The multimodal treatment of eating disorders

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The treatment of eating disorders is based on a multimodal model, recognizing that these disorders do not have a single cause or a predictable course. The treatment strategy is determined by the severity of illness and the specific eating disorder diagnosis. For the treatment of anorexia nervosa, the key elements are medical management, behavioral therapy, cognitive therapy and family therapy, while pharmacotherapy is at best an adjunct to other therapies. In bulimia nervosa, the treatment of choice is cognitive-behavioral therapy, but a greater improvement in mood and anxiety occurs when antidepressant therapy is added. In binge eating disorder, cognitive-behavioral therapy and interpersonal therapy produce substantial and long-lasting changes and pharmacological treatment has often a useful role.

**Key words:** Eating disorders, multimodal treatment, cognitive-behavioral therapy, pharmacotherapy, nutritional rehabilitation

The treatment of eating disorders is based on a multimodal model. This model recognizes that eating disorders do not have a single cause or a predictable course. They begin with dieting or restrained eating behavior. Often the dieting is for the purpose of becoming thinner and more attractive, or it may follow a severe stress or physical illness. Behaviors and influences antecedent to the dieting experience can be categorized as problems of biological vulnerability, psychological predispositions, family disturbances, and environmental-societal influences. The integrated effect of these disturbances on dieting behavior propels the individual person into developing an eating disorder. As the dieting continues, starvation effects, weight loss, nutritional effects, and psychological changes occur. A sustaining cycle of core dysfunctional eating behaviors develops with both psychological and physiological reinforcement.

For the anorexia nervosa patient, psychological reinforcement occurs as the patient develops a sense of security and effectiveness while she realizes that dieting and losing weight is something she can control very well with consummate skill. Physiological changes in the dopaminergic, serotonergic and opioid neurotransmitter systems most likely aid in reinforcing the starvation behavior. For bulimia nervosa, the psychological reinforcement comes about when the patient realizes that binge eating can alleviate anxiety in a manner similar to alcohol or drugs. During the process of self-induced purging, dopamine is released in the brain and likely contributes to the physiological reinforcement of the binge/purge behavior.

**RISK FACTORS**

There are several different categories of risk factors for developing eating disorders. Familial risk factors have been demonstrated with family studies. If one has a family member or relative with anorexia nervosa, bulimia nervosa or obesity, then one has a greater chance of developing an eating disorder (1). Also, if one has a family member or relative with depression or alcohol/drug abuse/dependence, one is at a greater risk for developing an eating disorder. Individual biological factors include being mildly overweight or having an early menarche (2).

Genetic studies have shown a significant linkage on chromosome 1 for restricting anorexia nervosa (3) and a significant linkage on chromosome 10 for bulimia nervosa (4). There have been no consistent and replicated findings for polymorphisms of specific genes with association studies. Possible genetic vulnerabilities include a predisposition to a particular personality type, predisposition to a psychiatric disorder (affective or anxiety disorders) or predisposition to neurotransmitter dysfunction. Thus, a genetic predisposition and vulnerability may become manifest under adverse conditions such as inappropriate dieting or emotional stress.

Biological vulnerability can include dysfunction of neurotransmitters such as serotonin, dopamine and norepinephrine that regulate eating behavior. Studies have shown that all three of these neurotransmitters are dysfunctional in eating disorder patients (5-7). Aberrations of neuropeptides regulating eating behavior are also present in eating disorders. Such changes are present in neuropeptide Y, opioids, leptin, cholecystokinin, ghrelin, melanocortins, adiponectin, agouti-related protein, and brain derived neurotrophic factor (8).

Signals from the periphery, including gut-related peptides and adipokines, interact with hypothalamic peptides in the regulation of feeding behavior and body weight. State related changes in nutrition and body weight influence cerebrospinal fluid and plasma levels and receptor activity of neuropeptides (9).

Individual psychological risk factors include a perfectionistic-obsessional personality, which is a risk especially for the restricting type of anorexia nervosa (10). Low self-esteem and a sense of ineffectiveness, lack of confidence and a feeling of inadequacy are risk factors for anorexia nervosa and bulimia nervosa (11). Affective disorders (depression), alcohol and drug abuse are risk factors especially for bulimia nervosa (12).

