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Comparing the Combination Effect of Propofol-Ketamine and Propofol-Alfentanil on Hemodynamic Stability during Induction of General Anesthesia in the Elderly

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Abstract

Background: Propofol (Diprivan), a modern intravenous hypnotic drug, produces a reduction in both cardiac index (CI) and mean arterial pressure (MAP) due to its sympatholytic activity. S-Ketamine (Ketanest), a potent analgesic, in contrast, causes an increase in both CI and MAP due to its sympathomimetic activity. This study was performed to compare the combination effects of propofol-ketamine and propofol-alfentanil on hemodynamic stability during induction of general anesthesia.

Methods: In a prospective study, 100 patients over 60 (ASA I, II) scheduled for elective lower abdominal interventions were randomly divided into two groups. For induction of general anesthesia, after injection of midazolam, the first group (A) received alfentanil and propofol and the second group (B) received S-ketamine and propofol. Each group received atracurium as muscle relaxant. Blood pressure (BP) and heart rate (HR) were measured before and 1 and 5 minutes after induction of anesthesia.

Results: The increase in HR and decrease in MAP were statistically significant in both groups 1 and 5 minutes after general anesthesia. The increase in HR and decrease in MAP were significantly more in Group A, 1 and 5 minutes after general anesthesia.

Conclusion: The dose of S-ketamine administered during induction of general anesthesia may not be enough to neutralize the cardio-depressant effect of propofol. A better hemodynamic activity was observed in Group B compared to Group A due to partial neutralization of the opposing action.

Keywords: Propofol; Ketamine; Alfentanil; Hemodynamic stability; General anesthesia

Introduction

Ketamine is used for induction and maintenance of general anesthesia. Clinical superiority of S-Ketamine has been described with regard to its anesthetic potency, the extent of analgesia, effects and side effects during and after operation, and undesirable psychological dysfunction.[1] In combination with midazolam, a significant reduction is achieved. In combination with propofol, the sympatholytic effects of this hypnotic agent were compensated by S-ketamine. Continuous infusion of ketamine and propofol allows total intravenous anesthesia (TIVA) with profound analgesia and spontaneous ventilation.[2] With respect to sympathoadrenergic and hemodynamic reactions, the clinical position of S-ketamine is unchanged. Nevertheless, a significant clinical progress can be expected due to improved recovery and reduced substance load, when racemic ketamine is replaced by S-ketamine.[3] Both isomers produced similar cardiovascular and hormonal responses during surgery.[4] Increases in systolic and diastolic arterial blood pressures and insufficient reduction of the stress response with respect to ACTH and cortisol seem to require a premedication, which reduces ACTH secretion. Because of a significant reduction in the quantitative

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drug load, S-ketamine offers a clinical advantage as compared with the currently used racemic ketamine.[5] Propofol (Diprivan), a modern intravenous hypnotic drug, produces a reduction in both cardiac index (CI) and mean arterial pressure (MAP). S-ketamine (ketanest), a potent analgesic, in contrast, causes an increase in CI and MAP.[6] The combination of propofol and ketamine for total intravenous anesthesia was shown to minimize the side effects of each drug used alone. Total intravenous anesthesia with propofol and ketamine proved to be very satisfactory from a clinical point of view.[7] The dose of ketamine administered during the induction of general anesthesia may have not been high enough to neutralize the cardio-depressant effect of propofol. However, during the maintenance of anesthesia, there is in fact a better hemodynamic stability in ketamine-propofol combination than that in propofol-fentanyl combination as a result of neutralization of the opposing actions. Fentanyl even intensifies the fall in MAP after propofol administration; cardio-depressant actions may also accumulate. Patients receiving ketamine-propofol combination showed a better vigilance as well as pain relief postoperatively. General intravenous anesthesia with propofol and ketamine offers the advantages of better analgesia, a higher state of vigilance, and the absence of respiratory depression during the postoperative phase compared with the anesthesia resulting from a combination of propofol and fentanyl.[7] The aim of this study was to compare the effects of the combination of propofol-ketamine and propofol-alfentanil on hemodynamic stability during induction of general anesthesia.

Materials and Methods

In a prospective study, 100 patients (ASAI, II) older than 60 were randomly divided into two groups and scheduled for elective lower abdominal interventions. For induction of general anesthesia, both groups received midazolam (0.05-0.1 mg/Kg). The first group (A) received propofol (2 mg/Kg during 30 seconds) and alfentanil (50 micro/Kg during 3 minutes) and the second group (B) received propofol (the same dose) and S-ketamine (1-2 mg/Kg). Both groups received atracorium (0.5 mg/Kg) as muscle relaxant. Blood pressure (BP) was measured with cuff (non-invasive method) and heart rate (HR) with ECG monitoring before, as baseline values, and 1 and 5 minutes after the induction of anesthesia. The data were analyzed, using SPSS software (version 11.5, Chicago, IL, USA). Paired sample test was used to compare the changes of HR and BP. T-test was used to compare the changes of HR and MAP.

Results

There was a significant decrease in MAP and a significant increase in HR in group (A) (alfentanil-propofol) 1 and 5 minutes after induction of anesthesia compared with the baseline values (Table 1) (p<0.001 for mean change of HR and MAP). There was a significant decrease in MAP and a significant increase in HR in group (B) (S-ketamine-propofol) 1 and 5 minutes after induction of anesthesia compared with the baseline values (Table 2) (p<0.001 for mean

Table 1: Changes of HR and MAP after induction of anesthesia compared with baseline value in Group A.

