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Effects of (acute) first dose selenium injection on the blood glucose level of diabetic and healthy rats

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ABSTRACT

The study was performed in healthy and streptozotocin diabetic rats. Blood glucose was measured before and at 30, 60 and 120 minutes after the first acute I.P. injection of sodium selenite and selenate. Acute I.P. injection of sodium selenite and selenate resulted in decreased blood glucose level of diabetic rats after 30 minutes of administration, whereas, the blood glucose of healthy ones increased slightly in response to selenium administration in a dose dependent manner this provided additional evidence of the significant effect of selenium on blood glucose in healthy and diabetes rats

INTRODUCTION

Results of studies carried out on the effects of selenium supplementation on serum glucose levels of normal animals are conflicting. Fillippi (1913) reported a marked glucosurea in rabbits chronically poisoned with selenate and slight glucsourea when given selenite. Later on Bunk and Combs (1980) observed a measurable increase in the plasma glucose concentration in chicks after oral administration of 0.205 mg/kg sodium selenite. Whereas, no difference in serum glucose concentration due to selenium supplementation in food and in drinking water was reported (Sugden *et al.,* 1978; Becker *et al*., 1996). On the other hand selenium given in drinking water to rats has no effect on glycolytic and citric acid intermediates (Shearer and Kinersly, 1973). However, Rasekh *et al.,* (1991) reported that acute interaperitoneal administration of selenium (1.6mg/kg or more) caused hyperglycemia in fed and 24 hour fasted rats (30, 60 and 90 minute) following selenium injection. Wright (1941) reported an increase in blood glucose of well-fed rats in response to sodium selenite in doses greater than 5.0 mg/kg., but his work did not focus on the short-term effects of this element. Likewise, Pellegrino and Galzzone (1928) observed an increase in the blood sugar levels of fasted rabbits after intramuscular injection of selenate. However, chronic administration of selenium like

vanadium, (Brichard *et al.,* 1988) had no effect on the serum glucose level of normal rats (Becker *et al*., 1996; McNeill *et al*., 1991; Berg *et al*., 1995; and Battell *et al.,* 1998). The study of Nonavinakere *et al.,* (1986) suggested that the threshold dose for selenium induced hyperglycemia 1 hour post-injection (I.P.) is 1.6 mg/kg. Other studies indicated that this hyperglycemic response to selenium has abated following adrenalectomy (Mallory *et al.,* 1988 and Rasekh *et al*., 1991).

It was reported that selenium has a marked influence on diabetic rats. Acute intrapretoneal injection of sodium selenite at a dose of 173µg/kg body weight drastically reduced the very high levels of serum glucose in acute slightly diabetic rats within 5 to 30 minutes after treatment, which was accompanied by un-significant slight increase of serum insulin (Lizuka *et al.*, 1992).

The objective of the study was to investigate the effects of intraperitoneal injection of selenium in diabetes mellitus and to detect if selenium is a typical insulin mimetic.

MATERIALS and METHODS

The study was carried out on 56 adult male albino rats weighing (180-210 g). The rats were housed in ordinary cages for 7 days prior to use. Three rats were housed per cage, and maintained at a constant temperature 25º C, with fixed cycle of 12 h light: 12h darkness (light on from 07.00 to 19.00).

Diabetes mellitus was induced in rats by a single interaperetonial injection of freshly prepared, streptozotocin (STZ) at a dose of 75 mg /kg body weight which was dissolved in 0.1 M citrate buffer pH 4.5. The animals were allowed a 7 day interval to recover before starting experiments. During this time blood samples were obtained from the tail for glucose analysis using an Accutrend analyzer (Boehringer Mannheim), in day 2, 4 and 7 after STZ injection. Rats with blood glucose levels > 300 mg /dl were considered to be diabetic.

Sodium selenite (0.175 and 0.350 mg/kg) and sodium selenate (2.8mg/kg) were prepared by dissolving it in sterilized distilled water. Each rat was injected I.P. with 0.1ml selenium solution. Healthy and diabetic untreated rats were injected with 0.1ml saline.

Blood glucose was measured by glucose oxidase method at just before injection of selenium and saline at 0 times and at 30, 60, 90, and 120 minutes after injection .

Statistical analysis was carried out by one way analysis of variance followed by Bartlett´s test, where ($P<0.05$) was taken as significant.

RESULTS

Results given in Table (1) indicated that the levels of the blood glucose of rats after STZ injection were higher (477 mg/dl) than that of the healthy ones (102 mg/dl). Immediately after the first dose of selenium administration (acute I.P. selenium injection) the two groups' responded differently i.e. the blood glucose of healthy rats increased, whereas that of the diabetic ones decreased in response to selenium administration. It's clear that sodium selenate (2.8 mg/kg) increased the level of the blood glucose of the healthy rats relative to that of the healthy selenite treated rats (0.350, 0.175 mg/kg). Likewise, selenate reduced significantly ($P < 0.05$) the level of the blood glucose of diabetic rats (320mg/dl) compared to that of selenite treated ones (452 and 445 mg/dl, respectively).

