BLOOD GLUCOSE AND PLASMA INSULIN RESPONSES TO XYLITOL ADMINISTRATED INTRAVENOUSLY IN DOGS

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Xylitol is a pentitol which is a normal intermediate in the glucuronate-xylulose pathway. Recently it was reported by Prellwitz and Bässler (1963) that the xylitol administrated intravenously was rapidly metabolized in both nondiabetic and diabetic subjects. Although there has been no previous report concerning a hypoglycemic effect of xylitol injection, we report in this paper a significant hypoglycemia produced in the normal dog following the intravenous administration of xylitol, which may stimulate strongly the insulin secretion of the pancreatic beta-cells.

Methods

Five normal male dogs weighing 9 to 13 kg and 3 diabetic male dogs weighing 8 to 12 kg were anesthetized with intravenous injection of sodium pentobarbital (30 mg per kg of body weight) after 16 to 20 hours starvation. In the three diabetic dogs mentioned above 80 mg of alloxan per kg of body weight had been injected intravenously on 10 to 14 days before the xylitol administration.

Blood samples were taken with the small polyethylene tube catheterized into the vena cava inferior through the femoral vein.

The first blood sample was taken at 60 minutes after the injection of the anesthetic. Following the first blood sampling, 10 % solution of xylitol ("Klinit", Eisai Co., Tokyo, Japan) was rapidly injected through the subcutaneous vein in the foreleg of the experimental animals. The dosage of xylitol administrated was 0.4 g per kg of body weight. Blood samples were taken at 10, 20, 30 and 60 minutes from the end point of the injection of xylitol. Blood sugar was determined with glucose oxidase method ("Glucostat", Worthington Biochemical Co., U. S. A.), and plasma was separated from blood cells immediately after taking blood and kept frozen at -20° C until insulin assay. The method of determination of plasma insulin was double-antibody radioimmunoassay reported by Hales and Randle (1963).

Results

In normal dogs:

The blood sugar levels decreased in all of 5 normal dogs receiving xylitol. The lowest levels ranging from 37 to 52 mg/dl were shown in 3 dogs at 30 minutes after the xylitol injection, whereas the remaining 2 dogs showed the lowest blood sugar levels, 41 and 47 mg/dl, at 60 minutes after the administration of xylitol. The average values of blood sugar concentration of these 5 dogs were as follows: 83 ± 7 mg/dl before injection of xylitol, 74 ± 8 mg/dl at 10 minutes, 58 ± 8 mg/dl at 20 minutes, 48 ± 9 mg/dl at 30 minutes, and 58 ± 17 mg/dl at 60 minutes after the injection. The lowest level in the average values was at 30 minutes, and the decrease of the blood sugar was considered to be highly significant.

The plasma insulin levels increased in all of 5 normal dogs re-

ceiving xylitol. The highest levels ranging from 180 to 257 microunit/ml were shown in 3 of the five dogs at 20 minutes after the xylitol injection, whereas the other 2 dogs showed the highest plasma insulin levels, 195 and 203 microunit/ml, at 10 minutes after the injection. The average values of plasma insulin concentration of these 5 dogs were as follows: 39 $\pm$ 11 microunit/ml before injection of xylitol, 194 $\pm$ 29 microunit/ml at 10 minutes, 209 $\pm$ 35 microunit/ml at 20 minutes, 145 $\pm$ 63 microunit/ml at 30 minutes, and 57 $\pm$ 26 microunit/ml at 60 minutes after the injection. The highest level in average values was at 20 minutes, and the increase of the plasma insulin produced by xylitol was highly significant (Table 1).

In diabetic dogs:

In contrast to the normal dogs, the blood sugar levels increased gradually in all of 3 alloxanized diabetic dogs receiving xylitol. The highest levels were shown at 60 minutes after the injection of xylitol.

Xylitol administration did not produce significant increases in the plasma insulin levels in the diabetic dogs receiving xylitol (Table 1).

Discussion

Although Mellinghoff (1961) reported that peroral administration of xylitol did not affect the blood sugar level in diabetics and Mehnert et al. (1964) reported that the blood sugar level of normal persons did not change by the intravenous infusion of xylitol, a significant hypoglycemia produced by xylitol was shown in this paper.

The peak of the plasma insulin concentration after the xylitol injection was observed prior to the obvious decrease of blood sugar level in normal dogs, and alloxanized dogs with diabetes showed neither increase of plasma insulin level nor decrease of blood sugar level

Table 1. Effect of intravenous injection of xylitol on blood sugar and plasma insulin concentrations in normal and diabetic dogs.

	Blood sugar mg/dl					Plasma insulin microunit/ml				
	0	10	20	30	60	0	10	20	30	60
		minutes after injection					minutes after injection			
Normal dog										
No. 1	92	76	51	47	79	38	195	180	130	96
No. 2	88	84	68	60	47	49	148	180	114	72
No. 3	84	78	62	52	74	30	203	192	69	36
No. 4	74	71	62	43	41	27	218	257	231	34
No. 5	78	63	48	37	48	51	218	236	181	49
Diabetic dog										
No. 6	165	174	190	198	244	21	15	18	30	30
No. 7	205	212	218	218	270	22	25	29	17	39
No. 8	260	267	260	278	293	28	25	58	32	53

following the xylitol injection. These results suggest that the hypoglycemia produced by xylitol is caused by the hypersecretion of endogenous insulin from pancreatic beta-cells. In our experiment the peak level of plasma insulin following the xylitol injection was about two times higher than that following the injection of equivalent dosage of glucose.

To explain the mechanism of stimulating effect of xylitol on the beta-cells, farther studies must be performed. Field et al. (1960) reported that glucose was chiefly metabolized through the pentose phosphate pathway in the pancreatic beta-cells, and he suggested that NADPH produced in this pathway stimulated the synthesis of insulin in the beta-cells. Therefore it seems interesting to assume that relatively large amount of NADPH might be produced by the conversion of xylitol to L-xylulose and stimulate the synthesis of insulin.

References

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