Z. Ernährungswiss. 16, 39–43 (1977)

ISSN 0044–264

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Serum mineral changes in alloxan diabetes before and after treatment with some hypoglycemic drugs

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With 1 table

(Received December 29, 1976)

After administration of alloxan, animals show a triphasic change in the blood sugar levels. Initial hyperglycemia, hypoglycemia, and permanent hyperglycemia (12). The development of these phases of alloxan diabetes are mainly due to insulin deficiency, insulin surplus, and then insulin lack, respectively (7).

Many authors reported increased serum zinc due to alloxan diabetes. *Maske* (10) stated that the islet cells have the distinctive property of concentrating zinc and the injury of these cells leads to a release of zinc in serum. However, *Rasin* (13) reported that insulin lowered the blood zinc levels in experimental dogs.

Jün-Bor et al. (8) found lower serum calcium content in the alloxan-diabetic rats and mice while *Herrera* (6) reported no significant change. On the other hand, *Zaets* (19) showed that the dialyzable calcium increased and that of protein-bound calcium decreased.

Increases in plasma magnesium in diabetes was reported by *Hammersten* and *Smith,* (5). They found also that it returns to the normal level after injection of insulin. *Herrera* (6) found a decrease in serum potassium in alloxan-diabetic animals, while *Milanov* et al. (11) reported unchanged potassium level in their diabetic animals. The effect of insulin administration to aloxanized adrenalectomized rats causes drop in serum potassium (4).

Many investigators reported decreased sodium level in diabetes (11, 1).

The present study was performed to study the metabolism of certain ingornic elements such as zinc, copper, iron, calcium, magnesium, potassium, and sodium in alloxan diabetes before and after treatment with different hypoglycemic drugs.

Materials and methods

This work was carried out on 180 normal male albino rats of body weight ranging from 200–250 g. The rats were maintained on the laboratory stock diet and allowed to eat ad libitum. Fasted rats were rendered diabetic by intraperitoneal injection of a freshly prepared alloxan monohydrate solution in a dose of 150 mg/kg body weight.

The rats were categorized into 8 groups, 30 normal rats used as controls, 30 rats treated with alloxan only, 20 alloxan-diabetic rats of each of the 6 following groups. A group of these was given glibenclamide (daonil) in a dose of 0.1 mg/kg body weight/day for 7 days. The second groups was given daonil for 14 days. The third group was given glucodiazine (lycanol) in a dose of 20 mg/kg body weight/day for 7 days and the fourth group for 14 days. The remained two groups were treated with insulin (1 unit/kg body weight/day) twice a day for 7 and 14 days, respectively.

Blood samples were collected from the heart of the animal by means of disposal needles and syringes. Each two blood samples were pooled together. A portion of the blood was used for estimation of glucose. The remaining portion was allowed to clot. The serum was reparated for analysis of zinc, copper, iron, calcium, magnesium, sodium, and potassium.

The method of *Nelson*'s modification of *Somogyi*'s (16) was used for determination of blood sugar. Serum zinc and copper were determined by the method of *Sinaha* and *Gabrieli* (15). Serum iron, potassium, and sodium were estimated by the method published in *Beckman*, Analytical method by Atomic absorption spectrophotometer. Serum calcium and magnesium were determined using the method of *Willis* (18).

Results and discussion

Our alloxan-diabetic rats showed high serum-zinc level compared to normal controls (table 1). These findings agree with those results obtained by *Shevchuk* (14) and *Maske* (10) who suggested that this phenomenon was due to release of zinc from the islet cells as a result of its destruction by alloxan. *Tarni* (17) found that urinary zinc in alloxan-diabetic rabbits was significantly increased 4 or 5 days after the onset of diabetes and remained constantly high. Remission of the diabetic state, however, tended to normalize the zinc excretion again.

In our study, the treatment of alloxan-diabetic rats with daonil led to lowering of serum zinc. On the other hand, when lycanol was administered to diabetic rats, they showed non-significant effect on serum zinc neither after 7 days nor after 14 days. Similarly, there was no return of serum zinc to the normal level when insulin was used. However, *Rasin* (13) reported that insulin lowered blood-zinc level directly after administration in diabetic dogs, but the zinc level increased again after few hours.

In the alloxan-diabetic rats, serum copper was higher than normal. This higher level may be due to hepatotoxic effects of alloxan. Seven days after the treatment of alloxan-diabetic rats with daonil, the serum copper decreased to some extent till on the 14th day of treatment it lowers to the normal level. When lycanol was administered to alloxan-diabetic rats, serum copper lowered down faster to the normal level till the 14th day. In case of insulin treatment, the copper level slowly lowered till it normalised on the 14th day.

In our study, alloxan diabetic rats showed significant increase in serum iron. This was in agreement with *Maske* et al., (9) who found increased urine- and blood-iron level in alloxan-diabetic rats. This increase may be due to haemolysis of the red blood cells. Treatment with daonil and insulin did not affect serum iron even after 14 days of injection. Lycanal lowered the serum-iron level to some extent. No explanation was traced in the literature in this respect.