Individual behavior such as dieting or involvement in activities or professions that emphasize weight control –
TREATMENT

Both the severity of illness and the specific diagnosis will determine the treatment strategy for an eating disorder. Guidelines have been developed for the treatment of different degrees of severity of illness and are established from hospitalization to day programs to intensive outpatient therapy to group therapy (16). There are no randomized controlled trials that adequately assess the intensity of treatment. The major categories of eating disorders are anorexia nervosa, bulimia nervosa and binge eating disorder. Variations of these disorders are treated similarly to the major diagnostic category which they approximate.

There are three reviews of new treatment research in eating disorders with critical analyses. These include the Cochrane reviews (17), the Australian and New Zealand practice guidelines for the treatment of anorexia nervosa (18) and the guidelines for treatment of eating disorders by the National Institute for Clinical Excellence in London (19).

Treatment of anorexia nervosa

For treatment of anorexia nervosa, the key elements are medical management, behavioral therapy, cognitive therapy and family therapy. Pharmacotherapy is at best an adjunct to the other therapies in this disorder. Nutritional rehabilitation and weight restoration are essential. Behavioral therapy is useful in managing weight gain and prevention of binge eating and purging. Cognitive therapy addresses the distorted cognitions of feeling fat, evaluating self-worth solely by body image and the pervasive sense of ineffectiveness and inadequacy. Family therapy is especially effective for children under the age of 18. Fluoxetine may prevent relapse in patients who have obtained at least 85% of a normal weight. Atypical antipsychotics may be useful in reducing severe anxiety and augmenting weight gain (20).

Nutritional rehabilitation programs usually employ emotional nurturance and a variety of behavioral interventions, which involve a combination of reinforcers that link exercise, bed rest, and privileges to target weight, desired behaviors and informational feedback. There are no randomized controlled trials to demonstrate the superiority of nasal gastric tube feeding over oral feeding in nutritional rehabilitation. Advocates claim that such intervention may hasten weight gain without deleterious effects. Supplemental nocturnal nasal gastric refeeding has been used for better short-term outcome in hospitalized adolescent girls with anorexia nervosa. Other centers have used voluntary nasal gastric tube feeding and have taught patients how to insert their own tube. Adequate controlled trials have not been conducted for this type of intervention.

For individual psychosocial interventions, there continues to be difficulty in recruiting and retaining patients. At least a one-third dropout rate or withdrawal due to relapse complicate the interpretation of randomized controlled trials (21). There is some indication that cognitive-behavioral therapy following weight gain may reduce the risk of relapse (22).

Family therapy is the most effective treatment for adolescents with anorexia nervosa and seems to be equally effective when administered as conjoint or as separated family therapy (23). Overall, 6 months of therapy also seems to be as effective as 12 months; however, patients with severe obsessive-compulsive disorder may require longer treatment (24). There is little formal study of the efficacy of group psychotherapy for the treatment of anorexia nervosa or the usefulness of support groups for this disorder.

Two core assumptions are made about anorexia nervosa in cognitive therapy. First, food avoidance, necessary to maintain a low weight, is essentially a food phobia. Second, anorexia nervosa serves a positive function: it provides an escape from aversive developmental issues and distressing life events often of an interpersonal nature.

One element in cognitive therapy is cognitive restructuring. In this approach the patient must identify specific negative thoughts, list the evidence for these thoughts, list the evidence against the thoughts, form a reasoned conclusion and use the reasoned conclusion to guide her behavior. Another element in cognitive therapy is problem-solving. In this procedure the patient identifies a specific problem, develops different strategies, considers the likely effectiveness and feasibility of each strategy to deal with the problem, selects the best strategy, defines the steps to carry out the strategy, carries out the chosen strategy and then evaluates the entire problem-solving process in light of the outcome. Another essential element in cognitive therapy is monitoring. For this the patients must make daily records of food intake, including the type of food ingested, the time of ingestion and the environment where the ingestion occurred. Monitoring also includes daily records of binge/purge behavior, exercise, mood and interpersonal difficulties (25).

Pharmacotherapy of anorexia nervosa is limited. Cyproheptadine facilitates weight gain in restrictive anorexia nervosa and has an antidepressant effect. Chlorpromazine or olanzapine may reduce severely obsessional, compulsive and agitated behavior; a side effect is weight gain. Fluoxetine may reduce relapse of weight and eating disorder behaviors in weight restored patients. There are few new randomized controlled trials of pharmacotherapy for anorexia nervosa. These trials have
shown fluoxetine in a dose of 60 mg/day adds no benefit to inpatient treatment of underweight anorexia nervosa patients. Another trial of 35 anorexia nervosa patients that were partially weight restored showed some indication that fluoxetine during weight maintenance may decrease the relapse rate (26). A third trial, which compared three drugs, clomipramine, fluoxetine and amisulpride, in inpatients showed that amisulpride had the best effect on weight gain (27).

