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ORIGINAL ARTICLE

Ketofol as induction agent in diabetic patients.

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ABSTRACT… Objective: To evaluate the role of ketofol as induction agent in diabetic patients. **Study Design:** Randomized Control Trial. **Setting:** Department of Anesthesia, Abwa Medical College, Faisalabad. **Period:** Dec 2021 to May 2022. **Material & Methods:** Patients after informed consent divided randomly into two groups 25 in each. Group A receiving propofol 1.5 mg/kg and Group B receiving ketofol 1:2 as induction agent. The dose given was 1ml for every 5Kg. Standard 5 parameter monitoring with pulse oximetry, ECG, noninvasive BP done starting from preoperative to 2 minutes, 5 minutes and 10 minutes after induction agent given. MAP and HR were monitored. Hemodynamic instability was defined as I) Heart rate >160/min or <50/min. II) MAP>120mmHg or <60 mm Hg. **Results:** Total 50 patients included in this study. 25 in each group. The results show significant stability in hemodynamics in group B. **Conclusion:** Ketofol has better hemodynamic stability as induction agent in diabetic patients when used in a 2:1 ratio. This makes it a good choice for this specific patient population.

Key words: Diabetes Mellitus, Ketofol, Pulse Oximetry.

INTRODUCTION

Diabetes mellitus is a disease which occurs due to impairment in carbohydrate metabolism either due to decreased production of insulin or insulin resistance. Disease effects millions of people and brings macro and microvascular changes effecting multiple systems like cardiovascular, neurological and renal.[1] Effects on cardiovascular system and autonomic nervous system are the one which pose challenges for anesthesiologist.[2] Induction of anesthesia is the most challenging time in this group of patients because of exaggerated responses to induction agent and disturbed physiology.

Propofol is the most commonly used induction agent now a days, and is readily available. It consists of a phenol ring substituted with two isopropyl groups, which effects on GABA receptors and induces sleep. Major cardiovascular effect exerted by propofol are hypotension as a result of decrease in systemic vascular resistance due to inhibition of sympathetic vasoconstrictor activity, decrease in pre load, and cardiac contravctility.[3] It also impaires normal baroreceptor reflex mechanism to hypotension. Rapid injection, large doses, and extremes of ages are associated with more pronounced cardiovascular effects.

Ketamine is another induction agent, it is a cyclic analogue of phencyclidine. It has multiple effects throughout CNS. It causes thalamic dissociation from limbic cortex resulting in dissociative anesthesia. It also demonstrate NMDA receptor antagonist action. As it is a sympathomimetic agent it can cause significant rise in BP and HR.[4] The cardiovascular effects are due to central stimulation of sympathetic nervous system and peripheral inhibition of norepinephrine reuptake at nerve terminals after its release. Along with these there is increase in pulmonary artery pressure and myocardial work load. The indirect stimulatory effects are beneficial for patients in shock.

Ketofol is the combination made by addition of

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ketamine to propofol in which both the drugs combat each others side effects and provide desired hemodynamic stability.[5] The two drugs can be combined in different ratios according to the requirement. We used A 1:2 ratio in this study.

MATERIAL & METHODS

This Randomized control trial was conducted at Department of Anesthesia Abwa Medical College, Faisalabad from Dec 2021 to May 2022 after approval from institutional ethical committee (ABWA MC/HR/1023/21). Patients after informed consent divided randomly into two groups 25 in each. Group A receiving propofol 1.5 mg/kg and Group B receiving ketofol 1:2 as induction agent. The mixture of two drugs is prepared by taking 50 mg ketamine diluted into 10ml and 100mg propofol. A total of 20ml prepared, having 5mg /ml propofol and 2.5mg /ml ketamine. The dose given was 1ml for every 5Kg. After informed consent, I/v line established and isotonic crystalloid fluid started at 20ml/hr. Standard 5 parameter monitoring with pulse oximetry, ECG, noninvasive BP done starting from preoperative to 2minutes, 5minutes and 10 minutes after induction agent given. MAP and HR were monitored.

