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Chapter 3

AN UPDATE ON TREATMENT STRATEGIES FOR BULIMIA NERVOSA

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Abstract

Objective: The purpose of this article is to provide an overview of the treatment literature on bulimia nervosa. The available published literature in this area was reviewed.

Method: Following computer searches the psychotherapy and pharmacotherapy literature were reviewed in detail.

Results: Psychotherapy remains the cornerstone of treatment for most patients with bulimia nervosa. The most intensively studied form has been cognitive behavioral therapy, although there are also data supporting the use of interpersonal psychotherapy, dialectic behavior therapy and family-based treatments for adolescents with bulimia nervosa. There is also a growing literature on the utility of self-help approaches. Two recently introduced therapies, which are currently being studied, include enhanced cognitive behavioral therapy and integrative cognitive-affective therapy. Relative to pharmacotherapy approaches, antidepressants remain the best studied form of drug therapy, focusing on the use of the serotonin reuptake inhibitors. Other medications which have been tried empirically include ondansetron and topiramate.

Discussion: The treatment of bulimia nervosa has evolved to the point where both psychotherapy and pharmacotherapy approaches appear to be affective. Overall remission rates appear to be higher with empirically supported manual-based psychotherapy approaches, although many patients have benefited from drug therapy as well.

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INTRODUCTION

A substantial treatment literature has developed regarding individuals with bulimia nervosa (BN) over the last 30 years. These treatments clearly impact on the course of this disorder, although further treatment development is needed.

In deciding on the proper treatment approach the goal is to provide the patient with the support and structure necessary for her to start eating regularly balanced meals and to cease binge eating and engaging in compensatory behaviors. Usually this can be accomplished effectively in outpatient treatment settings, but for some patients a more intensive setting, such as a partial hospital program or an inpatient stay may be necessary, particularly for patients who have co-occurring severe psychopathology or for those who fail to respond to outpatient care. Suicidality is the most common reason for such an increased level of care.

PSYCHOTHERAPY

Psychotherapy remains the cornerstone of treatment for most patients with BN. Unfortunately, the forms of treatment which have been shown to be effective have not been widely disseminated to the practice community, and many patients who are seen for treatment with eating disorders receive treatments that are not empirically validated (1). In considering psychotherapy certain general principles apply. First, both group and individual approaches are applicable. Second, there is evidence that more intensive treatment early on, such as seeing patients multiple times during the first few weeks of treatment, are helpful in achieving treatment success, eventually resulting in higher rates of abstinence (2).

Relative to specific techniques a variety of approaches have been studied. The one most intensively studied has been cognitive behavioral therapy (CBT). There are also data supporting the use of interpersonal psychotherapy (IPT), dialectic behavior therapy (DBT), and family based treatments for adolescents with BN. Recently there has been interest in a new generation of CBT-oriented approaches including enhanced CBT (CBT-E) developed by Fairburn and colleagues and integrative cognitive-affective therapy (ICAT) developed by Wonderlich and colleagues (3-6).

COGNITIVE BEHAVIORAL THERAPY

This therapy has been used in a variety of controlled trials and appears to be more effective than most treatments (with the possible exception of IPT), or waiting list controls (3,7).

Probably the leading evidence-based treatment for those with BN is a specific form of CBT developed for these patients (8). This therapy posits that low self-esteem enhances extreme concerns about weight and shape, which results in strict dieting, which then leads to binge eating and self-induced vomiting as a compensatory technique. This therapy is basically designed for those in a normal weight range. It focuses on the need to reduce dietary restraint and to address concerns about shape and weight. Emphasis early on is placed on the use of

food logs as a self-monitoring approach, which are reviewed with the therapist each session. Patients are also asked to engage in only weekly weighing.

In the first phase there is an emphasis on educating patients about medical complications, stressing the ineffectiveness of vomiting and laxatives as methods of weight control, and education about the biology of weight and shape. Also three forms of dieting are discussed: 1) avoiding eating for long periods of time; 2) avoiding certain types of food and, 3) restricting total amount of food eaten. In the first phase various behavioral techniques are used including the prescription of regular eating patterns, the use of alternative behaviors, stimulus control techniques and psychoeducation of laxatives and diuretics.

In the second phase of treatment emphasis is placed on cognitive restructuring, systematic problem solving and the reintroduction of "forbidden" foods as well as continued work to reduced body image disparagement. The third phase focuses on relapse prevention strategies.