From the recent promising pilot studies of psychopharmacotherapy in anorexia nervosa we can conclude that antipsychotic medications such as olanzapine and quetiapine may be helpful during the weight restoration phase. Citalopram may reduce depression and anxiety during weight restoration. Fluoxetine is not beneficial in weight restoration but may decrease relapse rate in anorexia nervosa patients. Nutritional supplements with L-tryptophan do not increase effectiveness of fluoxetine (28).

There are many problems with these treatment studies of anorexia nervosa. First, there are very few randomized controlled trials. Second, patients are not motivated for treatment. This is evident in that patients do not enter trials and dropout rates are high. Third, medical complications often require withdrawal from trials. Fourth, very small sample sizes are present in completed trials.

Treatment of bulimia nervosa

The treatment of bulimia nervosa has several key elements. Cognitive-behavioral therapy, which can be conducted as individual or in group format, has a psychoeducational component and requires self-monitoring. Other techniques are cognitive restructuring, problem-solving and cost benefit analyses. Behavioral therapy in the treatment of bulimia nervosa is usually in conjunction with cognitive therapy. In this form of treatment, restricting exposures to cues is common as well as developing alternative behaviors with response prevention techniques to stop vomiting. Interpersonal therapy focuses on interpersonal relationships and classifies the type of interpersonal problem. Pharmacotherapy has shown best results with selective serotonin reuptake inhibitor drugs, which reduce binger/purge behavior. These are preferred because of the lower side effect profile. Tricyclic antidepressants also reduce binger/purge behavior but have greater side effects.

In contrast to anorexia nervosa, treatment studies of bulimia nervosa have proliferated in the past 15 years. Controlled studies of specific therapy techniques such as behavioral therapy, cognitive therapy, psychodynamic therapy and psychoeducation therapy have been conducted in both individual and group therapy format. Multiple controlled drug treatment studies have also been conducted. Often a variety of therapy techniques are used together in either individual or group therapies. There is no way at present to predict which bulimic patient will respond to what type of treatment.

Cognitive-behavioral therapy is the first choice treatment for bulimia nervosa. It was the most effective treatment in 35 controlled studies, which showed 40 to 50% of patients abstinent from binging and purging at the end of treatment (16-20 weeks). Reduction in binging and purging occurred in 70 to 95% of patients. Thirty percent with no improvement post-treatment showed improvement to full recovery one year after treatment (29).

There is some evidence that treatment programs which include dietary counseling and managing are more effective than those that do not. The nutritional rehabilitation in bulimia nervosa involves establishing patterns of regular, non-binge meals. Increasing caloric intake and expanding macronutrient selection in meals is also important. This will likely correct any nutritional deficiencies that may be present.

Another psychotherapy shown to have some effect in treating bulimia nervosa is interpersonal therapy. Focus psychodynamic psychotherapy was not as effective as cognitive-behavioral therapy in short term trials. Behavior therapy with exposure and response prevention had no additive benefits over cognitive-behavioral therapy. A meta-analysis of 40 group psychotherapy treatment studies suggested moderate efficacy. Groups that included dietary counseling were more effective, as were groups with more frequent visits during treatment. Many clinicians favor a combination of individual and group therapy in the treatment of bulimia nervosa (30).

There are no randomized controlled trials of family therapy in the treatment of bulimia nervosa: it may be considered for adolescents. Self-help manuals and guided self-help manuals use cognitive-behavioral techniques: there are limited trials with varying results; more development of these self-help manuals and larger studies are needed. Dialectical behavioral therapy focuses on training in emotional regulation skills: one study showed significant improvement compared to a waiting list (31).

A summary of pharmacotherapy in bulimia nervosa concludes that all antidepressants are better than placebo for reducing binge eating. Over a dozen double-blind placebo controlled trials of antidepressants have been conducted with a dosage similar to the treatment of depression. Medications improved mood and preoccupation with shape and weight in about 20% of patients. Complete abstinence from binging and purging, however, occurred in only 20 to 30%. Some medications that have been effective in reducing binge frequency should not be used in treating bulimics because of their side effects. Bupropion has been associated with convulsions in bulimic patients. Trazodone has been associated with producing delirium in a few bulimic patients. The monoamine oxidase inhibitors can cause hypertensive crises if bulimic patients do not follow the required restricted diet (32).

