 32% in group2 (propofol predosing group). The combination has 1.35 times the potency of individual agents[12]. Using the loss of response to verbal command and tolerance to the placement of a facemask as end-points, the dose of propofol required to induce anesthesia was significantly smaller in the patients given propofol (1.87 mg.kg-1) or midazolam (1.71 mg.kg-1) when compared to the control group (2.38 mg.kg-1).In our study the dosage requirement in midazolam group(1)(n=30) was (mean=74.83 mgs),propofol predosing group(2)(n=30) was (mean=68.83 mg) and control group3 (n=30)was (mean=103.50 mg) which was significant (p=0.001).[13] It was concluded that Midazolam pretreatment was associated with a significant reduction in propofol dose requirement in both younger and older patients. The reduction in older patients was significantly greater than the equivalent response in younger groups. Hence one should be Cautious is in the use of midazolam as an agent for co-induction with propofol in the elderly. Hence in our study, the age group selected for the study were between 16 to 50 years. compared the hemodynamics, efficacy, safety, and postoperative recovery of patients following the use of either midazolam plus propofol or placebo plus propofol for induction and maintenance of general anesthesia for outpatient surgical procedures of less than two hours' duration [14]The study. included 203 ASA I, II, and III patients undergoing various outpatient surgical procedures. It was concluded that concomitantly administered midazolam and reduction-concentration propofol did not exacerbate the well-described hypotensive effects of full-strength propofol during induction of anesthesia In our study. there was a significant reduction in systolic blood pressure between group1 and group2 as well as group1 and group3.(p=0.001) [15] There was a significant reduction in pulse rate between the control group and the other two groups(f=20.47,p=0.001). Although midazolam may work synergistically with propofol51, a major clinical benefit is the rapid attainment of anxiolysis. We did not attempt to quantify or compare the anxiolysis achieved by the administration of either midazolam or propofol but the patients appeared to be more relaxed and settled and the associated reduction in sympathetic drive may have allowed induction of anesthesia with lower doses of propofol. [16]Pre dosing and coinduction both reduce the dose of induction agent required to achieve hypnosis and any form of pre-medication is likely to have a similar effect. Both midazolam and propofol groups(Group1&2) are therefore cost-effective, in that the propofol requirements in our study were limited to a single ampoule for each patient. [17]Pre dosing with propofol is as effective as midazolam in reducing the dose of propofol to induce anesthesia [18]We used two endpoints – loss of response to verbal command and response to placement of face mask. Of these, we found loss of response to verbal command the more reproducible. However, if we had used a different endpoint such as laryngeal mask insertion the results may have been different. Our study was blinded, the assessor being unaware of the pre-dosing agent, and we consider this essential for any objective assessment.[19,20]

Conclusion

Predosing of midazolam for propofol induction had less hemodynamic variability (fall in blood pressure

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and heart rate during and after induction) and was more cost-effective since it requires only a single vial of propofol for induction, whereas the control group had significant hemodynamic variability.,significant fall in blood pressure and heart rate .and requires more than a single vial of propofol for induction, hence it is not cost-effective. Predosing of propofol for induction with propofol had less hemodynamic variability(fall in blood pressure and heart rate) than the control group. It is more cost-effective when compared to the control group and midazolam co-induction group.

References

1. Aitkenhead A. Comparison of propofol and midazolam for sedation in critically ill patients. Lancet 1989: 704-8.
2. Anesthesia induction for laryngeal mask insertion--comparison of propofol with midazolam and propofol with thiopental. Masui. 1997Feb;46(2):188-92. Japanese.Art of reasonable combining drugs in anesthesia Cah Anesthesiol.1994;42(5):635
3. Bailey J, Mora C, Shafer S. Pharmacokinetics of propofol in adult patients undergoing coronary revascularization. Anesthesiology 1996; 84: 1288-97
4. Borgeat A, Wilder-Smith O, Sarah M, et al. Subhypnotic doses of propofol possess direct antiemetic properties. Anesth Analg 1992; 74: 539-41.
5. Boysen K. Induction and recovery characteristics of propofol, thiopental, and etomidate. Acta Anaesthesiol Scand 1989; 33: 689-
6. Bray R. Fatal myocardial failure associated with a propofol infusion in a child [letter]. Anesthesia 1995; 50: 494.
7. Bryson H, Fulton B, Faulds D. Propofol: an update of its use in anesthesia and conscious sedation. Drugs 1995; 50: 513-9
8. Coadministration of propofol and midazolam decreases bispectral index value as a result of synergic muscle relaxant action on the motor system. Anesthesiology. 2004 Sep;101(3):799;
9. Cockshott I. Propofol pharmacokinetics and metabolism—an overview. Postgrad Med J 1985; 61 Suppl 3: 45-50.
10. Co-induction of anesthesia: the rationale. Eur J Anaesthesiol Suppl. 1995 Nov;12:5-11. Review. 452-7.
11. Co-induction of anesthesia: day-case surgery. Eur J Anaesthesiol Suppl.1995 Nov;12:25-34. Review.
12. Doze V, Shafer A, White P. Propofol-nitrous oxide versus thiopental- isoflurane-nitrous oxide for general anesthesia. Anesthesiology 1988; 69: 63-71.
13. Eames W, Rooke G, Sai-Chuen R, et al. Comparison of the effects of etomidate, propofol, and thiopental on respiratory resistance after tracheal intubation. Anesthesiology 1996; 84: 1307-11.
14. Effects of midazolam on propofol-induced anesthesia: propofol dose requirements, mood profiles, and perioperative dreams. Anesth Analg. 1997 Sep;85(3):553-9.
15. Effect of midazolam pretreatment on induction dose requirements of propofol in combination with fentanyl in younger and older adults. Anesthesia. 2001 Feb;56(2):108-13
16. Effects of midazolam in propofol-induced anesthesia. Anesth Analg. 1998 May;86(5):1148
17. Fulton B, Sorkin E. Propofol: an overview of its pharmacology and a review of its clinical efficacy in intensive care sedation. Drugs 1995; 50: 636-57.
18. Gan T, Ginsberg B, Grant A, et al. Double-blind, randomized comparison of ondansetron and intraoperative propofol to prevent postoperative nausea and vomiting. Anesthesiology 1996; 85: 1036-42.
19. Gepts E. Infusion of propofol as a sedative technique for colonoscopies.Postgrad Med J 1985; 61 Suppl 3: 120-6.

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