This therapy is generally administered in a treatment "package" wherein patients are seen twice a week for the first four weeks and then once a week thereafter for a total of 20 visits. The empirical literature supporting the efficacy of this approach is substantial.

INTERPERSONAL THERAPY

Interpersonal therapy (IPT) was originally developed as a treatment for depression by Klerman and colleagues (9). In the late 1980's this approach was modified for patients with BN. Wilfley and colleagues (10,11) developed a group format for IPT and demonstrated that it was an effective treatment for patients with BED. It has also been shown to be an effective treatment for patients with BN (7).

The theoretical model for IPT posits that interpersonal functioning is a critical component of psychological adjustment. The interpersonal roles of particular interest for IPT therapists involve the family as well as friends, and fellow workers and those in the neighborhood and community.

IPT for those with BN is again time limited and attempts to link interpersonal relationships to eating disorder symptoms. Four social domains can be addressed in the treatment: 1) interpersonal deficits, 2) role transitions, 3) interpersonal role disputes, and 4) grief. Generally one or at most two of these areas become the focus for treatment. IPT is generally delivered in 15-20 sessions or 4-5 months and includes three phases. In the initial phase, problem areas are identified; in the subsequent phase therapist and patient work on the target problems and in the final phase gains are consolidated and patients are prepared to do future work on their own.

A critical part of IPT is the interpersonal inventory which involves a thorough examination of each individual's interpersonal history. This includes an examination of relationships, social functioning, expectations of relationships and other interpersonal issues. This then leads to the interpersonal formulation which includes the identification of the primary areas of focus. The therapist presents a written version of this formulation to the patient and this is frequently referred to later in therapy. The therapy includes the encouragement of affect. IPT places considerable importance on establishing a strong positive

therapeutic relationship with the patient. The therapy is goal directed. There is an ongoing need to draw connections between eating difficulties and interpersonal events.

DIALECTICAL BEHAVIOR THERAPY

DBT is a specialized form of CBT. It was originally developed to treat women with extreme emotion dysregulation, such as those with borderline personality disorder (12,13). This is skill-based approach that integrates dialectical philosophy derived from Zen that includes mindfulness skills and behavioral principles. It has now been adopted for use with patients with eating disorder and therefore may be particularly useful for patients with eating disorders who have comorbid personality disorders, a not uncommon pattern (14).

Two small non-randomized trials treating individuals with borderline personality disorder and eating disorders utilized the standard DBT (15,16). However, a form of DBT has been adapted specifically for patients with eating disorders, developed at Stanford University (17). Subsequently there has been one randomized trial in BN (17). In this study a wait list control was used as a comparison group. The results indicated higher rates of abstinence from binge eating and purging at the end of 20 weeks of treatment in the active treatment group (28.6%) versus the weight list control (0%).

In general DBT focuses on several issues, including self-acceptance, dialectic strategies, stylistic strategies, core strategies and case management strategies. Dialectical strategies focus on dichotomous thinking and behaviors and emotions. These may include the use of stories and metaphors. Stylistic strategies attempt to balance acceptance and the need for change. The therapist must convey interpersonal warmth and concern. Core strategies are those designed to promote acceptance and behavioral change and includes such things as an examination of antecedents and consequences and behavioral chain analysis. Case management strategies include teaching a patient to more effectively interact with the environment. Specific adaptations for patients with BN include a focus on decreasing mindless eating and food preoccupation, and capitulating or giving up to ones emotions and then binge eating. The model includes both individual and group sessions and includes an emphasis on distress tolerance, emotion regulation skills and relapse prevention.

FAMILY-BASED TREATMENT FOR ADOLESCENTS WITH BULIMIA NERVOSA

In contrast to the substantial literature on the treatment of adults with BN very little research has focused on the treatment of adolescents with BN. Only two randomized controlled trials have been published both using a family-based therapy for BN (18,19). In the first of these studies le Grange and colleagues assigned 80 patients with full or subsyndromal BN, ages 12-19, to family-based therapy for BN or to individual supportive psychotherapy. Both groups received 20 therapy sessions over 6 months. The family-based approach had a clinically and statistically significant advantage over the comparison group at the end of treatment and at six-month follow-up, with more patients abstinent from binge eating and purging (39% vs. 18%) at end-of-treatment. In the other randomized controlled trial family-

based therapy was compared to cognitive behavioral guided self-help. Subjects were age 12-20. Significantly more people in the CBT guided self-help group were abstinent from binge eating at post-treatment although there were no differences at six-month follow-up.

