
Pharmacotherapy

Obesity Treatment

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Pharmacologic Agents

- Fenfluramine
- Phentermine

Fenfluramine

- It affects the serotonergic system
- Serotonin agonist.
- It enhances the uptake of serotonin and blocks its reuptake.
- Decreases appetite and provide a feeling of fullness.
- Trade name: Pondimin.

Phentermine

- It affects the catecholaminergic system.
- It stimulates norepinephrine and dopamine release and blocks its reuptake.
- It decreases appetite and allows for less frequent eating.
- Trade name: Fastin, Obcap, Obenix, Zantryl, Phentol

Single Use of Phentermine

- Studies done on continuous or intermittent therapy were equally effective, leading to increased weight loss.
- Short-term studies from 3 to 6 months showed better success in wtg. loss.
- Insomnia, nervousness, irritability, and headache.

Single Use of Fenfluramine

- Short-Term studies appears to induce positive weight changes: 3 - 6 months.
- Long-Term studies does not necessarily induce any further significant reduction in body-weight.
- Increase in the thermic effect of food in rats/
no change on RMR.
- gastrointestinal disturbances, drowsiness, lethargy, depression.

Combined Drug Therapy: “Phen/Fen Miracle Drug”

- Rationale: drugs with different mechanisms of action might be used in smaller amounts, providing efficacy equivalent to or greater than that of the full dose of a single drug, with fewer adverse effects.

Phen/Fen

- Weintraub et.al., 1992: 4-year study.
- Multimodal intervention strategy:
- medications, behavior mod., caloric restriction, and exercise therapy.
- Monograph: Studies I thru VII

Studies I thru VII

- To study the benefits and adverse effects of the phen/fen use.
- Intermittent versus continuous therapy.
- Adjustments in medication dose in order to achieve 120% ideal body weight.
- Efficacy of medication.
- Cessation of medication.
- Serum lipid response.

Protocol

- 121 patients.
- men: 1500 to 1800 kcal.
- Women: 1000 to 1200 kcal.
- Exercise: 300 kcal/ 3 x per week.
- Counseling: behavior mod.
- Medical supervision.

Week 0 to Week 34

- Phen/Fen group: lost 14.2 kg
- Phen (15mg) / Fen (60mg).
- Control group: lost 4.6 kg

Week 34 to 104

- All patients on medication: n = 83
- Intermittent group: lost 11.5kg
- Continuous group: 12.6 kg
- Augmented group: lost 6.5 kg
- Phen(30 mg)/Fen(60mg).

Week 104 to Week 156

- N = 59
- To achieve 120% of ideal BW.
- 5 combinations of drug doses.
- Subjects gained an average 2.7 kg by week 156.
- 9.4 kg below baseline.

Week 156 to Week 190

- N = 51
- Placebo group: gained 6.9 kg.
- Phen/Fen group: 15 mg./ 60mg: 4.4 kg.
- Subjects 4.1 kg less than baseline.

Week 190 to Week 210

- N = 48
- Participants tapered-off medication.
- End of study: 1.4 kg less than baseline.

Lipid Profile

- HDL-C: 15% higher at week 210
- Total Cholesterol/HDL-C ratio: 8% less at week 210
- Triglycerides: 16% lower at week 210.

Summary

- Moderate weight loss during the first year.
- Peak weight loss: week 34 / 14 kg with medication.
- No evidence that body weight was reset at a lower level with long-term use of medication.
- Week 210: average loss, 3 lbs.

Conclusions

- Single- drug and combined therapy studies: 3 to 6 months modest success.
- Most weight loss during: first 3 to 4 months.
- Long-term treatment: 1st year weight maintained / slightly increased.
- Over 1 year: BW gradually regained.

Recommendations

- The National Task Force on Obesity, 1996: Until more data are available, pharmacotherapy cannot be recommended for routine use in obese individuals.
- TNEJM Editorials, 1996: BMI greater than 30/unsuccessful treatments/pts with medically important obesity/adjunct to diet and exercise.