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The Role of Pineal Gland on Blood Glucose in Rabbit Pups was Born from Hypoxic Mothers

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ABSTRACT

It has been showed that maternal hypoxia leads to postnatal dysfunctions such as abnormalities in endocrine function and also pineal gland has a variety of physiological functions. We aimed role of maternal hypoxia interaction with pineal gland effect on blood glucose of rabbit pups. We used fifteen healthy pregnant rabbits, medium breeds and divided them into three groups according thirds of pregnancy. In each group two rabbits were used as controls in which they inspired normal air. The remaining three rabbits as cases were subjected to hypoxia for 10 days during three thirds of pregnancy. Epiphysectomy operation was performed on 31st day of life at all of rabbit pups. Blood samples of rabbit pups were collected and plasma glucose was determined one day before and ten days after epiphysectomy. The mean values for plasma glucose concentrations were 106.71±8.00 and 114.21±13.04 mg/dl in case and control groups in all of thirds of pregnancy respectively before epiphysectomy. After epiphysectomy glucose concentration decreased at all of rabbit pups both case and control groups but this gradient was more in controls than cases. We suggested influence of epiphysis gland on plasma glucose concentration in rabbit pups.

Key Words: Maternal, Hypoxia, Pineal gland, Blood glucose, Rabbit.

INTRODUCTION

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 (McMillen and Robinson 2005). 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 (Bertram and Hanson 2001). 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 (Fowden et al 2006). Oxygen is implicated in the regulation of trophoblast differentiation and invasion (Seeho et al 2008) thus induction of intrauterine growth retardation (IUGR) by maternal stress such as hypoxia leads to postnatal abnormalities in cardiovascular, metabolic, and endocrine function (Fowden et al 2005). It has been showed that maternal hypoxia leads to postnatal dysfunctions in many of laboratory animals (Sadler 2006). 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 (Harcourt 2002; Naresh 2005). Also there are functional inter-relationships between the beta cells of the endocrine pancreas and the pineal gland (epiphysis) where the synchronizing circadian molecule melatonin originates (Peschke et al 2006). The initially important, yet poorly understood aspects of pathogenesis take place following in uterus insult prior to the recognition of the aberrant development noted days or weeks later at term. Thus, these phenomena can only be explored by careful study during ontogenesis (Weisborth et al 1974). In this research we studied role of maternal hypoxia interaction with pineal gland effect on blood glucose of rabbit pups.

MATERIALS AND METHODS

Fifteen healthy pregnant rabbits (8-10 month aged), medium breeds Chinese Hare (Lepus sinensis) divided into three groups. In each group two rabbits were used as controls in which they inspired normal air. The remaining three rabbits as cases were subjected to a 20 minutes daily period of hypoxia for 10 days during first third (1-10 days) of pregnancy for first group, during second third (11-20 days) for second group and during last third (21-30) for third group 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;

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30, 30, 40cm. Sixteen newborn rabbit pops (8 controls and 8 cases) in each group grew up until 30-days. Epiphysectomy operation was performed on 31st day of life at all of rabbit pups were born from pregnant mothers. Blood samples of rabbit infants were collected from marginal vein of ears and plasma glucose was determined one day before and ten days after epiphysectomy. Blood glocuse monitoring was performed by On Call Now system ACON/USA with stripe method. Surgery was performed on thirty first day of life in all control and case rabbit pups by Aulov method. Animals anesthetized by Ketamine (50mg/kg) and Xylazine (10 mg/kg).

All animals were supervised in the animal care facility for at least 30 days before any studies. Animasl were used under ethical approval of department.

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

According to results there was a significant difference in glucose concentration between case and control groups before and after epiphysectomy. The mean values for plasma glucose concentrations were 106.71±8.00 and 114.21±13.04 mg/dl in case and control groups in all of thirds of pregnancy respectively before epiphysectomy. After epiphysectomy glucose concentration decreased at all of rabbit pups both case and control groups (Table 1) but this gradient was more in controls than cases (Figure 1). Analysis of results also showed significant differences at both case and control groups according to third of pregnancy before and after epiphysectomy except in controls of last third. Highest gradient in controls was found in first third group (28.12±16.91) but lowest in last third (10.00±13.50). However, there was no any significant difference in gradient between case and control groups at all thirds.

