Prospective Randomized Comparative Clinical Study of Hemodynamic Changes with Etomidate Versus Ketofol during Induction Under General Anaesthesia

Rampal Singh[1], Sarfraj Ahmad[2], Gopal Krishan[3], Gautam Kumar Goel[4], Tamanna Baktier[5], Sachin Kumar[6]

ABSTRACT

Introduction: General anaesthesia is associated with marked cardiovascular changes. Induction with propofol is accompanied by decrease in mean blood pressure and heart rate but etomoidate and ketofol provides stable perioperative hemodynamics during induction of general anaesthesia. So we compared etomidate and ketofol (propofol and ketamine combination) in terms of hemodynamic response. The aim of this study was to, compare the effects of etomidate and ketofol (propofol and ketamine combination) on hemodynamic changes during induction of general anaesthesia.

Material and methods: It was a prospective randomized clinical comparative study in which, 60 patients of ASA grade I or II were posted for elective surgery under general anaesthesia and were enrolled into one of the two groups according to the agents to be given for induction of general anaesthesia. Patients of group 'A' were induced with etomidate 0.3 mg/kg and group 'B' were induced with ketofol (ketamine 1 mg/kg and propofol 1.5 mg/kg) through intravenous route.

Results: The results show almost equal hemodynamic stability during anesthesia induction and intubation using etomidate compared with ketofol.

Conclusion: The results of our study suggest that both etomidate and ketofol produce stable hemodynamics and satisfactory induction conditions in patients undergoing noncardiac surgery.

Keywords: Etomidate, Endotracheal Intubation, Hemodynamic Response, Ketofol.

INTRODUCTION

Endotracheal intubation is the translaryngeal placement of endotracheal tube into the trachea via mouth (oro-tracheal intubation) or nose (nasotracheal intubation). It acts as a noxious stimulus which provokes a transient but marked sympathetic response associated with release of catecholamines and cortisol. These responses are not significant in a normotensive patient but can be detrimental in individuals who are hypertensive, those with a cerebrovascular disease or patients with glaucoma and penetrating injuries.

Laryngoscopy and endotracheal intubation is a painful procedure. It is most commonly used for airway management during induction of general anesthesia. This procedure is most frequently associated with hemodynamic changes which include tachycardia, hypertension, arrhythmia etc. These hemodynamic changes are among the hazardous complications of general anaesthesia.[1]Such cardiovascular responses, although transient but may be dangerous in some patients particularly those suffering from cardiovascular and cerebrovascular disease. These changes are produced by lifting the base of tongue and epiglottis by the laryngoscope blade and tracheal stimulation during laryngoscopy and intubation.[2] Ketamine causes dissociative anaesthesia and has cardiac stimulatory properties, increases blood pressure, heart rate and cardiac output whereas propofol is a widely used sedative-hypnotic anaesthetic agent, which has potent cardiovascular depressant effects that produce hypotension and bradycardia. So, the hemodynamic effects of these two drugs are neutralizing and reduce the incidence of overall cardiovascular side effects. In balanced anesthesia, combination of two or more anaesthetic agents is currently administered, which enhances the benefits and decreases the unfavourable side effects of each agent in the combination. Many studies have demonstrated the beneficial effects of ketamine propofol combination in sedation as well as non-cardiac surgeries.[3]

This study was an attempt to compare hemodynamic changes during induction with etomidate and ketamine, propofol combination so that we can choose a safe induction agent establishing stable hemodynamics.

The aim of this study was to compare the effects of etomidate versus ketofol (propofol and ketamine combination) on hemodynamic changes during induction under general anaesthesia.

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METHOD AND MATERIALS

After approval from the institutional ethical committee. This study was conducted on 60 patients. After taking written informed consent for participating in the study. Patients were randomly divided into two equal groups: Group- 'A' and Group- 'B' consisting of 30 patients each.

The following vital parameters were studied in both groups: systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), heart rate (HR), percentage of oxygen saturation (SpO_2), pain on injection, post-operative nausea and vomiting (PONV), myoclonus. Patients of ASA (American Society of Anaesthesiologist) grade I or II, age between 20-60 years, patients requiring general anaesthesia, either sex who gave informed written consent were included in the study. Patients who refused for procedure, patients with history of seizure disorder, drug allergy, cardiovascular diseases and uncontrolled hypertension, high intra cranial pressure (ICP) and obesity (BMI>30kg/m^2) were excluded from study.

