

13380 COMPETITIVE PROBLEMS IN THE DRUG INDUSTRY

COMPARISON OF SUBJECTS WITH NORMAL GLUCOSE TOLERANCE

In the between group comparison no significant difference was seen in the number of subjects with normal glucose tolerance tests between the placebo and each of the drug groups (table 3). Unpaired t-tests showed the glucose values at the various time intervals to be comparable between the placebo and each of the drug groups. The within group comparison showed that compared with the appropriate initial test: (a) a greater number of subjects had normal glucose tolerance in test 2 but not in subsequent tests in the placebo group; (b) a significantly greater number of subjects had normal glucose tolerance tests in test 2, 3 and 4 in the chlorpropamide group; (c) a significantly greater number of subjects had normal glucose tolerance in test 2 and 3 in the tolbutamide group; (d) no significant change in the number of subjects with normal glucose tolerance tests in the follow up years despite the decrease in percent ideal weight in test 2 and 5 in the phenformin group and (e) a significantly greater number of subjects had normal glucose tolerance in test 3 in the acetohexamide group. A comparison of glucose levels was done by paired 't' analysis where each individual's initial test served as the control. The following results were obtained: (a) in the placebo group the blood glucose levels were lower at 30 min and 60 min in test 2 and higher at 0 min and 120 min in test 4; (b) in the chlorpropamide group the blood glucose levels were lower at fasting, 30 min, 60 min and 120 min in test 2 and at 30 min and 60 min in test 3; (d) in the phenformin group the blood glucose levels were higher at 0 min and 30 min in test 5 and (e) no significant change was observed in the acetohexamide group.

COMPARISON OF INSULIN SECRETION

In fig. 3 the insulin response to oral glucose was calculated as the total incremental area above fasting for the stated time interval ($\mu\text{U}/\text{ml}/\text{min}$). Similarly the insulin response relative to glucose stimulus was calculated as the total incremental area for insulin divided by the total incremental area for glucose for the stated time interval. In the between group comparison by the unpaired 't' test, no significant difference was noted between the placebo and each of the drug groups in each of the five tests in all the four variables shown. The mean ($\pm$ S.E.M.) time peak insulin during the initial test for the five groups were: placebo = 93.2 ($\pm$ 5.7) min, chlorpropamide = 96.6 ($\pm$ 11.8) min, tolbutamide = 85.4 ($\pm$ 7.9) min, phenformin = 99.1 ($\pm$ 9.5) min and acetohexamide 87.9 ($\pm$ 9.1) min. The placebo group did not differ significantly from each of the drug groups in all five tests the mean time of peak insulin. In the within group comparisons by paired 't' analysis, the only significant differences between test one and each of the subsequent tests in the above five variables was seen in the chlorpropamide and acetohexamide group. In the former group the 0-60 min and 0-180 min insulin/glucose area ratios were significantly higher in test 2 compared with those in test 1. In the latter group, the 0-180 min insulin/glucose area ratio of test 3 was higher than test 1. These differences were due not to an increase in insulin secretion but to a decrease in glucose area.

COMPARISON OF FASTING LIPID LEVELS

Table 4 shows the number of subjects with normal fasting serum triglyceride levels in each test and group. As a group, 76 of the 120 chemical diabetics had normal fasting triglyceride levels in the initial test. In the between group comparison by chi square analysis, the following results were obtained: compared with the placebo group (a) the tolbutamide group had a significantly greater number of subjects with normal fasting triglycerides in test 3, 4 and 5; (b) the phenformin group had a greater number of subjects with normal fasting triglycerides in test 3 and (c) the acetohexamide group had a greater number of subjects with normal fasting triglycerides in test 2 and 3. Unpaired 't' analysis indicated that, compared with the placebo group, the tolbutamide group showed lower fasting triglycerides in test 4 and 5 whilst the other groups showed no differences. In the within group comparison both by chi square analysis and the paired 't' test, no significant differences were seen between the fasting triglyceride levels in test 1 and each of the follow up tests in all five groups.

Table 5 shows the number of subjects with normal fasting serum cholesterol levels. In the initial test 85 out of the 120 chemical diabetics in the whole group