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Adjunctive Use of Appetite Suppressant Medications for Improved Weight Management in Bariatric Surgical Patients

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Background: Patients who undergo bariatric surgery sometimes experience late onset of weight gain, when they lapse into negative eating patterns, which adversely affect weight management. Long-term weight management is a process, with a surgical foundation, and requiring adjunctive strategies for best results. We sought to determine if appetite suppressant medications could be safely incorporated into a comprehensive program of weight management.

Methods: Subjects were at least 18 months post-operative, were accessible for weekly follow-up, and weighed at least 9 kg more than their ideal body weight. Phentermine and fenfluramine were prescribed in combination, at the lowest dose necessary to achieve comfortable appetite suppression.

Results: Weight losses ranged from 4.5 to 22.7 kg, over a 12-week course of treatment, corresponding to 8–65% of excess body weight. Most side-effects were minor, and did not require cessation of treatment. Two patients discontinued treatment due to side-effects which were unacceptable to them.

Conclusion: Phentermine and fenfluramine are a safe and useful adjunct to a comprehensive program of weight management.

Introduction

Drug therapy for obesity has long been a goal in medicine, since the number of people afflicted with the disease is significant. Over the years, pharmaceutical chemists have changed the available drugs, to alter structure-activity relationships, in an effort to maintain effectiveness while decreasing adverse side-effects.

We recently embarked on a major retrospective study of our patients 5–6 years following Gastric Bypass, Roux en-Y (GBPRY) or Bilio-Pancreatic Diversion (BPD), performed for surgical treatment of morbid obesity. As we reviewed our early data, we discovered a subset of patients who maintained their weight loss nicely for several years, and then began to regain weight.

In our practice, patients are introduced to the concept that their surgical procedure creates a 'tool', with which they can manage their weight, by adhering to a comfortable and simple pattern of behavior. Patients who begin to lose control of their weight have ceased to properly use the tool created by surgery. The precipitating factors are generally major life stresses such as job loss, marital changes, or death in the family. We sought a way to help these patients over these hurdles, and to assist them to attain and maintain their target weight. Phentermine (Ionamine®, Fastin®) and fenfluramine (Ponderal®, Pondimin®) have been reported to support prolonged weight management, when used in combination.[1] We chose to explore the adjunctive use of these drugs in post-surgical patients, and to assess their safety, when used in a comprehensive weight management program.

Methods

Eligible subjects were at least 18 months post-operative, accessible for weekly, prospective follow-up, and were 9 or more kg above their ideal body weight, as determined from standard actuarial tables.

Therapy was supervised by two bariatric surgeons, and managed by a registered nurse practitioner, who has herself undergone gastric bypass. Each patient was interviewed, the medical and

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dietary history was reviewed, and physical examination was performed. The informed consent process included a printed information pamphlet, as well as individual counselling regarding the known effects, risks and side-effects of the drugs. Safety issues relative to post-surgical use were specifically discussed. Patient comprehension was confirmed by a pre-treatment true-false examination. Patients were evaluated weekly by the nurse practitioner, including a screening questionnaire for side-effects, and a 1-week supply of medication was dispensed at each visit, to encourage compliance with follow-up.

Treatment was instituted at minimal dosage levels, since the absorption and effects of the drugs are not known in this group of patients. According to their history, patients were placed into one of three dietary categories; overeaters, snackers or sweets-eaters. These dietary challenges were treated differently, based upon expected and observed differences in the effects of the drug. Overeaters were initially treated with phentermine 15 mg in mid to late morning. Sweet-eaters generally were begun on phentermine 15 mg late morning and fenfluramine 20 mg at night. Snackers were started on either drug, independently or both together, depending on their temporal pattern of disordered eating. Patients who 'graze' throughout the day require broader medication support, while those with a specific time to lapse into snacking may be treated with timely dosing. Hypertensive or cardiac patients were preferentially treated with fenfluramine alone.

Close follow-up was maintained prospectively, on a weekly basis, to provide close surveillance for adverse side-effects, and maximum support for behavioral change and dietary compliance. The entire regimen of post-surgical instructions and behavioral changes were re-emphasized to each patient, in an effort to renew successful use of their 'tool':

1. Eat 2–3 meals daily, and consume a protein portion at the beginning of each meal.
2. No between meal snacking (no caloric intake between meals).
3. At least 64 oz of water intake daily.
4. A minimum of 30 min of aerobic exercise at least 3 times weekly.

Drug dosages were evaluated on a week-to-week basis, based upon variables such as weight change, side-effects, blood pressure, negative answers on questionnaires, and the patient's feeling of satiety on the currently prescribed drugs and dosages. Our goal was to maintain the patient on the fewest drugs at the lowest doses and still provide an adequate weight loss pattern.

Results

Thirty-six patients met the criteria for the study, and two did not complete the regimen. Of those completing the study, two were males and 32 were females, with age ranging from 27 to 65 years of age. Twenty-two (60%) had undergone BPD and 12 (40%) had undergone GBPRY. Body Mass Index (BMI) ranged from 27–50 $kg\,m^{-2}$, with median 38 $kg\,m^{-2}$ and mean 34 $kg\,m^{-2}$. Excess body weight ranged from 14.5 kg to 59.1 kg above ideal body weight, as determined from standard actuarial tables.