Methodology

Thorough pre-anesthetic check-up was done. In group "A" etomidate 0.3 mg/kg where as in group "B" ketofol (ketamine 1 mg/kg and propofol 1.5mg/kg) was used for induction of the anaesthesia through intravenous route. All patients of both the groups received ranitidine 150 mg and alprazolam 0.25mg by oral route the night before surgery.

All patients were kept fasting overnight 6 hrs for solids and 3 hrs for liquids. After arrival at operation theatre, an 18G intravenous line was secured. All vital parameters were attached and baseline readings were taken. Patients were premedicated with injection glycopyrrolate 0.004 mg/kg, ondansetron 0.08 mg/kg, butorphanol 0.02 mg/kg and midazolam 0.02 mg/kg though intravenous route and were preoxygenated with 100% oxygen for 3 minutes. In each group patients were induced with respective drugs. In both the groups above mentioned vital parameters were recorded respectively at different time interval. Subjective pain on injection was recorded as per complaint of patient. Myoclonus was noted if found in any patient. At the end of the surgery, reversal was done with injection neostigmine 0.05mg/kg and glycopyrrolate 0.008mg/kg by intravenous route. Amount of blood loss and fluid given was assessed. Pharyngo-tracheal suction was done and then patients were extubated after confirming the adequate recovery of muscle power and were monitored post-operatively for nausea and vomiting.

When patients were able to keep their eyes open, elevate head and breathe normally, they were shifted to post-operative recovery room. Any complications or side effects like nausea, vomiting was evaluated and noted postoperatively as early (0 to 6 hrs) and late (6 to 24 hrs). Patients with nausea or vomiting in post-operative period, received injection ondansetron 4 mg IV intravenously as a rescue antiemetic.

STATISTICAL ANALYSIS

The statistical analysis was performed using SPSS version 23. The clinical profile in patients was analyzed by chi-square test for qualitative variables. The data was presented in mean and standard deviation. Independent *t*-test was used to compare mean between two groups of different variables. Five percent (5%) probability level was considered as statistically significant ($p<0.05$).

RESULTS

In this study group A and group B were comparable in terms of age, sex distribution, body weight, ASA grade and duration of surgery. There was no statistically significant difference between two groups ($p>0.05$).

In our study, we compared the hemodynamic responses of etomidate with ketofol for induction of anesthesia in the patients undergoing surgery under general anesthesia. The results showed almost equal hemodynamic stability during anesthesia induction and intubation using etomidate compared with ketofol (Table 1-2 & Graph 1-2).

DISCUSSION:

Haemodynamic Response: Considering the opposing effects of propofol and ketamine on hemodynamic parameters, it seems that combination of them at a lower dose can decrease overall side effects and summates the advantages of each agent.[4]

In our study, we compared the hemodynamic responses of etomidate versus ketofol for induction of anesthesia in the patients undergoing surgery under general anesthesia. The results showed almost equal hemodynamic stability during anesthesia induction and intubation using etomidate compared with ketofol. These results are contradictory with the results of Baradari AG et al.[3] This may be due to the selection of patients as they selected the patients with compromising left ventricle in their study, but in our study, we selected healthy patients (ASA Grade I& II).

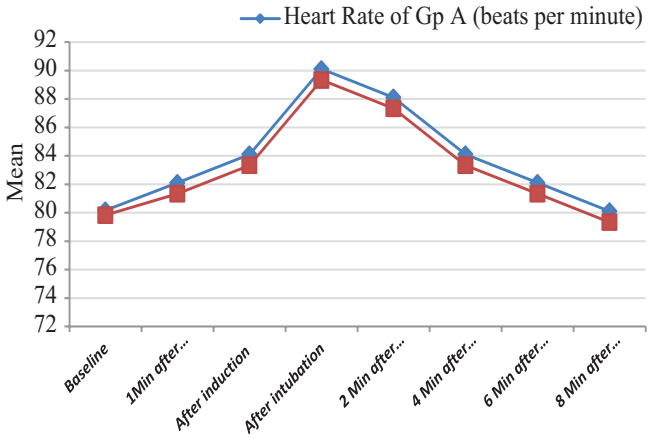
Aghdaii N et al. found propofol-ketamine combination and etomidate-midazolam combination acceptable for induction of anaesthesia in left ventricular dysfunction patients undergoing coronary artery bypass graft (CABG) surgery.[5]