Fluoxetine in a dose of 60 mg/day is the drug of first choice because of beneficial effects and a favorable side effect profile. If the first trial is unsuccessful there is evi-
dence that another antidepressant trial may be effective. Minimal duration of successful treatment should be 6 months. Baseline laboratory assessments such as cell blood count, serum electrolytes, liver function tests, blood urea nitrogen/creatinine ratio, thyroid function and electrocardiogram should be obtained.

Ondansetron, a 5HT3 antagonist, decreases afferent vagal activity and has been shown to have a mild effect on reducing binge/purge behaviors in bulimic patients. However this drug has serious side effects of constipation, headaches and abdominal pain. Topiramate has been shown to effectively reduce binge/purge behavior in a double-blind placebo-controlled trial in bulimia nervosa patients: this medication must be initiated in a very low dose of 25 mg/day and gradually increased with a maximum of 400 mg/day. A slow increase of dosage will help prevent side effects of fatigue, paresthesia, difficulty concentrating, and influenza-like symptoms. The opiate antagonist naltrexone, in a dose of 200-300 mg/day, has been shown to reduce binge/purge behavior. However, there is a concern of liver toxicity at this dosage (33).

Three randomized controlled studies comparing cognitive-behavioral therapy and pharmacotherapy showed that the combination was superior to medication alone. One study showed that the combination was superior to cognitive-behavioral therapy alone, while the other two studies did not show this (34).

In conclusion, the treatment of bulimia nervosa can be summarized by stating that binge eating, purging, and core eating disorder attitudes respond best to cognitive-behavioral therapy. A greater improvement in mood and anxiety occurred when antidepressant therapy was added.

Treatment of binge eating disorder

Binge eating disorder is still considered in the category of eating disorders not otherwise specified. This disorder is distinguished from bulimia nervosa by a lack of compensatory behaviors to counteract the caloric intake and weight gain from binge eating episodes. These patients do not purge, exercise or engage in dieting. Randomized controlled treatment trials have used the same techniques as those for bulimia nervosa. Patients with binge eating disorder have responded well to cognitive behavioral therapy and antidepressants that have been effective in treating bulimia nervosa (35).

A summary of psychotherapy treatment research for binge eating disorder is as follows. Cognitive-behavioral therapy and interpersonal therapy produce substantial and long lasting changes in the specific and general psychopathology of binge eating disorder. Cessation of binge eating is associated with weight loss and maintenance of this loss over a 1 year period. Double-blind placebo controlled trials of antidepressants have shown that desipramine, fluvoxamine, fluoxetine, sertraline and citalopram all reduce binge eating and are associated with weight loss in the treatment of binge eating disorder. Other drugs shown superior to placebo for binge eating disorder are phenytoin and topiramate. There is one open study for zonisamide. Pharmacological treatment should be considered as an option in all cases of binge eating disorder, not just those with concomitant mood disorders. It should be considered strongly in those who fail to respond to psychological treatment. One should consider trials of topiramate, a selective serotonin reuptake inhibitor, sibutramine, venlafaxine, bupropion (no purging or history of bulimia nervosa or anorexia nervosa) and zonisamide. Be prepared if necessary to conduct a minimum of three trials to obtain an optimal response. Choose medication based on patient comorbidity and preference in side effect profile. Use doses similar to those for approved indications. Treat for a duration similar to that for bulimia nervosa or major depressive disorder: for example, 6 to 12 months at a level of substantial improvement before attempting discontinuation of the drug. In some cases treatment may need to be continued indefinitely (36).

CONCLUSIONS

In conclusion, the treatment of eating disorders is based on a multimodal approach. Patients need to be treated with a multidisciplinary team, including a psychiatrist for pharmacotherapy and psychotherapy, a nutritionist for nutritional education and meal planning, an internist or pediatrician for medical care and a family therapist for children under the age of 18.

For the treatment of anorexia nervosa, the key elements are medical management, behavioral therapy, cognitive therapy and family therapy, while pharmacotherapy is at best an adjunct to other therapies. In bulimia nervosa, the treatment of choice is cognitive-behavioral therapy, but a greater improvement in mood and anxiety occurs when antidepressant therapy is added. In binge eating disorder, cognitive-behavioral therapy and interpersonal therapy produce substantial and long-lasting changes and pharmacological treatment has often a useful role.

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