Table 1. Plasma glucose concentration before and after epiphysectomy in all of rabbit pups according to group

P-value	SD	Mean	Measurement time	Group
P<0.001	8.00	106.71	Before Epiphysectomy	Case N=24
	10.04	95.67	After Epiphysectomy	
P<0.001	13.04	114.21	Before Epiphysectomy	Control N=24
	19.38	97.17	After Epiphysectomy	
P<0.001	11.35	110.46	Before Epiphysectomy	Total N=48
	15.29	96042	After Epiphysectomy	

DISCUSSION

Effect of pineal gland on blood glucose

Melatonin, which is synthesized in the pineal gland (epiphysis) and other tissues, has a variety_of physiological, immunological, and biochemical functions (Nishida 2005). There are functional inter-relationships between the beta cells of the endocrine pancreas and the pineal gland, where the synchronizing circadian molecule melatonin originates (Peschke et al 2006). The Romanian group of C.I. Parhon was the first to perform and report systematic research on the importance of the pineal gland in connection with carbohydrate metabolism. In the following years, many publications opened a discussion concerning the importance of the pineal for glucose metabolism, which is still controversial today (Peschke 2008). Recent studies have shown opposite effects of melatonin on the human carbohydrate metabolism. Daily administration of melatonin reduced glucose tolerance and insulin sensitivity, while the prolonged application of melatonin in elderly women did not influence significantly glucose and serum lipids levels (Robeva et al 2008).

Our study results indicated decreasing effect of epiphysectomy on plasma glucose in 30 days-aged postnatal rabbit pups.

Gorray et al showed A significant hypersecretion of insulin in the pancreatic islets from the pinealectomized animals (Gorray et al 1979). Some results substantiated the observation of hyperglycemia because of the application of pineal extracts (Peschke 2008). In another study Single melatonin injection caused hypoglycemia in the newly-hatched parakeet and adult pigeon, and hyperglycemia in newly-hatched pigeon (Mahata et al 1988). These data suggest that melatonin can exert an influence on the secretion and/or action of insulin; however, studies on pinealectomised animals have demonstrated contradictory results, such as reduction of blood glucose and hyperinsulinemia, or low basal insulin levels and hyperinsulinemia under certain photoperiod and feeding conditions in pinealectomized animals (Lima et al 2001). Also Aliyev et al showed blood glucose elevation from 24 hour until 15 days after epiphysectomy but it was decreased 20 days after it (Aliyev et al 2003). Some reports on avian species are ambivalent in this respect as well. Whereas John et al. stated in 1983 that melatonin did not lead to an alteration of the blood glucose levels in turkeys, a later result from 1990, on pigeons, confirmed the blood glucose-increasing effect of melatonin after application. Particular attention should be given to those publications that take the age of the animals under examination or the duration of the photoperiod into consideration. For example, melatonin caused hyperglycemia in newborn pigeons, whereas, in the adult bird, hypoglycemia was detected (Peschke 2008). Results of other study indicated plasma glucose elevation by mid-light intraperitoneal injection of melatonin. Thus, melatonin may act directly on the liver to elevate the plasma glucose level, and changes in plasma glucose level itself may in turn affect hepatic melatonin binding (Poon et al 2001). Furthermore, it has been published that high melatonin levels, because of blinding, or of exogenous melatonin application, raise blood glucose levels, whereas blood glucose levels decrease and insulin level increases because of pinealectomy (Peschke 2008).

