A TRIAL OF HYPOGLYCAEMIC AGENTS FOR WEIGHT INCREASE IN PSYCHIATRIC PATIENTS*

By

SUSANNE SHAFAR

FORMER attempts to restore weight loss in psychiatric patients have included hyperalimentation (Weir Mitchell, 8) and sub-coma insulin therapy (Debenham *et al.*, 2; Sargant and Craske, 5; Sullivan, 7). The aim of the present trial was to compare weight gains in a group of patients given repeated small doses of insulin with two other groups to whom oral hypoglycaemic agents were administered, and with a control group. The drugs used were tolbutamide and chlorpropamide, both of which are sulphonylureas used in the management of diabetes mellitus, and known to induce hypoglycaemia in non-diabetic subjects (Hoenig and Gittleson, 4; Cardonnet *et al.*, 1; Garcia Reyes *et al.*, 3). Pharmacologically there are no qualititative differences in their mode of action. Stowers *et al.*, (6) found the half-life of tolbutamide to be 3·5 hours and that of chlorpropamide 34·5 hours. The prolonged action of chlorpropamide permits once daily dosage, but tolbutamide, being a shorter acting drug, was given in divided doses to maintain depression of blood sugar over the 24 hours.

The subjects were in-patients in a general hospital psychiatric unit who had suffered weight loss prior to admission. As the average length of stay in this unit is four weeks, patients could not serve as their own controls. The trial comprised 42 patients, 31 women and 11 men, with an age range of 23 to 68 years. Patients were allocated to the four groups at random. No selection on clinical grounds was made except that patients suffering from serious physical disease were excluded. Weighing took place at the start of the trial and thereafter twice weekly, patients being weighed in the same night attire on each occasion. The weights were checked by two nurses. Patients were not told of the nature or purpose of the medication. Each patient's fasting blood sugar was examined before starting the trial; in all cases levels were normal.

The insulin group (3 men, 8 women) commenced with 5 units of soluble insulin 30 minutes before each of the three main meals, with daily increases up to 10 units, if tolerated; the tolbutamide group (3 men, 7 women) were given 1·0 gram of the drug 30 minutes before main meals; the chlorpropamide group (3 men, 8 women) were given 0·5 gram of the drug at 6.30 a.m. each day. The control group consisted of 2 men and 8 women. The patients also received appropriate physical and psychotherapeutic measures: 34 received ECT, 18 modified narcosis, 14 phenothiazines and 2 Tofranil. Diagnostic categories included: affective psychosis (16 patients), personality disorder (11), and abnormal psychogenic reactions (15). The four treatment groups were statistically compared in respect to age, length of stay, diagnosis, "other treatments given", and psychiatric outcome. All significance tests were made at the $P=0·05$ level. There were no significant differences between the groups.

RESULTS

The hypoglycaemic medication produced no side-effects. Table I presents the mean daily weight gains in ounces. Because of the disparity in numbers of the male and female samples, the sexes were analysed separately.

* This is a shortened version of a more detailed paper which can be obtained on request from the author.

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TABLE I

Group	No. of patients		Ounces per day	
	M	F	M	F
I	3	8	+14·3	+2·2
T	3	7	+1·4	+1·9
CH	3	8	+0·4	+3·7
C	2	8	+0·3	+1·4

Significant Difference (P=0·05): 10·9

I=insulin, T=tolbutamide, CH=chlorpropamide, and C=control

Thus the 3 male insulin patients, but not the 8 female insulin patients, had significantly higher weight gains than the tolbutamide, chlorpropamide and control groups. Gains in the other groups did not differ significantly. In both the male and female sample weight gains of the control group were the smallest. Age had no significant effect on results. Correlation co-efficients between initial weights and mean weight gains did not reach significant levels. For the purpose of assessing psychiatric outcome, patients were rated as follows: "excellent", "good", "fair" and "poor". Mean daily weight gains in respect to outcome are shown on Table II. Abbreviations are as in Table I.

TABLE II

Outcome	Number of patients				Mean gains, ounces per day			
	I	T	CH	C	I	T	CH	C
Excellent	2	4	4	5	10·7	2·2	4·6	2·9
Good	4	3	2	1	2·6	1·7	2·9	0
Fair	4	2	4	0	6·5	1·2	1·5	—
Poor	1	1	1	4	0	1·1	3·2	−2·3

Highest weight gains obtained in patients rated "excellent", and least gains in those rated "poor". In the "good" and "fair" categories the weight gains did not correlate with psychiatric improvement.

CONCLUSION

Though numbers are small, it emerges that the two oral hypoglycaemic drugs in the dosage used in this trial were no more effective than insulin in producing weight gains. Only the male insulin group showed significantly higher weight gains than the controls.

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Susanne Shafar, M.B., Ch.B., D.P.M., *Assistant Psychiatrist, Crumpsall Hospital, Manchester*