Hemodynamic instability was defined as

I) Heart rate >160/min or <50/min.
II) MAP>120mmHg or <60 mm Hg.

Data analysis done by using SPSS 16.
Mean and standarad deviation calculated for quantitative variables (age, weight)
Frequency and percentage calculated for qualitative variables. (gender)
Confounders controlled through stratification chi square will be applied keeping significance <0.05 to 0.1.

RESULTS

Age range in this study was from 30-70 yrs. Majority of patients. were in 50-60 yrs (84%). Out of 50 patients 26% were of 60-70kg and 24% were in 70-80 kg. 30% patients were ASA III and 20% ASAII.

Total 50 diabetic patients were included in this study. Anyone with uncontrolled hypertension was excluded. Preoperative heart rate and Mean Arterial Pressure were recorded. Heart rate and Mean Arterial pressure at baseline were comparable. There was no significant difference in the two groups preoperatively.

After 2 minutes of induction 24% patients in group A had bradycardia among whom 2% had heart rate less than 50/ minute with hypotension and needed ionotropic support for which ephedrine 10 mg was used as rescue drug. while in group B 22% had stable heart rate while 8% showed tachycardia. None of the patients in group B went into bradycardia. At 5 minutes after induction 2% patients. in group A showed bradycardia but not in need of rescue drug. It was managed with titration of inhalational agent. None in group B. after 10 minutes heart rate become stable in both groups.

Similarly, Mean Arterial Pressure after 2 minutes of induction fall in 22% pts. While in Group B it remained stable.

After 5 minutes of induction 10 % patients in group A showed hypotension while group B remain stable. At 10 minutes after induction both groups showed hemodynamic stability.

		After 2 min						After 5min						After 10 min				
Group A	Upto 50/ min	50-60/ min	60-70/ min	70-80/ min	80-90/ min	90-100/ min	100-110/ min	50-60/ min	60-70/ min	70-80/ min	80-90/ min	90-100/ min	100-110/ min	60-70/ min	70-80/ min	80-90/ min	90-100/ min	100-110/ min
	2.0%	22.0%	24.0%	2.0%	0.0%	0.0%	0.0%	2.0%	26.0%	18.0%	4.0%	0.0%	0.0%	12.0 %	34.0 %	4.0 %	0.0 %	0.0 %
Group B	0.0%	0.0%	2.0%	22.0%	18.0%	4.0%	4.0%	0.0%	0.0%	18.0%	24.0%	8.0%	0.0%	6.0 %	30.0 %	12.0 %	2.0 %	0.0 %

Table-I. Heart rate changes

	After 2 min					After 5 min					After 10min			
Group A	60-70 mmHg	70-80 mmHg	80-90 mmHg	90-100 mmHg	100-110 mmHg	60-70 mmHg	70-80 mmHg	80-90 mmHg	90-100 mmHg	100-110 mmHg	70-80 mmHg	80-90 mmHg	90-100 mmHg	100-110 mmHg
	22.0%	16.0%	12.0%	0.0%	0.0%	10.0%	34.0%	6.0%	0.0%	0.0%	0.0%	16.0%	30.0%	4.0%
Group B	0.0%	0.0%	20.0%	24.0%	6.0%	10.0%	36.0%	30.0%	18.0%	6.0%	0.0%	16.0%	30.0%	4.0%

