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Effects of Azetazoleamide (Diamox) Upon Blood Sugar of Normal and Diabetic Patients. (22724)

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Moseley *et al.*(1) observed insulin shock in a diabetic patient receiving azetazoleamide as a diuretic and subsequently made studies on normal subjects to evaluate the effect of this drug on glucose tolerance. No significant change in the intravenous glucose tolerance curve was noted when studied with and without the administration of azetazoleamide. They concluded from the oral glucose tolerance curve that azetazoleamide may interfere with the absorption of glucose from the gastrointestinal tract.

Since Moseley did not study diabetic patients and limited his study to an acute problem, our studies were designed to determine whether azetazoleamide influences the fasting blood sugar of normal and diabetic patients after acute and chronic administration and whether the oral glucose tolerance curves can be affected.

Acute study. Acute experiments were carried out in 20 normal and 20 diabetic subjects. Half of each group were given either 500 mg of azetazoleamide* orally and fasting blood sugars determined (method of Folin-Wu)(2) 3 hours later or followed without drug administration for a similar period. One week later, to eliminate biologic variation, the subjects were re-studied but the procedure

reversed. The results of this experiment are summarized in Table I. Azetazoleamide did not alter the fasting blood sugar 3 hours after its administration in the normal and the diabetic group of patients when studied as an acute experiment. The blood sugar taken at 3 hour intervals was practically the same with and without the drug.

Chronic study. Chronic experiments were carried out in 6 normal and 6 diabetic patients. Azetazoleamide was given in doses of 500 mg daily for a 3 week period to 3 normal and 3 diabetic patients. Fasting blood sugars were determined (method of Somogyi)(3) at weekly intervals. As a control, a similar group was followed without drug administration. In Table II average values of blood sugars are recorded. With chronic administration of 500 mg of azetazoleamide there was no significant change in the fasting blood sugar in either the control patients or those receiving the drug for a period of 3 weeks.

Oral glucose tolerance. The final experiment was related to the effect of azetazoleamide on the glucose tolerance curve. Three normal and 3 diabetic patients received the standard oral glucose tolerance test utilizing 100 g of glucose. The procedure was repeated at a later date with 500 mg of azetazoleamide being given 3 hours prior to the

* Supplied by Lederle Laboratories Division, American Cyanamid Co.

TABLE I. Influence of Azetazoleamide upon Blood Sugar of Normal and Diabetic Patients. (Value of fasting blood sugar in mg %.)

Subjects	Without drug				After oral admin. of 500 mg			
	Control		3 hr		Control		3 hr	
	Range	Avg	Range	Avg	Range	Avg	Range	Avg
Non-diabetic (20)	95-132	114	100-124	112	83-140	112	93-132	113
Diabetic (20)	85-380	233	83-320	202	106-367	237	103-340	222

TABLE II. Chronic Experiment on Normal and Diabetic Patients. (Avg value of fasting blood sugar in mg %.)

Weeks	Control*				500 mg azetazoleamide O.D. daily*			
	0	1	2	3	0	1	2	3
Non-diabetic	86	84	91	97	79	76	82	87
Diabetic	137	135	144	158	118	118	120	127

* 3 subjects for each group.

administration of glucose. The glucose tolerance curves are recorded in Table III. Although there was considerable individual variation in the curves obtained, the blood sugar curve for each of the subjects studied was not different with and without azetazoleamide. The differences in the curves obtained are within the range of technical and biologic variation.

improves, the insulin requirements may be decreased and eventually discontinued. Since azetazoleamide is used in diabetic patients for its diuretic properties, it is conceivable that the drug resulted in a change of cardiac status and insulin requirements, and azetazoleamide *per se* has no significant effect on sugar metabolism or insulin sensitivity. Any diuretic agent would have the same action and it is unnecessary to postulate a specific effect of azetazoleamide upon the blood sugar of diabetic subjects.

Conclusions. 1. The influence of azetazoleamide upon fasting blood sugar and the glucose tolerance curve was studied in a group of diabetic and normal subjects. Azetazoleamide was given either as a single dose or for a period of 3 weeks. 2. No significant alter-

TABLE III. Effect of Azetazoleamide on the Glucose Tolerance Curve. (100 g glucose orally—value of fasting blood sugar in mg %.)

	Min.	Control				500 mg azetazoleamide 3 hr before test			
		0	30	90	150	0	30	90	150
Non-diabetics	1. A.B.	76	109	107	100	79	106	106	101
	2. C.P.	88	138	126	115	90	123	104	101
	3. J.K.	89	162	200	138	100	151	132	112
Diabetics	1. H.D.	127	200	308	313	128	181	268	258
	2. A.F.	96	99	172	236	107	112	189	245
	3. H.B.	159	192	267	300	178	213	251	305

Comment. Maren *et al.* (4) previously observed in chronic acidotic dogs maintained on azetazoleamide that the fasting blood sugar had slight but definite tendency to rise. However, an insulin tolerance test was found to be normal in a dog treated with azetazoleamide.

The response that Moseley noted was probably due to a well recognized clinical observation of diabetic patients with congestive heart failure. During this time they may be uncontrollable and require an increased dose of insulin. As the congestive heart failure

of the fasting blood sugar or the glucose tolerance curve was noted following the administration of azetazoleamide.

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