Habibi MR et al. found that using a ketamine-thiopental combination for anesthesia induction in patients with impaired ventricular function undergoing CABG was associated with greater hemodynamic stability compared with etomidate.[6] However, in another study Baradari AG et al. found that etomidate provides better hemodynamic values compared with the ketamine-propofol combination.[3] A study by Yang et al. demonstrated that induction with propofol reduces myocardial systolic and diastolic function in patients with normal left ventricular function who underwent non-cardiac surgery.[7] Furthermore, propofol causes vasodilation and hypotension due to decreased sympathetic tone and decreasing SVR, and has a direct depressant effect on smooth muscle. Additionally, its myocardial depressant effect may be related to alterations in intrinsic myocyte contractile function.[8] Regardless of any underlying conditions, studies indicate that anesthesia induction with propofol at a dose of 2 mg/kg to 2.5 mg/ kg can reduce blood pressure by 25% to

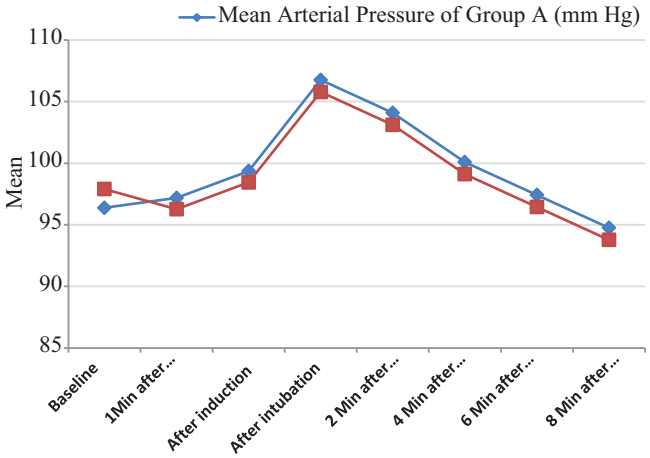
40%.[9] Theoretically, it seems that concurrent administration of propofol and ketamine with divergent hemodynamic effects might be neutralizing and reduce the overall adverse effects.[10] This assumption has been completely confirmed by our study.

Unlike our interpretation a study by Abbasivash et al. revealed that propofol-midazolam-ketamine co-induction in patients scheduled for elective non-cardiac surgery provides more hemodynamic stability than etomidate.[9] Contradiction in results may be due to extra addition of midazolam to ketofol combination.

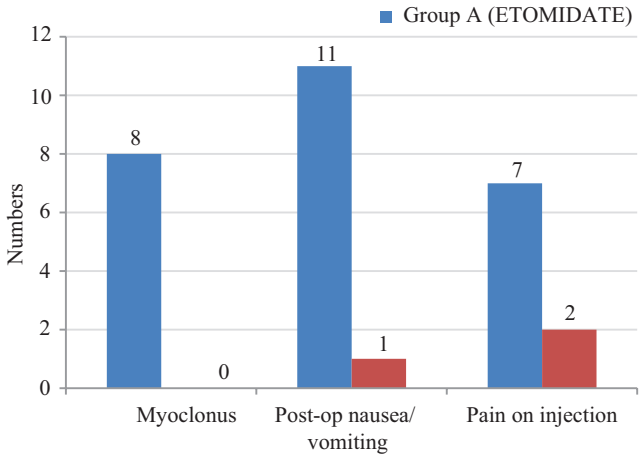
In our study, we compared the hemodynamic responses to etomidate versus ketofol for anesthetic induction in the patients. The results show that both etomidate and ketofol



Graph-2: Comparison of mean heart rate between group A and group B



Graph-1: Comparison of mean arterial blood pressure between group A and group B



Graph-3: Comparison of complicatons/side effects of group A and group B

Time interval in minutes	HR* of Gp A (n=30) (mean±SD)	HR* of Gp B (n=30) (mean±SD)	t value	p value
Baseline	(80.17±6.17)	(79.83±5.95)	0.213	0.832**
1min after premedication	(82.1±5.54)	(81.33±5.13)	0.556	0.580**
After induction	(84.1±5.54)	(83.33±5.13)	0.556	0.580**
After intubation	(90.1±5.54)	(89.33±5.13)	0.556	0.580**
2 min after intubation	(88.1±5.54)	(87.33±5.13)	0.556	0.580**
4 min after intubation	(84.1±5.54)	(83.33±5.13)	0.556	0.580**
6 min after intubation	(82.1±5.54)	(81.33±5.13)	0.556	0.580**
8 min after intubation	(80.1±5.54)	(79.33±5.13)	0.556	0.580**

