9. Study No. 2545

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The above-named investigators used the identical protocol and the same study plan. This is described below:

EXPERIMENTAL DESIGN

Each study consisted of 32 subjects who were grouped into one of the four cells indicated below prior to double blind assignment into one of four dosage schedules. Such random assignment was predicated on a randomization schedule based on appropriate tables selected from ——— and Oakford, Tables of Random Permutations, Stanford University Press, 1962.

The cells are described as follows: Eight male patients who were 15 to 30 pounds overweight, and 8 male patients who were 30 to 75 pounds overweight; 8 female patients who were 15 to 30 pounds overweight, and 8 female patients who were 30 to 75 pounds overweight.

The subjects were 21 to 65 years of age with mature, non-endocrine obesity as evidenced by being 15 to 75 pounds heavier than the desirable weight. Special inclusion criteria were an expressed desire to lose weight, and an expressed interest in and willingness to participate in this drug trial, on either Ponderex or placebo for a period of 12 weeks.

EXCLUSION CRITERIA

1. Endocrine or other metabolic causes of obesity.
2. Evidence of abnormal fluid retention.
3. Obesity of childhood onset.
4. History of weight loss regimen in the last 6 months.
5. Inability to reasonably ensure accurate reporting of any deviation from the dosage schedule, side effects, etc.
6. Severe hypertension.
7. Marked coronary artery disease.
8. Severe renal impairment.
9. Severe hepatic impairment.
10. Pregnancy or apt to become pregnant.
11. Lactation.
12. Overt depression.
13. Have taken in the last 2 weeks, or currently taking or likely to take any of the excluded concomitant drugs (anorexigenics, tranquilizers, sedatives, MAO inhibitors, diuretics, thyroid preparations, and steroids).

DOSAGE SCHEDULE

One group received Fenfluramine tablets 60 mgs/day (one tablet t.i.d. of a 20 mg strength); the next group received an equivalent sized placebo tablet t.i.d.; the next group received Fenfluramine tablets in a dose range of 60 to 120 mgs/day given in three divided doses, and, the fourth group received a placebo dose that was equivalent to the Fenfluramine high does schedule. So, we have groups of patients properly randomized, two received a low dose schedule of either Fenfluramine or placebo, and two groups receiving a high dose schedule of Fenfluramine or placebo. The treatment was for 12 weeks continuous, and not crossed-over.

The drugs were packaged in appropriately labbled bottles (double blind, coded), containing a two-weeks' supply of tablets. The investigator issued a bottle at the first, third, fifth, seventh, ninth and eleventh visit to each patient and requested the subject to return the unused tablets in two weeks so that the remaining ones may be counted and recorded.

No special diet was recommended. It is felt that a rigid low calorie diet is not necessary to determine appetite suppressant qualities of any drugs.

OBSERVATIONS

The following observations were made at the initial visit, and every 7 days for the entire 12-week period:

1. Weight—Every effort was made to ensure accuracy and to minimize the extraneous variations from visit to visit; i.e., personnel were to be carefully instructed. The same person, if possible, was to do all the weighing; medically