BRIEF NOTES and COMMENTS

The Editors invite investigators to submit short communications of potential interest to the readers of the Journal for this new department which begins in the current issue.

They may cover any aspect of the subject matter of diabetes: clinical notes, observations on therapeutic agents, socio-medical problems, or unusual clinical experiences.

Communications should not exceed 1,000 words except in unusual circumstances. Figures and tables should be limited to one of each, and references should be ten to twenty in number.

These communications should not be used to establish priority of observation for work in progress, or for work that is intended for publication in extenso, within the near future.

If this department proves useful by attracting well-written, short papers dealing with findings of interest to most of our readers, it will become a regular feature. Its success will depend upon the quality of the contributions offered. The Editors welcome correspondence concerning the department during its trial.

EFFECT OF ORAL SULFONYLUREA ON PLASMA TRIGLYCERIDES IN DIABETICS

J. Harold Morris, M.D., Donald A. West, A.B., and Robert E. Bolinger, M.D., Kansas City

SUMMARY

The effect of sulfonylurea compounds on the plasma triglycerides was tested in eighteen adult diabetics. Sulfonylurea caused a mean reduction in plasma triglyceride of 19 mg. per cent. The magnitude of the reduction did not correlate with the hypoglycemic effect. The reduction in triglyceride was apparent in spite of weight gain in some subjects.

The correlation between the incidence of coronary artery disease and elevation of the plasma triglycerides establishes the latter as one of the best indices in the prediction of arterial degenerative disease.[1-7] Of particular interest is hypertriglyceridemia in diabetes associated with a higher incidence of arterial degenerative disease.[6,8] Hamwi et al.[9] have noted the greatest triglyceride elevations to occur in poorly controlled diabetics. Albrink et al.[7] have emphasized the role of high carbohydrate intake in the genesis of hypertriglyceridemia. Since Hirsch et al.[10] observed a good correlation between hyperglycemia and hyperlipidemia, control of the blood glucose suggests itself as the most practical approach to the hyperlipidemia problem in diabetes. The group of diabetics who are most prone to atherosclerotic disease are the adult obese diabetics with often only mild hyperglycemia. This group is best managed with diet with the occasional addition of oral hypoglycemic agents. Shipp and Munroe[11] have reported lowering of serum lipids in two diabetics with hyperlipemia upon treatment with sulfonylurea compounds.

The following study is designed to determine the effect of sulfonylurea compounds on plasma triglycerides of diabetic patients in an outpatient setting where dietary control is admittedly poor.

From the Diabetic Clinic, Kansas University Medical Center, Kansas City, Kansas.

MATERIALS AND METHODS

Patients for this study were stable diabetics not dependent on insulin. All had been on diabetic diets (30 per cent of calories as fat) with varying degrees of cooperation for at least a year before the study was undertaken and were continued on the same diet throughout the study.

Plasma triglycerides were determined by the method of von Handel et al.[12] in the fasting state at two weekly intervals. Each patient was observed in this fashion for a period of approximately twelve weeks on diet alone, and for another twelve weeks on diet plus sulfonylurea. The latter was given as tolbutamide in doses of 0.5-1.5 gm. per day or as chlorpropamide in doses of .125-.500 gm. per day. Blood glucose was determined by the method of Somogyi-Nelson.

RESULTS

Results of the plasma triglyceride determinations for the period of diet alone and diet plus sulfonylurea are shown in table 1 for the eighteen patients studied. It is seen that a reduction in the mean triglyceride level

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TABLE 1

Effect of sulfonylurea

	Diet						Sulfonylurea					
Case no.	Number of samples	Δ Wt.	Fasting blood glucose mg. per 100 ml. Mean	σ *	Triglyceride mg. per cent Mean	σ	Number of samples	Δ Wt.	Fasting blood glucose mg. per 100 ml. Mean	σ	Triglyceride mg. per cent Mean	σ
1	6	− 1¼	205	15	107	11	6	+ 4	192	77	83	25
2	4	+ 2	129	10	161	14	5	+ ¼	114	11	136	21
3	5	+ 9½	143	17	107	26	5	− 1	147	16	76	10
4	5	− 8	204	25	139	14	5	+ 4	146	28	116	17
5	6	—	191	52	121	30	8	—	146	25	114	20
6	7	− 9	167	34	177	41	5	− 1¾	151	17	137	34
7	5	+ ½	179	20	113	26	8	− 5¼	152	19	90	16
8	3	− 3	279	13	182	96	6	− ¼	251	51	128	14
9	6	− 6½	176	17	242	34	6	+10½	143	24	175	40
10	6	− 5	111	7	83	5	6	−17¾	104	15	92	12
11	5	− ¼	191	29	166	63	5	+ 6½	127	15	126	13
12	5	− 4¼	174	26	129	34	5	+ 5¾	157	11	80	12
13	6	− 1¾	183	17	215	63	6	+ 1¾	152	4	209	23
14	8	−11	191	40	73	12	6	+ 4¼	139	14	70	26
15	5	+ 1½	119	7	78	19	5	+ 2	101	15	100	23
16	6	− 3¾	138	41	202	34	6	+ ¾	131	18	230	57
17	7	−12	89	12	123	11	3	− 1	82	6	116	12
18	6	−12	333	25	374	75	4	+ 8¾	288	42	317	91

