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THE USE OF DIAZEPAM ON REDUCING KETAMINE HEMODYNAMIC SIDE EFFECTS (HEART RATE BLOOD PRESSURE) DURING INDUCTION PERIOD OF ANAESTHEIA

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Summary

The study was designed to see the effect of diazepam 0.2mg/kg I.V. before the usual induction dose of ketamine 2 mg/kg I.V. on the cardiovascular parameters (heart rate, diastolic and systolic blood pressures). Eighty patients were scheduled for elective surgery allocated in two groups: [group A: (n=40) received ketamine 2mg.kg IV and cardiovascular parameters were measured], and [group B: (n=40) diazepam 0.2mg/kg I.V. preceded ketamine by 5 minutes and cardiovascular parameters were measured]. Group A showed a significant increase in (heart rate and blood pressure) on test period. In group B: there is a significant decrease in (heart and blood pressure). The study support the idea that diazepam is effective in reducing cardiovascular effects of ketamine to make smooth induction of anaesthesia.

Introduction

A major goal of anaesthetic administration is maintaining optimum homeostasis in the patient. The autonomic nervous system (ANS) is our primary defense against challenges to that homeostasis, it provides involuntary (out side of consciousness) content most important control of heart rate is the effect of the (ANS).

Diazepam (valium) was synthesized by Stench in 1959 [1]. It is 98% bound to plasma proteins[2]; rapid distribution to muscle and fat, with the major metabolite, plasma methyldiazepam with elimination half-life of 24hourse, excretion of metabolite is mostly in the gut and urine[3]. Biotransformation of diazepam occurs in liver to form two active metabolites oxazepam and desmethyldiasepam both of which add to and prolong its effect. It exerts their general effects by occupying the benzodiazepine receptor that modulates GABA (the major inhibitory neurotransmitter in the brain). Cardiovascular effect of diazepam includes slight reduction in arterial blood pressure resulting from a decrease in systemic vascular resistance. The hemodynamic effects of diazepam is

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dose related, the higher the plasma level, the greater the decrease in systemic blood pressure, however there is a plateau plasma drug effect above which little change in arterial blood pressure occurs[1]. It could abolish or modulate the central sympathetic and cardiovascular stimulation [4].

Ketamine is chemically related to phenycyclidine [5]. It was synthesized in 1962 by Stevens[3] and it was used in anaesthesia in 1965 by Domino Corssen[1] it produces dissociate anaesthesia, achieves induction of anaesthesia in about 60 seconds after intravenous administration of ketamine 1-2mg/kg and within 2-4 minutes after intramuscular injection 5-10 mg/kg. It is useful for induction of anaesthesia and even maintenance of anaesthesia in patients who are hypovolemic[6]. There is evidence that ketamine will attenuate baroreceptor function via an effect on NMDA receptor (n-methyl-D-aspartate), it has a unique effect in stimulating the cardiovascular system and is associated with increase in blood pressure, heart rate, cardiac output and work[1].

The aim of this study is to evaluate diazepam in reducing cardiovascular stimulation caused by ketamine (heart rate and blood pressure) during induction period of anaesthesia.

Patients and Method

Eighty patients (18-40) yr., (50-75) kg, and ASA I and II scheduled for elective surgery, where allocated into two groups. Group A: (n=40) anaesthesia was induced with ketamine (2mg/kg), I.V. while group B: (n=40) was taking diazepam 0.2 mg/kg I.V. 5 minutes before induction with 2mg/kg of ketamine. Heart rate and blood pressure were checked before and after ketamine injection. Regarding statistical evaluation Z-test and t-test were used when applicable and a p-value of less than 0.05 was consider significant.

Results

In table I, the z-test was performed to estimate the difference bewteen the two means (heart rate and blood pressure) of group A (pre and post test of patients that received ketamine only) and statistically is highly significant. Table II, the z-test was performed to estimate the difference between two the means (heart rate and blood pressure) of group B (pre and post test of patients that received ketamine preceded by diazepam) and statistically is highly significant.