Table-II. Mean arterial pressure changes

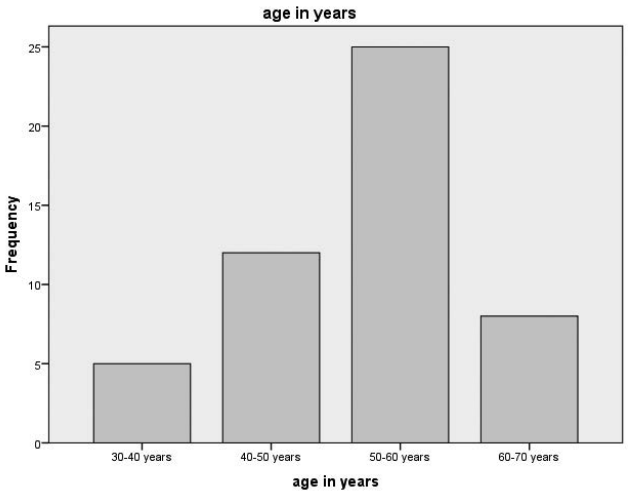

Figure-1. Age segmentation of patients

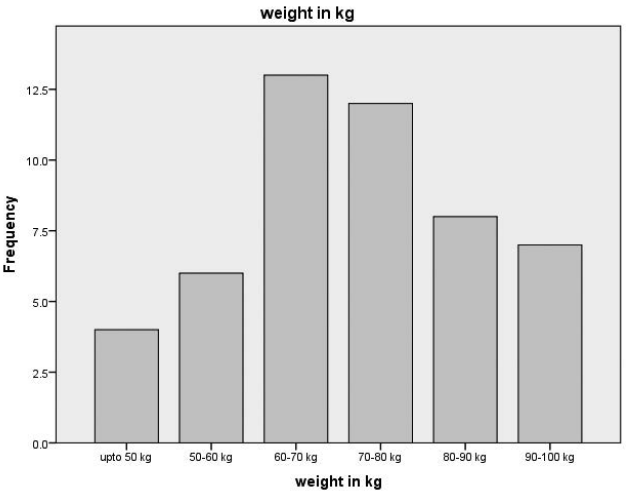

Figure-2. Weight segmentation of patients

DISCUSSION

Diabetes mellitus a world wide medical illness effecting millions of people poses challenges for anesthesiologist due to its multiorgan effects. Induction is the most stressful time for anesthetist in regard to cardiovascular stability. In this study we tried to find out a best possible induction agent in diabetic patients as there is very little data available on this. Ketofol has been used mostly either in critical patients or for procedural sedation. No studies addressed diabetic patients specifically for induction agent selection. We found out that diabetics when given propofol alone as induction agent shows cardiovascular instability in terms of fall in Mean arterial Pressure and heart rate. Instead if we combine propofol with ketamine in diabetics as induction agent it results in hemodynamic stability.

Ketofol in ratio 1:1, 1:2 has been used in some studies as induction agent in patients undergoing laparotomy or laproscopic surgery and better hemodynamic stability was observed in the group receiving combination of drug.[11,12,13] Smichney NJ et al performed a study in critically ill pts requiring intubation and they compared propofol and ketofol as induction agent in these pts the results were similar to our study i.e. hemodynamic stability in ketofol group while hypotension and bradycardia in propofol group.[5]

Aboeldahab H et al performed a study in ASA I pts. Undergoing hernia repair they compared propofol, ketamine and propofol ketamine mixture as induction agent. The result showed that propofol group had reduction in Heart rate and Mean Arterial pressure while Ketamine group had increase in Heart rate and Mean arterial Pressure while ketofol group showed hemodynamic stability.[6]

Another study conducted by Aberra B et al compared the two drugs for LMA insertion and monitored the ease of insertion and hemodynamic stability. The results about hemodynamics are comparable to our study. The difference in this study is that it showed an increase in mean arterial pressure after LMA insertion in Ketofol

group maximum mean arterial pressure being 81.5 +- 11.5 mm Hg in this group immediately after insertion of LMA.[7] A similar study done by Yousef GT et al showed similar results.[8]

Ketofol has been widely used in procedural sedation because of better hemodynamic stability, good analgesia, better airway control than propofol alone.[9,10] Little data is available on ketofol as induction agent in ASA II, III patients as induction agent especially in diabetic population. This study was done to find out a better induction agent in this specific population as the prevalence of this disease is increasing in our population day by day. The difference in our study is that we used a 1:2 ratio of mixture in this specific population.

As far as limitations of this study are concerned, most of the diabetic patients have hypertension as well, we selected the patients having only diabetes. More studies are needed to find the effect of ketofol in diabetic and hypertensive patients with a larger sample size and different ratios.

CONCLUSION

Ketofol has better hemodynamic stability as induction agent in diabetic patients when used in a 2:1 ratio. This makes it a good choice for this specific patient population.

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