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The effect of maternal hypoxia on blood glucose before and after administration of ketamine in rabbit kits

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Abstract

Commonly used anesthetics such as ketamine can differentially affect a number of physiological parameters include hyperglycemia. We aimed this study to determine the effect of maternal hypoxia on blood glucose before and after ketamine administration. Six healthy pregnant rabbits, divided into two groups. Control pregnant rabbits inspired normal air. The case rabbits were subjected to 20 minutes daily period of hypoxia for 10 days during first third of pregnancy for first subgroup and during second third for second subgroup. Blood glucose levels were measured immediately before administration of ketamine (50 mg/kg) and 30, 60, 90 and 120 min after injection. According to results there was a significant difference in glucose concentration between case and control groups before injection. Elevation of blood glucose levels occurred 30 minutes after injection only in control group but it decreased in both subgroups of case animals. Elevation of blood glucose continued in control and began in case group 60 minutes after injection of ketamine but blood glucose decreased 90 minutes after it at all of animals. Taken together, these findings verified influence of maternal hypoxia on postnatal blood glucose. According to results maternal hypoxia caused contrary effect of ketamine on blood glucose in rabbit kits.

Key words: Hypoxia, Ketamine, glucose, Rabbit

INTRODUCTION

In preclinical animal models, it is generally assumed that physiological parameters of the animal under general anesthesia represent the basal state of the animal. However, different anesthetics can variably affect cardiovascular, neurohumoral, and behavioral parameters [1]. Commonly used anesthetics can differentially affect a number of physiological parameters in experimental models; these parameters include cardiovascular, neurohumoral, behavioral and metabolic one of which is hyperglycemia [2-4]. Ketamine is widely used as a short-acting anesthetic and analgesic agent that induces a trance-like anesthetic state known as dissociative anesthesia in both animals and humans, although data on its use and the associated side effects are generally lacking [5,6]. According to some experiments in commonly used laboratory anesthetic agents such as ketamine had dramatic effects on blood glucose levels [5,7]. Administration of ketamine causes neurohormonal and metabolic changes similar to stress, including increased plasma glucose concentrations [8]. Plasma glucose and insulin concentrations can influence clinical outcome [9]. Acute hyperglycemia may influence the outcome in a number of critical illnesses. The adverse effect of hyperglycemia is also reflected in animal models of myocardial infarction [1]. Together, animal experiments and human epidemiological data show that a wide range of individual tissues and whole organ systems can be programmed in uterus with adverse consequences for their physiological function later in life [10]. Animal studies have also demonstrated that the timing, duration, and exact nature of the insult during pregnancy are important determinants of the pattern of intrauterine growth and the specific physiological outcomes [11]. Changes in the intrauterine availability of important material including oxygen, program tissue development and lead to abnormalities in adult cardiovascular and metabolic function in several species [12].

Little is known regarding the effect of pregnancy period hypoxia interaction with ketamine on plasma glucose metabolism; therefore we aimed this study to determine the role of maternal hypoxia on blood glucose before and after ketamine administration.

MATERIAL and METHODS

Experiments were carried out in six healthy pregnant rabbits, medium breeds divided into two groups; two animals as controls and four ones as cases that replaced into two subgroups. All animals were supervised in the animal care facility for at least 30 days before any studies. Control pregnant rabbits inspired normal air. The case rabbits were subjected to a 20 minutes daily period of hypoxia for 10 days during first third (1^{st} -10^{th} days) of pregnancy for first subgroup and during second third (11^{th} -20^{th} days) for second subgroup in which 7% O_2 and 93% N_2 instead of air was passed into the non-poisonous nylon with rubber materials bag. Case animals have been placed in *baro* camera with dimensions; 30, 30, 40cm. Fifteen newborn rabbit kits; 5 controls and 10 cases (2 subgroups) grew up until 30^{th} -days. Experiments were performed at approximately 10 AM each day. To collecting blood samples, food was withdrawn 18 hrs before the start of the experiment. Blood samples of rabbit kits were collected from marginal vein of ears. Baseline blood glucose levels were measured immediately before the intramuscular (IM) administration of ketamine (50 mg/kg). Blood samples also were obtained at 4 time-points; 30, 60, 90 and 120 min after injection. Blood glucose levels were

measured by the glucose strip method.

Collected data were analyzed by SPSS software. Statistical significance was calculated using the Student's t test (Paired for comparison between before and after, Independent for comparison between case and control groups). The level of significance in all cases was set at a two-tailed $p<0.05$.

RESULTS and DISCUSSIONS

Blood glucose levels were measured before and at different times over approximately 2 hrs following the administration of ketamine. According to results there was a significant difference in glucose concentration between case and control groups before injection (Table, $P<0.05$). In the present study, elevation of blood glucose levels occurred 30 minutes after injection only in control group but it decreased in both subgroups of case animals. Elevation of blood glucose continued in control and began in case group 60 minutes after intramuscular administration of ketamine in rabbit kits but it decreased 90 minutes after injection at all of animals (Table, $P<0.05$). However, results were different 2hrs after injection so that blood glucose level decreased in control whereas increased in first subgroup of case ($P<0.05$) and not differ in second subgroup ($P>0.05$).

Table: Plasma glucose concentration before and after injection of ketamine in all of rabbit kits according to group

Groups		Before injection	Minutes after injection			
			30	60	90	120
Control		73.20±4.44	106.00±7.37	116.40±4.93	66.60±4.62	50.20±3.77
Case	Subgroup1	132.60±7.43	114.40±7.63	122.60±5.86	108.80±5.40	112.60±6.84
	Subgroup2	135.40±8.41	106.20±7.63	108.60±7.96	105.40±9.02	105.20±7.12

This study results indicated decreasing effect of maternal hypoxia on plasma glucose in 30 days-aged postnatal rabbit kits. Oxygen is implicated in the regulation of trophoblast differentiation and invasion [13] thus induction of intrauterine growth retardation (IUGR) by maternal stress such as hypoxia leads to postnatal abnormalities in cardiovascular, metabolic, and endocrine function [14]. Evidences suggest that hypoxia can independently contribute to disorders of glucose metabolism. Hypoxemia is an important stimulus for altering autonomic activity, with larger desaturations causing greater increases in sympathetic activity can influence glucose homeostasis by increasing glycogen breakdown and gluconeogenesis in rabbits [15, 16].

According to results of this study, maternal hypoxia also caused decreasing effect of ketamine on blood glucose in postnatal rabbit kits. Brady and Koritnik observed that ketamine has no effect on plasma glucose in African green monkeys [17]. However, ketamine used alone may cause changes in stress-related biochemical variables in plasma [8]. Saha et al demonstrated that commonly used anesthetic agents, such as ketamine produce acute hyperglycemia in rats [1]. Other researchers also have confirmed this effect [5, 9]. Reyes et al suggest the existence of an inhibitory tone on insulin secretion and a glycogenolytic response in ketamine anesthetized rats, probably mediated by adrenergic inervation of the pancreas and liver and by circulating catecholamines secreted from the adrenal medulla [18]. Other study strongly suggests the involvement of insulin, GH, ACTH, and corticosterone released via the $_2$-adrenoceptor pathway in producing ketamine-induced hyperglycemia [1]. Therefore the hyperglycemic effect after injection of ketamine has to be considered for any experimental procedures in rabbits [19].

Taken together, findings verified influence of maternal hypoxia on postnatal blood glucose. According to results of this study maternal hypoxia on first and second third of pregnancy caused contrary effect of ketamine on blood glucose in rabbit kits.

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