Table-1: Comparison of heart rate of group A & group B

Time interval in minutes	MAP* of Gp A (n=30) (mean±SD)	MAP* of Gp B (n=30) (mean±SD)	t value	p value
Baseline	(96.38±1.86)	(97.9±2.62)	1.821	0.072**
1min after premedication	(97.18±2.06)	(96.27±1.76)	1.839	0.071**
After induction	(99.36±1.93)	(98.44±1.71)	1.936	0.058**
After intubation	(106.76±1.99)	(105.78±2.24)	1.787	0.079**
2 min after intubation	(104.09±1.99)	(103.11±2.24)	1.787	0.079**
4 min after intubation	(100.09±1.99)	(99.11±2.24)	1.787	0.079**
6 min after intubation	(97.42±1.99)	(96.44±2.24)	1.787	0.079**
8 min after intubation	(94.76±1.99)	(93.78±2.24)	1.787	0.079**

Table-2: Comparison of mean arterial pressure of group A and group B

produce stable hemodynamics and satisfactory induction conditions in patients undergoing noncardiac surgery under general anaesthesia. The results showed almost equal hemodynamic stability during anesthesia induction and intubation using etomidate compared with ketofol. These results are contradictory with the results of Baradari AG et al.[3] This may be due to the selection of patients as they selected the patients with compromising left ventricle in their study, but in our study, we selected healthy patients (ASA Grade I& II). Like our observations Singh R et al.[11]also evaluated the hemodynamic effects of anaesthesia induction with propofol, etomidate, midazolam, thiopentone combination and found that there were no significant differences in hemodynamic changes between the groups.

In accordance with our results Nahid Aghdaii et al. also reported comparable hemodynamic stability during anesthesia induction and intubation using etomidate midazolam combination and propofol ketamine combination in patients with left ventricular dysfunction undergoing coronary artery bypass graft surgery. These combinations provide rapid, pleasant and safe anesthesia with only a few side effects and minor hemodynamic fluctuations.[5]There were no adverse hemodynamic changes from induction until the end of their investigation. But in our study we observed postoperative nausea vomiting in 11 patients, pain on injection in 7 patients and myoclonus in 08 patients in etomidate group (group A) and postoperative nausea vomiting in 1 patient and pain on injection in 2 patients and no myoclonus was observed in any patient in ketofol group.

Like our results the findings of a study of Aghdaii N et al. regarding basic hemodynamic parameters, showed a comparable increase in heart rate, systolic, mean and diastolic blood pressure in both groups after induction, which may be due to the sympathetic stimulation on induction.[5] These results were similar to the results of various other studies[11-14] and was in contrary with the result of study of Singh Bajwa et al. for the propofol-ketamine group that reported minimal increase in SBP and DBP after induction, which slowly reduced to normal values due to antagonistic properties of propofol (decrease in blood pressure) and ketamine (increase in blood pressure). They also observed that all of these variables increased near baseline or above baseline in both groups one minute after intubation, which was probably due to hemodynamic response to laryngoscopy and intubation.[15]In most of these studies the addition of a low dose of ketamine has been shown to attenuate the cardiovascular depressing effects of propofol.[20]

The study of Pandey AK et al.[16] reported that more stable hemodynamic parameters were provided by etomidate presumably due to prevention of cortisol flow on induction by temporary suppression of cortisol synthesis and concluded that maintenance of several studies have investigated the effects of a wide variety of induction agents on these patients. In a study Gholipour Baradari et al.[1] compared the effects of etomidate, combination of propofol-ketamine and combined thiopental ketamine as induction agents on hemodynamic response to laryngoscopy and intubation. One of the major findings of this study was that the patients receiving propofol-ketamine combination as an intravenous induction agent had better hemodynamic stability compared with the other groups. Saleem et al. showed that ketamine-propofol combination provides superior hemodynamic stability compared to propofol-thiopental combination during anesthesia induction, laryngoscopy and tracheal intubation.[17]

Conclusion

In conclusion, the results of our study suggest that both etomidate and ketofol produce stable hemodynamics and satisfactory induction conditions in patients undergoing noncardiac surgery. These combinations provide rapid, pleasant and safe anesthesia with only a few side effects and minor hemodynamic fluctuations. There were no adverse hemodynamic changes from induction until the end of surgery. So, both etomidate and ketofol may be considered for induction of anesthesia in cardiac patients undergoing noncardiac surgery but due to cost effectiveness we recommend ketofol as preferred alternate in low socioeconomic patients. However more studies are required for better understanding of side effects of the drugs because of limitations of our study.

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