$$* \sigma = \sqrt{\frac{\Sigma x^2}{N}}$$

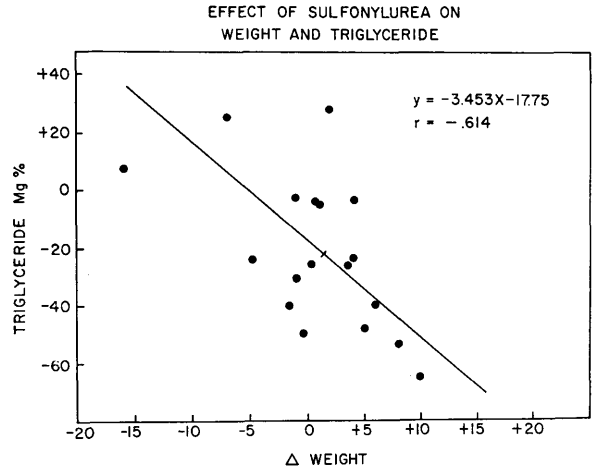

FIG. 1. The relation of the change in triglyceride to the change in weight between the periods of diet alone and of diet plus sulfonylurea is shown with a correlation of —.614.

occurred in all but four of the cases during the period of sulfonylurea treatment. The mean reduction for the group was 19 mg. per cent, which is highly significant ($P < .001$, see footnote).

The mean reduction in the blood glucose (26 mg. per 100 ml.) was also significant ($P < .001$) with the sulfonylurea indicating that dosage was adequate to produce hypoglycemia effect. These was no correlation, however, between the magnitude of the sulfonylurea effect on the triglycerides and on the blood glucose.

In most patients a weight change was noted during sulfonylurea treatment; however, there was no significant trend. Weight changes during the dietary period showed no correlation with triglyceride changes, but during the sulfonylurea period there was a significant negative correlation ($r = -.614$, $P < .01$). This would imply that in spite of weight gains in many patients the depressant effect of sulfonylurea on plasma triglycerides was still apparent (figure 1). Symptomatically, at least half of the patients complained of increased appetite during the period of sulfonylurea treatment.

DISCUSSION

The significant reduction in plasma triglycerides with sulfonylurea treatment is not surprising, since the primary effect of these drugs is an increase in the secretion of insulin.[14-16] The lowering effect of insulin on

*Analysis of Variance of Plasma Triglyceride Values[13]

Source of variance	Degrees of freedom	Sum squares	Variance	F	P
1. Between treatments	1	24,684	24,684	15.78	<.001
2. Between patients	17	879,189			
3. Within groups	165	256,454	1,554		
4. Interaction (1x2)	17	25,846	1,520		>.05
Total	200	1,186,173			

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the plasma triglycerides is well known[7,9] and constitutes the best explanation for this effect by sulfonylurea compounds.

In these studies the sulfonylurea effect on the lowering of plasma triglycerides was frequently accompanied by a weight gain such that a significant negative correlation was noted ($r = -.614$). This, again, is best explained by the known effect of insulin in reducing lipolysis from the fat depots and promoting storage of fat.[17] The reduction in lipolysis decreases free fatty acid available to the liver for triglyceride synthesis,[18] thus explaining the lowering of the plasma triglycerides. Since weight gain induced by primary increase in dietary intake is associated with elevation of the plasma triglycerides,[1] the reduction in triglyceride shown in these studies is even more striking. If the hypertriglyceridemia is an index of poor prognosis,[1-7] then reduction of this value suggests an improvement in prognosis. In most of the patients in this series there was no strict indication for an oral hypoglycemic agent based on parameters of carbohydrate metabolism alone, but in many of these persons a lowering of the triglyceride was significant in spite of some weight gain. That the weight gains were probably the result of increased caloric intake induced by the appetite stimulating effect of the hypoglycemic agent seems apparent. However, in an outpatient setting where dietary control is admittedly poor, the triglyceride reducing effect of the sulfonylurea would seem to constitute an advantage to be considered in selected patients.

SUMMARIO IN INTERLINGUA

Effecto de Sulfonylurea Oral Super Triglyceridos Plasmatic in Diabeticos

Le effecto de compositos de sulfonylurea super le triglyceridos plasmatic esseva essayate in dece-octo diabeticos adulte. Sulfonylurea causava un reduction medie de 19 mg per 100 ml in triglyceride plasmatic. Le magnitude del reduction non esseva in correlation con le effecto hypoglycemic. Le reduction de triglyceride esseva apparente in despecto de augmento de peso in alicun subjectos.

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