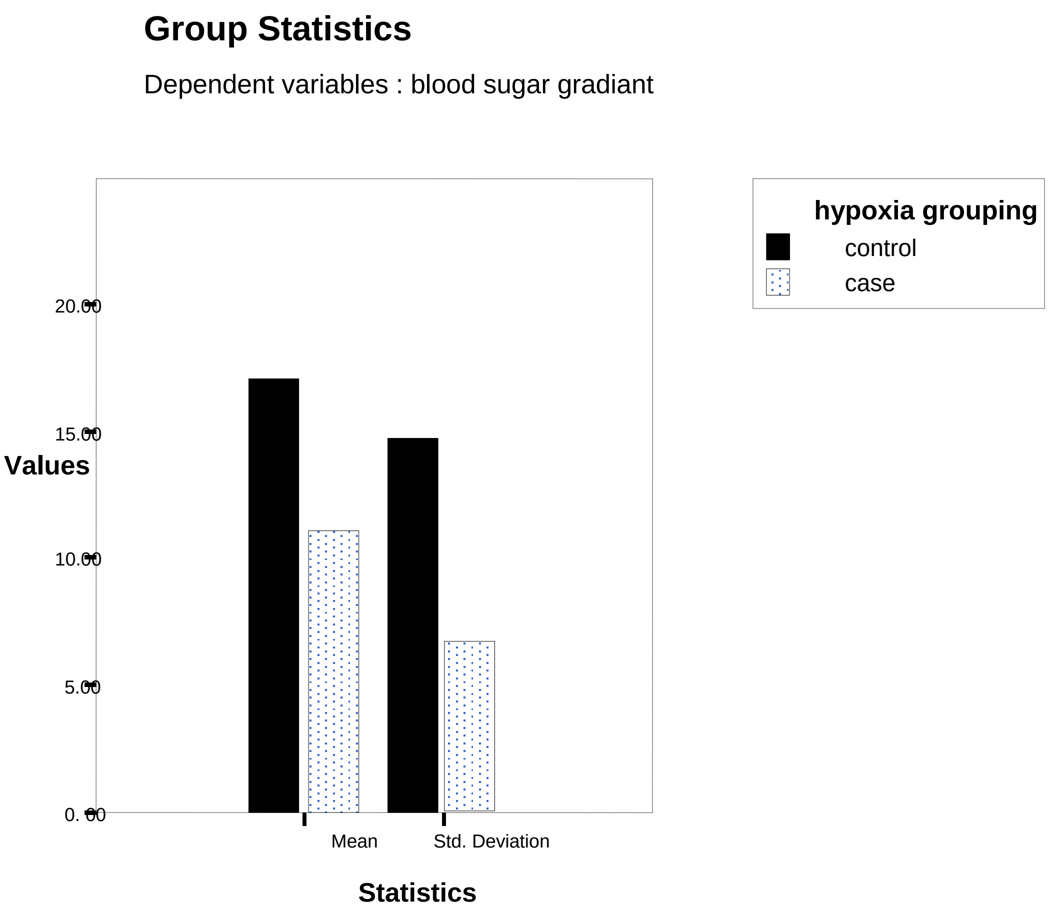

Figure 1. comparison plasma glucose concentration before and after epiphysectomy gradient* between case and control groups (* Gradient = Difference between Plasma glucose concentration before and after epiphysectomy)

Effect of maternal hypoxia

In spite of differences in our results there was not any significant relationship between hypoxia and glucose concentration before and after epiphysectomy gradient at all of thirds of pregnancy groups.

In published results of Lueder, et al fetal plasma glucose concentrations were similar in hypoxic and control fetuses (Lueder et al 1995). Hypoxia for the first 7 days of life resulted in an increase in insulin with no change in plasma glucose in the rats (Raff et al 2001). In other study plasma glucose was equal in the hypoxic and the normoxic control sessions (Oltmanns et al 2004).

Taken together, our finding verified influence of epiphysis gland on plasma glucose concentration in rabbit pups. Our study showed maternal hypoxia does not influence the effect of pineal gland on postnatal blood glucose.