The action of selenium on blood glucose was significantly affected by time. The healthy and diabetic-untreated rats injected I.P. with saline showed slight increase in blood glucose level 30 minute after injection and then decreased gradually. However acute I.P. injection of diabetic rats with sodium selenate (2.8mg/kg) significantly decreased the blood glucose level at 30, 60, 90, and 120 minute. Likewise, acute selenite injection into diabetic rats decreased slightly the blood glucose level at all-time point (30, 60, 90, 120 minute) after injection. The decrease in blood glucose was clear with the higher selenite dose (0.350mg/kg) relative to the lower dose (0.175mg/kg), (Table 1). It is evident that selenite and selenate treated diabetic rats showed the lowest glucose level at 30 minutes after treatment.

Table 1: Effect of first dose selenate and selenite injection in diabetic and healthy rats on blood glucose level

Treatment	Before selenium injection	Time after injection (Min.)			
		Glucose level (mg/dl)			
	0	30	60	90	120
Healthy) (saline0.85%)	102.6±6.49	115.4±6.49	108.2±6.49	106.5±6.49	105.0±6.49
Healthy (2.8mg/kg) selenate	118.7±3.77	138.3±3.77	157.3±3.77	154.7±3.77	145.0±3.77
Healthy (0.350mg/kg selenite	114.3± 5.3	121.7±5.3	134. 7±5.3	128.3±5.3	123.3±5.3
Healthy 0.175mg/kg) selenite	97.3±3.9	115.3±3.9	118. 3±3.9	130.3±3.9	115. 7±3.9
Diabetic untreated (saline)	4 77.0±32	489±32	482.0±32	424.0±32	479.0±32
Diabetic (2.8mg/kg) selenate	440.2±21.	282.6±21.1*	301.2±21.1*	288.0±21.1*	292.2±21.1*
Diabetic(0.350mg/kg)selenite	511.0±41.2	427±41.2	446.0±41.2	441.0±41.2	439.0±41.2
Diabetic (0.17mg/kg) selenite	481.0±49.21	410±49.21	425.0±49.21	436.0±49.21	447.0±49.21

Values are Means ±SEM *P<0.05

DISCUSSION

Results of this study proved that acute (I.P.) administration of selenium to severely diabetic rats reduced significantly the elevated blood glucose level at each time interval (30, 60, 90,120 minutes) with the lowest value observed at 30 minutes. The reduction occurs in a dose dependent manner. These results proved that the prompt reduction of the blood glucose level of the diabetic rats may suggest that selenium may have acted in a manner resembling that of insulin. The probable explanation for this insulin like effect of selenium may be through its effect on enzymes involved in hepatic glucose metabolism. The reduced glucose levels caused by selenium treatment observed in this study were in agreement with the previous observation of lizuka *et al*., (1992) who stated that, acute I.P. administration of selenite caused hypoglycemia to slightly diabetic rats 5 and 30 minutes following injection. The authors suggested that the hypoglycemic effect of selenium was to some extent similar to that of insulin (5, 30 minute). They also observed that the glucose level slightly decreased

when selenite was administered to pancreaectomized rats.

At the same time the acute I.P. Injection of selenium to healthy rats increased the level of glucose at different time intervals after injection (30, 60, 90, and 120 minute) in a dose dependent manner and did not drop back to the starting level up to 120 minutes after injection. (Though this effect of selenium is not like that of insulin). These results were not in line with the previous results reported by Bunk and Combs, (1980) and Rasekh *et al.,* (1991), which stated that plasma glucose level dropped back to normal levels 90 minute after selenite injection. Previous findings reported by Nonavinakere *et al*., (1986) and Rasekh *et al*., (1991) stated that the threshold dose for selenite to induce hyperglycemia one hour post-intraperitoneal injection was 1.6mg/kg.

The results of the present studies proved that both selenium salts (selenate and selenite) elevated the blood glucose level in a dose dependent manner, likewise Fillipi, (1913) observed a marked glucosurea in rabbit poisoned with selenate and slight glucosurea when given selenite.

It is evident that these results suggested a divergent effect of acute selenium injection to diabetic rats (insulin-like action) and normal rats (antagonized insulin action), suggesting that probably more than one mechanism is involved in acute effect of selenium injection. Shearer and kinersely, (1973) stated that acute selenium administration does not cause inhibition of enzymes within glycolysis or the citric acid cycles. Previous studies reported by Rosenfeld and Beath, (1946); Jensen, (1975) and Glover *et al.,* (1979) suggested a possible pituitary gland involvement in hyperglycemia response of healthy subjects to acute selenium administration. These findings were confirmed by Schamberger, (1983) and Thorlacius-Ussing and Danscher, (1985) who found an intracellular accumulation of selenium in secreatory granules and lysosomes of B cells following an interaperitoneal injection of 5mg /kg of sodium selenite. They suggested that this hyperglycemic response represents phenomenon originating in the pituitary gland. Rasekh *et al*., (1991) suggested that the hyperglycemia observed during acute selenite injection to normal rats is not mediated through a decrease in plasma insulin levels. They attributed the hyperglycemic effect of selenium to a significant increase in plasma corticosterone levels. They added that selenium did not cause any change in plasma glucose level of adrenectomized rats which suggests that the adrenal glands play a major role in hyperglycemia response. The authors added there might be other explanation that the hyperglycemia might be mediated by a neural mechanism which induces glucagon secretion by neurogenic stimulation of the pancreas via the vagus and splanchnic nerve.

CONCLUSION

The present study provided additional evidence that acute I.P. administration to healthy and diabetic rats significantly affect the blood glucose level. The divergence of acute selenium action on healthy (hyperglycemia), and diabetic subject (hypoglycemia) suggest that selenium has its own action and probably more than one mechanism is involved.

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