Weight loss ranged from 4.5 kg to 22.7 kg and from 8 to 65% of excess body weight at 12 weeks. BMI post-treatment ranged from 24 to 44 $kg\,m^{-2}$, with median 35 $kg\,m^{-2}$ and mean of 31 $kg\,m^{-2}$.

Table 1 shows the mean weight lost for the study period at 4-week increments, for BPD and GBPRY.

Table 2 shows mean percentage weight loss, as percentage of Excess Body Weight, for all patients. Weight loss between BPD and GBPRY groups was not significantly different. One patient demonstrated weight loss significantly less than the mean. Table 3 shows weight loss results, excluding this outlier.

Patients consistently reported subjective suppression of appetite and food craving. Side-effects included constipation, dry mouth, and sleep disturbances the latter is usually improved after 2–3

Table 1. Average weight lost at 4-week intervals

Week	BPD (kg)	GB (kg)
4	6.8	5.5
8	9.5	8.8
12	11.8	11.4
20	20.5	16.8

Table 2. Per cent excess body weight lost at 4-week intervals

Weeks	No. of patients	Excess lost (%)	Range (%)
4	34	21	2–39
8	29	29	5–65
12	20	34	8–65

Table 3. Per cent excess body weight lost/time (minus outlier)

Weeks	No. of patients	Excess lost (%)	Range (%)
4	33	22	8–39
8	28	30	14–65
12	19	35	15–65

weeks of constant dosage of phentermine. Memory loss was observed in several patients, and was reversed when medication was completed and discontinued.

Two persons ceased treatment due to unacceptable side-effects: one demonstrated significant memory loss, attributed to fenfluramine, and the other developed a rash on fenfluramine.

Discussion

Every bariatric surgical procedure produces powerful changes in physiology, control of eating behaviour, and nutrition. Yet every procedure has its failures, in terms of patients who either do not reach their weight loss goals, or who experience loss of weight control, even several years after surgical treatment. We sought safe and effective methods of enhancing and restoring weight loss for this unfortunate group of patients, and evaluated adjunctive use of appetite suppressant medications in the context of an intensive follow-up program.

GBPRY produces a major restriction of food intake, and is associated with the rapid onset of profound satiety, which usually lasts for several hours. Our post-operative instructions endeavor to take advantage of that physiology, to minimize caloric intake. Patients are instructed to eat protein first, both to ensure adequate intake, and because protein seems to rapidly stimulate the sense of satiety. They are encouraged to eat slowly and to chew food thoroughly, to provide time for the satiety response to occur.

Snacking is typically due to impulsive behaviour, not to physical hunger, and is forbidden. Water intake reinforces the sense of satiety, especially when taken between meals, in lieu of caloric intake. Exercise is considered essential, both to preserve muscle mass during caloric restriction, and to improve physical conditioning.

Typically, a GBPRY patient who has lost control of her weight will confirm that she can still eat only a small portion at mealtime. Weight gain is overwhelmingly associated with snacking, often initiated as an impulsive behavior, which rapidly progresses to systematic or compulsive snacking. For many patients, increased stress or a life crisis precipitates a return to old eating habits and patterns. In some instances, misguided family physicians have prescribed a regimen of six meals daily, 'to improve nutrition'. Restoration of control requires resumption of a more productive behavior pattern, for which suppression of hunger can be a valuable adjunct.

BPD alters absorption, particularly of fats and starches. Although these patients have more dietary freedom, they must still restrict intake of sugars, and will suffer uncomfortable steatorrhea if fat intake is excessive. Loss of weight control is usually associated with high sugar intake. Our BPD patients are instructed in a dietary and behavior regimen similar to that described above, for GBPRY. Their portion size will be larger, and they experience less satiety response.

A BPD patient who gains weight has often begun snacking frequently, and usually has developed a large intake of simple sugars. Often such patients will manifest pathological degrees of denial, emphatically denying sugar intake, or excessive fat intake, even as they complain of weight gain.

Patients fail to maintain follow-up for many reasons, one of which is shame over weight gain itself. We believe that major life stresses act to 'force' people back into old, and sometimes self-destructive patterns. Our early results indicate that there is a marked beneficial effect from anorectic drugs for our bariatric surgical patients, when used in a comprehensive weight management program.

We believe that person-centered and empathic management enables patients to accept the need for continuing assistance in weight management, to trust in the information given to them, and to participate in the process of modifying behavior. Regular, weekly follow-up provides the necessary support to establish new eating and behavior patterns, while the medications provide the power. The medications are generally well-tolerated. When doses were kept to the minimum needed to produce suppression of appetite, no major ill effects were observed in those patients completing the course of treatment. Occasional patients will find the drug effects unacceptable.

Morbid obesity is a chronic, irreversible illness. While surgery provides the essential foundation for successful treatment, lifelong weight

management may require adjunctive modalities. Post-surgical patients who have inadequate weight loss, or who are experiencing a loss of weight control, can safely achieve additional benefits, even several years following surgical treatment, from an intensive weight management program involving adjunctive use of appetite suppressant medications.

References

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