The theoretical underpinnings of family-based treatment for BN are an adaptation of an approach originally developed for treatment for anorexia nervosa (AN). In this model parents understanding of and the need to help their child are mobilized to promote changes in eating and weight. Since adolescents with BN tend to deny the importance of their symptoms parents are recruited to help move the adolescent toward a healthier adjustment. The approach is symptom focused and includes a strong emphasis on encouraging the parents to not assume a role of guilt. The role of the therapist is to serve as a consultant and educator while leaving decisions up to the parents.

In the first phase of this treatment, emphasis is placed on reestablishing healthy eating patterns. The sessions begin with a brief meeting between the therapist and the patient before meeting with the rest of the family. In the family meeting the therapist directs the discussion so as to strengthen the parental alliance. The family is carefully educated about medical and psychiatric sequellae of BN. Measures are taken to make it clear that the adolescent and the disorder are two separate things. This early part of therapy includes a family meal. This allows the therapist to establish rules around eating. The second phase of treatment focuses on helping the adolescent establish healthy eating behavior on their own, and the third phase of treatment focuses on adolescent issues and termination.

Self-Help for Bulimia Nervosa

The literature in this area has recently been thoroughly reviewed (20-22). The meta-analytic analyses, although hindered by a relatively small number of studies and relatively small sample sizes, suggests that partial self-help or guided self-help approaches do have some utility in the treatment of those with BN, and the follow-up results suggest that gains tend to be maintained. However, there isn't as of yet any firm evidence favoring one approach over another. However, the study by Walsh et al. (23) found that guided self-help provided by nurses did not add to the effectiveness of anti-depressant treatment, and was associated with a high dropout rate. This suggests that specialist care is probably needed for these types of interventions. Much of the development in this area has been motivated by health economic reasons but also problems with the availability of treatment. Clearly more work needs to be done looking at such approaches.

Enhanced Cognitive Behavior Therapy for Bulimia Nervosa

Fairburn and colleagues have modified the traditional CBT for treatment to a transdiagnostic model designed to treat people with a variety of types of eating pathology. The full transdiagnostic treatment has been described in detail (4,5,24). Enhanced CBT or CBT-E posits that eating disorders are essentially cognitive disorders and that the core psychopathology is usually overvaluation of shape and weight, while for a subgroup the core

is to control eating. The approach acknowledges that much diagnostic crossover exists in patients with eating disorder; hence, the needs for a transdiagnostic approach. Early in treatment a formulation is made that is personalized and then revised throughout treatment.

CBT-E is done in two forms, a focused version and a broad version which includes examination of mood intolerance, clinical perfectionism, low care self-esteem and/or interpersonal difficulties.

Therapy is delivered in 20 sessions over 20 weeks with a review session 20 weeks later. It is conducted in four stages. In the first stage patients are seen two times a week for four weeks. Emphasis is placed on engaging the patient, formulating the processes that maintain the disorder, and instituting weekly weighing and regular eating. The second stage is transitional in which progress is reviewed, barriers to change are identified and the formulation may be modified. Stage three is the main body of treatment and includes 8 sessions. Stage 4 is designed to insure that the changes are being maintained.

INTEGRATIVE COGNITIVE-AFFECTIVE THERAPY FOR THE TREATMENT OF BULIMIA NERVOSA

This therapy grew out of the observation that CBT does not sufficiently help many patients with BN. It has been argued that CBT might be improved by maintaining a stronger focus on affective and interpersonal issues (25) and enhancement of treatment techniques by integrating concepts for constructivist theories (26) including narrative strategies (27) utilizing the therapeutic relationship more thoroughly (28) and placing greater emphasis on developmental issues (29). In this model, greater emphasis is placed on self-discrepancy, interpersonal patterns, self-directed styles of behavior and emotional experience. The therapy is delivered in 21 sessions. A clinician manual and a patient workbook have been developed and palm top computers provide part of the therapy.

In terms of clinical principles ICAT attempts to increase awareness of emotional responses, identify situations that frequently illicit prominent emotional responses and to modify action tendencies in the face of situation-emotion units. It is delivered in four phases. The first is characterized by motivation and education, the second by meal planning, the third by a self-directed examination of interpersonal problems and the fourth by relapse prevention and work on termination.

PHARMACOTHERAPY

Considering CBT as the treatment of choice, it is unfortunate that CBT availability may be limited in the community. In a study by Crow and colleagues, (1) in a population of 353 women who were seeking treatment for BN, 65.4% had received previous treatment and of these, 96.7% reported receiving psychotherapy; however, only 6.9% of those reporting having received psychotherapy reported that the therapy included basic elements of CBT. With this in mind pharmacotherapy has been investigated for over twenty years (30).