Parameters	Pre-$\bar{x}$	Post $\bar{x}$	d	Z	p-value
Heart rate	80.27	97.44	-17.16	11.85	<0.01
Systolic blood pressure	117.6	144.75	-27.12	21.08	<0.01
Diastolic blood pressure	75	93.96	-18.96	22.06	<0.01

Pre-$\bar{x}$: mean resting value (pre-induction) of group A.
Post-$\bar{x}$: mean resting value (post-induction) of group A.
d: the difference between 2 means
P: probability <0.01
bpm: beat per minute

Table I. The means of cardiovascular parameters before and after induction of anaesthesia, the differences between them, z-test and p-values of groups A.

Parameters	Pre-x	Post x	d	Z	p-value
Heart rate	78.15	76.15	1.94	3.3	<0.01
Systolic blood pressure	118.5	131.3	-12.84	5.68	<0.01
Diastolic blood pressure	73.25	83.65	-10.2	4.62	<0.01

Pre-x: mean resting value of group B (before diazepam).
Post-x: mean resting value of group B (after diazepam).
d: the difference between 2 means

Table II. The means of cardiovascular parameters before and after induction of anaesthesia, the differences between them, Z-test and p-value of group B.

Parameters	Group A		Group B		t	d.f	p-value
	Post-x1	S.D.	Post –x2	S.D.			
Heart rate	97.44	10.99	76.15	7.21	10.23	78	<0.01
Systolic blood pressure	144.75	13.08	131.3	12.31	4.71	78	<0.01
Diastolic blood pressure	93.96	6.84	83.65	9.58	5.53	78	<0.01

Pre-x1: mean value of post-induction of group A.
Post-x2: mean value of post-induction of group B.
d.f: degree of freedom
p: probability

Table III. Comparison between A and B groups by using t-test.

Table III, the t-test was performed to estimate the difference between the two groups A and B for comparison and show the difference is significant and the p-value less than 0.05. So in brief there were highly significant difference in all the measure parameters (heart rate and diastolic and systolic blood pressures).

Discussion

The administration of diazepam to patients before ketamine is a part of many anaesthetic techniques and procedures, but this is mainly used to control restlessness, relieves tension, or to reduce hallucination and amnesia. Induction of anaesthesia with ketamine is achieved in about 60 seconds after I.V administration, amnesia is present, analgesia is intense and hypertonus of skeletal muscle helps maintain a patent upper airway and decrease in airway resistance[6]. Many studies have been performed on ketamine and diazepam e.g. ketamine / diazepam infusion anaesthesia with special attention on cerebrospinal fluid pressure and arterial blood pressure which showed decrease in both parameters [7]. Others showed that diazepam-ketamine induction in cardiac surgical patients did not result in clinically significant central sympathetic or cardiovascular stimulation [4], and on other hand, cardiovascular and respiratory effects of ketamine-diazepam anaesthesia follows micro (mini) drip technique [8]. In our study, results show that ketamine 2mg/kg I.V produces a significant changes in heart rate (HR), systolic and diastolic blood pressure (BP) in 100% of patients, increase during induction period of (21%, 23% and 25.5%) for heart rate, systolic and diastolic BP respectively. It is possible to reduce the tachycardia and hypertension caused by ketamine by using adrenergic antagonist of both (α and β), a continuous infusion of diazepam and the inhalation anaesthetics will blunt the hemodynamic effect of ketamine [1]. On other hand, verapamil prevent the rise in BP but the chronotropic effect of ketamine is not blocked [3]. However, we used diazepam 0.2mg/kg I.V 5 min. before ketamine administration in group B, results in heart rate increased of 3% from the resting values in 8 patients, the diastolic pressure increased of 11.1% from the resting values in 12 patients and the systolic pressure increased of 9.5% from resting values in 10 patients. The heart rate, the systolic and diastolic blood pressures were not significantly changed throughout the study period so it reduced the hemodynamic effect of ketamine and was considered as simple and smooth induction.

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