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REFERENCES

Aliyev AH, Khalilov RI, Neymanzade NK, Mikailova UT, Aliyeva FA, and Aliyev AV (2003). The role of the changes in the state of brain for regulation of some lipid and carbohydrate metabolic processes. NATO science series I: Life and Behavioral Sciences 342: 183-190.

Bertram CE, and Hanson MA (2001). Annual models and programming of metabolic syndrome. Br Med Bull 60: 103–121.

Fowden AL, Giussani DA, and Forhead AJ (2005). Endocrine and metabolic programming during intrauterine development. Early Hum Dev 81: 723–734.

Fowden AL, Giussani DA, and Forhead AJ (2006). Intrauterine Programming of Physiological Systems: Causes and Consequences. Physiology 21:29-37.

Gorray KC, Quay WB, and Ewart RB (1979). Effects of pinealectomy and pineal incubation medium and sonicates on insulin release by isolated pancreatic islets in vitro. Horm Metab Res 11:432-436.

Harcourt BF. Textbook of Rabbit Medicine. (2002). Butter Worth-Heinmann, Oxford.

Lima LMB, Reis LC, and Lima, MA (2001). Influence of the pineal gland on the physiology, morphometry and morphology of pancreatic islets in rabbits.Rev Bras Biol 61:333-340.

Lueder FL, Kim SB, Buroker CA, Bangalore SA, and Ogata ES (1995). Chronic maternal hypoxia retards fetal growth and increases glucose utilization of select fetal tissues in the rat. Metabolism 44:532-537.

Mahata SK, Mandal A, and Ghosh A (1988). Influence of age and splanchnic nerve on the action of melatonin in the adrenomedullary catecholamine content and blood glucose level in the avian group. J Comp Physiol 158: 601-607.

McMillen I, and Robinson JS (2005). Developmental origins of the metabolic syndrome: prediction, plasticity, and programming. Physiol Rev 85: 571–633.

Naresh M Punjabi, and Vsevolod Y (2005). Disorders of glucose metabolism in sleepapnea. J Appl Physiol 99: 1998-2007.

Nishida S (2005). Metabolic effects of melatonin on oxidative stress and diabetes mellitus. Endocrine 27:131-136.

Oltmanns KM, Gehring H, Rudolf S, Schultes B, Rook S, and Schweiger U (2004). Hypoxia causes glucose intolerance in humans. Am J Respir Crit Care Med 169:1231-1237.

Peschke E, Frese T, Chankiewitz E, Peschke D, Preiss U, and Schneyer U (2006). Diabetic Goto Kakizaki rats as well as type 2 diabetic patients show a decreased diurnal serum melatonin level and increased pancreatic melatonine-receptor status. J Pineal Res 40: 135-143.

Peschke E (2008). Melatonin, endocrine pancreas and diabetes. J Pineal Res 44:26–40.

Poon AMS, Choy EHY, and Pang SF (2001). Modulation of Blood Glucose by Melatonin: A Direct Action on Melatonin Receptors in Mouse Hepatocytes. Biol Signals Recept 10:367-379.

Raff H, Bruder ED, Jankowski BM, and Colman RJ (2001). Effect of neonatal hypoxia on leptin, insulin, growth hormone and body composition in the rat.Horm Metab Res 33:151-155.

Robeva R, Kirilov G, Tomova A, and Kumanov Ph (2008). Melatonin–insulin interactions in patients with metabolic syndrome. Journal of Pineal Research 44:52-56**.**

Sadler TW (2006). Langman′s Medical Embryology. 10th Edn. Lippincott, Williams&Wilkins, Philadelphia.

Seeho SK, Park JH, Rowe J, Morris JM, and Gallery ED (2008). Villous explant culture using early gestation tissue from ongoing pregnancies with known normal outcomes: the effects of oxygen on trophoblast outgrowth and migration. Hum Reprod 23:1170-1179.

Weisborth SH, Flatt RE, and Kraus AL (1974). The Biology of the Laboratory Rabbits. Academic press, New-York.