	Paired differences				*P value*
	Mean	**Std. Deviation**	**95% Confidence Interval of the Difference**		
			Lower	Upper	
HR before HR1 min	-9.5800	4.5089	-10.8614	-8.2986	<0.001
HR before HR 5 min	-10.6000	15.4722	-14.9971	-6.2029	<0.001
MAP before MAP 1 min	9.1200	6.2813	7.3349	10.9051	<0.001
MAP before MAP 5 min	11.7400	7.7901	9.5261	13.9539	<0.001

change of HR, $p<0.01$ for mean change of MAP). The increase in HR and decrease in MAP was significantly more in group A than in group B (Table 3). The mean heart rate increased significantly more in group A (2.58) than in group B (4.72) one minute after induction of anesthesia. These changes were also significantly more in group A (10.6) than in group B (4.84) 5 minutes after induction of anesthesia. The decrease in the mean arterial pressure was significantly more in group A (11.74) than in group B (4.02) one minute after induction of anesthesia while these changes after 5 minutes were also significantly more in group A (9.12) than in group B (2.5).

Discussion

One of the important factors during induction of anesthesia and intubation of the elderly patients is prevention of hemodynamic instability. Due to sympatholytic activity of both propofol and alfentanil, the patients may develop hypotension during the induction of anesthesia, and coronary blood supply disturbance and ischemia may also happen. The sympathomimetic activity of S-ketamine may neutralize the sympatholytic activity of propofol during the induction of anesthesia.[8,9] So comparison of the hemodynamic properties of a combination of propofol-S-

Table 2: Changes of HR and MAP after induction of anesthesia compared with baseline value in Group B.

	Paired Differences				*P value*
	Mean	**Std. Deviation**	**95% Confidence Interval of the Difference**		
			Lower	Upper	
HR before HR1 min	-4.7200	4.8278	-6.0920	-3.3480	<0.000
HR before HR 5 min	-4.8400	6.6497	-6.7298	-2.9502	<0.000
MAP before MAP1 min	2.5000	6.4658	0.6624	4.3376	0.009
MAP before MAP 5 min	4.0204	7.9175	1.7462	6.2946	0.001

Table 3: Changes of HR and MAP after induction of anesthesia compared with baseline value between two groups.

		Levene's test for equality of variances		T-test for equality of means		
		F	**Sig.**	**t**	**df**	**Sig. (2-tailed)**
DH1	Equal variances assumed	0.180	0.894	-5.202	98	0.001
	Equal variances not assumed			-5.202	97.546	0.001
DH2	Equal variances assumed	1.191	0.278	-2.419	98	0.017
	Equal variances not assumed			-2.419	66.505	0.018
DM2	Equal variances aAssumed	0.037	0.848	4.890	97	0.001
	Equal variances not assumed			4.889	96.870	0.001
DM1	Equal variances assumed	0.061	0.806	5.193	98	0.001
	Equal variances not assumed			5.193	97.918	0.001

ketamine and that of propofol-alfentanil is of great value. In our groups, a significant decrease in MAP and a significant increase in HR were detected one and five minutes after induction of anesthesia. Combination of S-ketamine-propofol produced less decrease in MAP and less increase in HR compared with the combination of propofol-alfentanil. Due to cardio-depressant activity of both propofol and alfentanil, producing a reduction in CI and MAP and compensating for tachycardia, the induction of anesthesia with propofol-alfentanil caused more hemodynamic instability than that with the other combination. As it was shown by Habib *et al.*[10], MAP decreased after induction of anesthesia with alfentanil but HR remained stable and increased significantly after intubation. Similar results were reported by Salihoglu *et al.*[11] Adams *et al.*[8] showed that 5 minutes after the induction of anesthesia, SAP and HR were significantly lower in the alfentanil group compared with those in the S-ketamine group. Mayer *et al.*[7] showed a moderate drop of MAP after induction of anesthesia with both propofol-ketamine and propofol-fentanyl but a slight decrease in HR in the fentanyl group and no change in the ketamine group. The increase in HR in our study may present the compensatory mechanism for decreased MAP and may be due to the effect of intubation which can cause stress-induced tachycardia as we didn't investigate the hemodynamic changes after intubation and after induction separately. The reported decrease of HR in other studies may be due to preoperative medications such as beta and alpha blockers and clonidine which prevent tachycardia during operation. As we expected, cardiovascular stimulating effect of S-ketamine (increase in MAP and CI) minimized the cardio-depressant effect of propofol. There was still a significant decrease in MAP and an increase in HR after induction of anesthesia with propofol and S-ketamine. This finding indicates that the dose of S-Ketamine administered during the induction of anesthesia may not be high enough to neutralize the cardio-depressant effect of propofol. Induction of general anesthesia with S-Ketamine and propofol proved more satisfactory from a clinical point of view than that with propofol-alfentanyl compound as it caused less hemodynamic instability.[10,11] Shuttler *et al.*[6] reported that the hemodynamic changes during the induction of anesthesia with propofol-ketamine combination was minor. Thus, the combination of S-ketamine-propofol is preferred to the combination of alfentanyl-propofol under conditions such as hypotension, hypothyrosis, adrenocortical insufficiency and in old patients who have a diminished physiological reserve, alteration in autonomic function, an increased incidence of coexisting cardiovascular disease and increased sensitivity to opoids and anesthetic drugs. Such problems increase the cardiovascular liability during induction of anesthesia, with the attendant risks of myocardial ischemia, stroke, cardiac arrhythmia or sudden death.

Propofol-S-ketamine combination produces better hemodynamic stability than propofol-alfentanyl combination in geriatric patients during induction of anesthesia. For elimination of cardiovascular effects of intubation, it is advisable to investigate the cardiovascular responses after intubation. For selection of the best combination of drug in the elderly patients for general anesthesia, cardiovascular responses of drug compounds should be considered during maintenance as well as during induction of anesthesia. It is also advisable to match the members of each group according to sex, race, preoperative disease and medication to eliminate the effects of preoperative risks on cardiovascular responses.

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