ANTIDEPRESSANTS

Research over the past twenty years indicates that most antidepressants have efficacy in the treatment of BN (31). Classes of agents that have shown efficacy include the tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs) and selective serotonin reuptake inhibitors (SSRIs). The core agents utilized currently are the SSRIs and one agent (fluoxetine) carries an FDA indication for treatment of BN. Although in most studies there has been a significant advantage for active drug over placebo, the exceptions appear to be moclobemide and fluvoxamine. Responses to antidepressant medication in BN are not dependent upon the existence of a pretreatment depression (32). In a study of BN patients the effect of fluoxetine 60 mg/day was found to not correlate with the baseline Hamilton Depression Rating Scale (HAM-D) score or comorbid depression diagnosis (33).

RESPONSE VERSUS REMISSION

Despite multiple studies showing greater efficacy than placebo (34-36) questions remain as to the extent of antidepressant treatment efficacy. Several trials have not been able to differentiate active drug from placebo on important outcome variables (37,38). Also, despite impressive reductions in the frequency of target symptoms, the percentage of subjects free of symptoms (abstinent) at the end of treatment is also disappointingly low.

The mean abstinence rate associated with pharmacotherapy has been reported to be 24 % (39). In one sequential treatment controlled trial (40) those who did not achieve a 75% reduction in binge eating frequency with desipramine over 8 weeks were switched to fluoxetine. Pharmacological treatment occurred in combination with CBT, supportive psychotherapy or alone. Overall, 74% of eligible patients required the switch to the second pharmacological treatment. Cessation of binge eating behavior was then found in 29% of the medication only subjects by the end of the second treatment period. Studies of the combination of pharmacotherapy and CBT reported average remission rates of 42 to 49% versus average rates of 23 to 36% with any single therapy (24). However, response rates to subsequent therapies for patients who fail initial treatment have been variable. In one study, non-responders to CBT or IPT were given fluoxetine or placebo. The active drug was superior to placebo in improving symptoms (41). In another study of patients in whom CBT had not resulted in remission, the rate of response to subsequent IPT was 16%, and the rate of response to pharmacotherapy (fluoxetine followed by desipramine if indicated) was only 10% (36).

Maintenance studies utilizing pharmacological agents have demonstrated efficacy over placebo (42,43). However these studies have been characterized by high drop-out rates, which make them difficult to interpret. The largest and most recent maintenance trial was reported by Romano and colleagues (44). Subjects were treated in a single blind acute treatment phase, with those meeting response criteria (a minimum of 50% reduction of baseline frequency of vomiting during one of the final 2 weeks of a single blind phase) being randomized to fluoxetine 60 mg/day or placebo. One hundred and fifty patients were randomized to active drug or placebo for a period of one year. However, only 17.7% of the 150 patients were abstinent at the time of randomization. Of the 150 patients who entered the

double blind phase only 19 completed the trial. The total number of patients who relapsed did not differ between groups, although fluoxetine did prolong the time to relapse. Thus, the weight of the evidence suggests that single agent pharmacological treatment does not provide a robust maintenance therapy for BN and patients achieving response but not remission appear to benefit little from maintenance treatment.

There is a strong need to develop new and better pharmacological approaches for these patients. Unfortunately there are no studies to date on the use of medication combinations or augmentation of pharmacological treatments, strategies that have been used with success in several other pharmacotherapy areas including the treatment of depression and anxiety disorders.

The concept of treating to remission has been developed as a focus in the treatment of affective disorders. It has been demonstrated that achieving remission (Hamilton Depression Rating Scale score < 8) versus only response (Hamilton Depression scale reduction of 50 %) is associated with better functioning (45) and prognosis (46,47). Unfortunately, studies which provide data on the outcome of patients who achieve abstinence in BN are few. In general, abstinence persisting at one year of follow up is quite variable (48) and in light of this, no consistent predictors of outcome have been identified (24). Thus an exploration of techniques to enhance symptom reduction is needed. Sequencing medication after failure to respond to CBT has shown mixed evidence. Medication addition was found helpful in a pilot trial by Walsh and colleagues (41). However a subsequent trial by Mitchell, et al. (40) found that after failure of CBT those who were randomized to medication derived little benefit. Yet combinations of medicine are often prescribed in clinical practice without evidence regarding efficacy or tolerability (49).