Table 1. Fasting blood glucose and serum electrolytes in controls and other treated groups of rats.

Item	Controls	alloxan diabetes	daonil 7 days	14 days	lycanol 7 days	14 days	insulin 7 days	14 days
Glucose	116.7	451.9	303.8	147.7	216.6	221.9	137.6	110.5
mg/100 ml	± 18.8	± 33.4	± 31.7	± 23.9	±42.7	±56.2	± 39.3	± 11.3
P >		0.005	0.005	0.05	0.005	0.005	0.1	n. s.
Zinc	131.6	220.8	167.6	141.4	210.9	187.0	240.2	171.4
μg/100 ml	± 15.8	± 74.3	± 22.8	± 16.6	± 52.8	± 57.6	± 23.0	± 41.7
P >		0.005	0.025	0.15	0.005	0.025	0.005	0.025
Copper	116.9	188.8	172.3	128.6	119.0	116.4	156.8	116.3
μg/100 ml	± 20.1	± 41.1	± 57.6	± 30.0	± 20.4	± 30.3	± 12.5	± 34.5
P >		0.025	0.025	0.15	n. s.	n. s.	0.025	n. s.
Iron	132.1	173.5	171.4	185.3	140.4	139.8	164.4	176.5
μg/100 ml	± 19.7	± 38.3	± 54.9	± 20.8	± 21.8	± 23.2	± 12.1	± 21.1
P >		0.01	0.01	0.01	0.15	0.15	0.01	0.01
Calcium	7.55	5.95	7.07	8.63	7.71	8.09	6.64	7.69
mg/100 ml	±0.8	±0.9	±0.3	±0.5	±0.3	±1.2	±0.4	±0.7
P >		0.025	0.15	0.05	0.15	0.025	0.1	n. s.
Magnesium	3.92	5.65	3.91	2.96	3.80	3.59	3.61	3.47
mg/100 ml	±0.44	±1.2	±1.04	±0.27	±0.54	±0.39	±0.19	±0.46
P >		0.005	n. s.	0.025	n. s.	0.15	0.15	0.15
Potassium	23.28	19.88	21.87	20.24	19.46	17.23	20.25	19.92
mg/100 ml	± 2.19	± 1.31	± 2.99	± 0.86	± 1.12	± 1.86	± 1.50	± 0.97
P >		0.025	n. s.	n. s.	0.15	0.005	n. s.	0.15
Sodium	225.3	178.8	178.4	212.5	196.3	211.5	183.4	203.9
mg/100 ml	± 10.8	± 13.8	± 11.5	± 10.6	± 10.7	± 10.0	± 10.0	± 5.7
P >		0.005	0.005	n. s.	0.05	n. s.	0.01	0.15

Calcium level in the alloxan-diabetic rats was significantly lower than normal. Our finding was in agreement with those values obtained by *Jün-Bor* et al. (8). Howeyer, when the hypoglycemic agents were used, the calcium levels returned to the normal ones after 7 days.

Statistically significant increase in serum magnesium was observed in alloxan-diabetic rats, which returned to the normal levels after 7 days from treatment with the three hypoglycemic drugs. After 14 days of treatment with daonil, the serum magnesium was even lower than normal controls. However, *Berthaux* and *Maurat* (2) found that a slow simultaneous intravenous injection of insulin and glucose caused decrease in the serum-magnesium level. Similar findings are reported by *Binet* (3).

The potassium level of our experimental diabetics was significantly lower than normals. This was concordant to the results obtained by *Herrera* (6), who found that 24 hours after an intravenous injection of alloxan, a decrease in potassium level was observed. On the other hand, *Milanov* et al. (6) found no change in his experimental animals. After treatment with daonil and insulin, the potassium level became somewhat higher, but still below the normal level, while lycanol coused a further decrease in potassium level. However, *Dury* (4) reported that insulin administration induced a significant decrease in potassium level in alloxanized adrenalecomized rats. This was explained on the basis that when there is deficiency in glucose, due to insulin injection, no intracellular synthesis of proteins from glucose occurs and, therefore, no entry of potassium from tissue fluids into the cells takes place (4).

The mean serum sodium in alloxan-diabetics was considerably lower than normal. These are in agreement with data obtained by many investigators (11, 1). *Milanov* et al. (11) ascribed this drop in serum sodium that it was due to diuresis which followed the diabetic state. After treatment with the hypoglycemic agents, the sodium level tends to normalize after 14 days injections. This may be due to the relief of the diabetic state as indicated in table 1 of the lowering of the glucose levels.

Summary

In alloxan diabetes, serum zinc, copper, iron and magnesium were significantly higher than in normal rats, while the level of serum calcium, sodium, and potassium was lower than normal. Treatment with daonil or insulin led to a normalization, as expected of the level of serum glucose and most of the other elements, except for iron and potassium. When lycanol was used for treatment, the level of all elements returned to the normal except for blood glucose, zinc and potassium.

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