ONDANSETRON

Non-antidepressants have also been demonstrated to have efficacy in the treatment of those with BN. The serotonin 3 receptor (5-HT3) antagonist, ondansetron, was found to be efficacious in a randomized, double-blind trial (50). This agent is an antiemetic active at the vagus nerve terminals peripherally and at the chemoreceptor trigger zone centrally (51). Ondansetron is used extensively in chemo- and radiation- therapy induced nausea and vomiting. It is suggested that BN patients have satiety defects caused by post-binge eating vagal stimulation. In a four week randomized, double blind trial patients receiving ondansetron 24 mg/day reduced binge-vomit frequency from 12.8 ± 5.0/week to 6.5 ± 3.9/week, an estimated reduction of 6.8 episodes/week ($p < 0.0001$) while the placebo group reduced their mean binge-vomit frequency from 13.4 ± 9.9 to 13.2 ± 11.6 episodes per week.

TOPIRAMATE

Topiramate, an anticonvulsant associated with weight loss, has been explored for BN treatment. Topiramate's multiple pharmacological actions include a reduction of voltage-gated sodium currents, activation of potassium currents, increased postsynaptic GABA-A receptor currents, a reduction in the activation of AMPA-kainate glutamate receptor subtypes,

and weak inhibition of carbonic anhydrase (52). There have been two randomized controlled trials of topiramate for BN treatment published (53,54). In addition, a recent review article summarizes the efficacy and tolerability of topiramate in the treatment of BN and binge eating disorder (55). The controlled trials in BN (53, 54) were both ten-weeks in duration and demonstrated reductions in binge/purge frequency as well as body weight with topiramate relative to placebo. Hoopes and colleagues (53) demonstrated that at a median topiramate dose of 100 mg/day (range 25-400 mg/day), binge and/or purge days were significantly reduced (44.8%) relative to the reduction observed with placebo (10.7%). Body weight also differed significantly between groups; with a 1.8 kg mean weight loss in the topiramate group compared with a 0.2 kg increase in the placebo group. Similarly, Nickel and colleagues (54) found that binge/purge frequency decreased by 3.3 episodes per week with topiramate (titrated to 250 mg/day) relative to placebo. The topiramate group in this study experienced significantly more weight loss (4 kg) compared to the placebo group (0.3 kg). Treatment-emergent adverse effects in the study by Hoopes and colleagues were reported more frequently with topiramate versus placebo. Effects reported by at least 10% of patients, included the following: fatigue, influenza-like symptoms, paresthesia, hypoesthesia, nausea, constipation, difficulty with concentration or attention, and nervousness. Study attrition due to adverse events was low, however, including only one of 34 patients in the topiramate group who experienced nausea. The study by Nickel and colleagues (54) reported headache as the only adverse effect which occurred more frequently with topiramate than with placebo, but the dosage used was not stipulated.

MISCELLANEOUS MEDICATIONS

Other treatments that have been studied include the androgen-antagonist flutamide, spironolactone, d-fenfluramine (no longer marketed), lithium, phenytoin and naltrexone, but none have evidenced clear efficacy, and none are commonly clinically employed in the treatment of those with BN at this time (56,57).

FUTURE PHARMACOTHERAPY RESEARCH

The first phase of investigation of pharmacotherapy for the treatment of BN has been completed. A variety of drugs have demonstrated benefit over placebo. However, the outcome for BN patients at this time is not optimal. It is time to embark on the second phase of pharmacotherapy investigation with BN. A next step in this search is exploring the augmentation of primary pharmacotherapy with secondary agents. Investigations to explore the efficacy of selected secondary agents can determine if symptom reduction is achievable after partial efficacy has been seen with the primary agent. This type of research is vital to explore the “next level” of pharmacotherapy.

SUMMARY

Both psychotherapy and pharmacotherapy approaches appear to be useful in the treatment of patients with bulimia nervosa. Established forms of psychotherapy include cognitive behavioral therapy, which has been the form most intensively studied, dialectical behavioral therapy, interpersonal therapy and, two recently introduced approaches, enhanced cognitive behavioral therapy and integrative cognitive-affective therapy. Pharmacotherapy approaches have relied primarily on the use of antidepressant drugs, particularly the serotonin reuptake inhibitors. The only FDA approved drug for the treatment of bulimia nervosa remains fluoxetine hydrochloride although a number of other agents are also effective. Ondansetron and topiramate have also been studied in placebo-controlled trials.

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