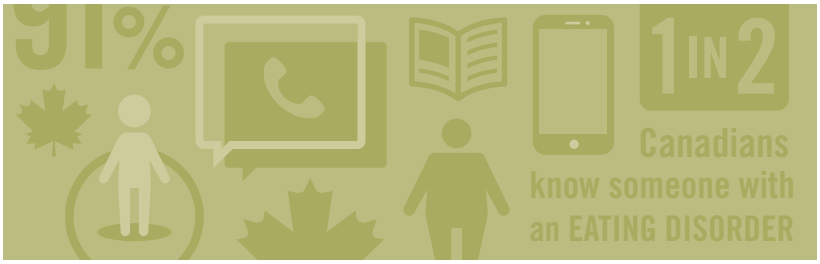
National Eating Disorder Information Centre

BULLETIN



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Pharmacological Treatment of Eating Disorders

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Eating disorders, which often develop in adolescence, can be highly debilitating and become chronic. They are traditionally treated with nutritional rehabilitation and behavioural management/psychotherapy within a multimodal context (psychiatrists, psychologists, dietitians, social workers, etc.). However, patients often wonder: *can medication help?* In general, eating disorders have not been found to be as responsive to medication as other mental health disorders. There is limited evidence for the efficacy of medication in the treatment of eating disorders; however, it may be useful for the management of comorbid conditions, e.g., depression and anxiety. This article highlights current evidence for pharmacological options for the treatment of anorexia nervosa (AN), bulimia nervosa (BN), and binge eating disorder (BED).

ANOREXIA NERVOSA (AN)

There are only a few pharmacological studies in patients with AN. Because the neurobiological mechanisms underlying AN are largely unknown, many pharmacological approaches have by necessity relied on shared features with other mental disorders (e.g., depression or anxiety). Main outcome criteria have been the restoration of body weight or the maintenance of body weight after weight restoration. Large investigations (meta-analyses) have been conducted to provide evidence for the efficacy of medications, but findings have shown little promise of efficacy for the pharmacological treatment of AN (de Vos et al. 2014). As a result, treatment guidelines for AN emphasize the lack of utility for medications and there is no medication approved by either Health Canada or the United States Food and Drug Administration (FDA) for the treatment of AN (Watson and Bulik 2013).

Antidepressants

Antidepressants were considered for the treatment of AN for two main reasons: a) weight gain is a common side effect of older drugs in this class, and b) patients with AN often suffer from comorbid depression. Unfortunately, most antidepressant studies in patients with AN have yielded rather disappointing results. Additionally, antidepressants

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may be associated with side effects that may hinder their use in those who are underweight (e.g., with regard to heart functioning). One study examined the selective serotonin reuptake inhibitor (SSRI) antidepressant fluoxetine versus placebo in patients with AN receiving behavioural treatment; although all patients in this study showed improvements in weight, as well as mood and anxiety, there were no differences between the fluoxetine- and placebo-treated groups. Another large clinical trial in weight-restored individuals with AN again showed no benefit of fluoxetine in rate of relapse compared with placebo up to one year after hospital discharge (Walsh et al. 2006). Overall, antidepressants do not seem to render significant improvements in patients with AN, although it remains unclear to what degree malnourishment might contribute to their lack of efficacy.

Anxiolytics (anxiety-reducing agents)

Patients with AN struggle with anxiety with regard to food intake. Thus, medications that may reduce pre-meal anxiety were considered as treatment options. Data on anxiolytic use in AN is very limited at present. The only robust available data showed no benefit of the benzodiazepine alprazolam compared with placebo in reducing pre-meal anxiety in a small group of hospitalized patients with AN (Steinglass et al. 2014). In addition, benzodiazepines may become addictive.

Antipsychotics

Antipsychotics were compelling as a class of drugs due to their potential to mitigate the rigid, often delusion-like thought processes around food, weight, and shape that are often observed in patients with AN. Also, weight gain is a common side effect with this type of drugs. The newer classes (the so-called second and third generation antipsychotics), however, show a very much improved overall side effect profile compared with older agents. Initial studies have shown that the antipsychotic olanzapine may be beneficial in terms of weight gain in adult patients with AN, and others have shown that it may bring about improvements in obsessional thoughts about eating (Bissada et al. 2008, Attia et al. 2011). Olanzapine may therefore be a useful treatment option for patients with AN, and possibly in adolescents with AN according to a recent small study by Spettigue et al. (2018); however, the mechanisms are not well understood. Conclusiveness about the efficacy of olanzapine will require findings drawn from larger future studies.

Treatments targeting bone mass loss

Among the several medical complications attributed to the effects of underweight in patients with AN, bone mass loss (osteoporosis) may be the single medical complication that may not fully normalize with weight restoration. A series of pharmacological interventions have been studied, including oral and over-the-skin (transdermal) hormone replacement, growth factors like insulin-like growth factor 1, and bisphosphonates. Only one study in adolescents of estrogen/progesterone delivered over the skin has shown some significant improvement in bone mineral density (Misra et al. 2011). Studies with bisphosphonates have also shown noticeable improvements; however, this class of drugs is contraindicated for use in women of reproductive age due to the risk of birth deformities in the newborn.

BULIMIA NERVOSA (BN)

There is evidence suggesting that the combination of medication and psychotherapy may be more efficacious then either intervention alone in BN, while pharmacotherapy alone may be inferior to psychotherapy alone. Therefore, pharmacotherapy of BN is best considered an add-on to evidence-based psychotherapy. Most randomized controlled trials examining the efficacy of pharmacological options in the treatment of BN have been short in duration (approximately 8 weeks). In the very few trials with longer observation periods, dropout rates were high. Therefore, the ideal length of pharmacotherapy for BN is unknown. In the absence of data, 6 to 12 months of treatment are recommended for patients with BN – following evidence-based recommendations for the pharmacological treatment of depression. Main outcome criteria in studies have been bingeing and purging behaviours.

Antidepressants

Placebo-controlled trials have shown that several types of antidepressants significantly improved binge eating, purging and depression in BN compared to placebo (Flament et al. 2012). However, tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs) are generally not recommended as first line treatments for BN due to their side effect profile, as well as the necessity to follow a specific diet (in the case of MAOIs). The pharmacological intervention of choice for adult patients with BN is the

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SSRI fluoxetine, which is not only the most widely studied medication in BN but also approved by Health Canada and the FDA for this indication. Fluoxetine is normally prescribed at a dose of 20mg per day for depression but has been shown to be effective in reducing binge eating, purging, weight and shape concerns, and depression in patients with BN at a dose of up to 60 mg per day. Similarly, other SSRIs such as citalopram, fluvoxamine, and sertraline have shown significant benefits in reducing symptoms of BN. The only antidepressant contraindicated in the treatment of BN is bupropion due to the increased risk of seizures.

Antiepileptic (antiseizure) drugs

A further option for BN appears to be the antiepileptic drug topiramate. Topiramate has shown efficacy with regard to frequency of bingeing and purging and was associated with a more pronounced weight reduction compared with placebo in randomized control trials. Thus, it is important to consider the potential psychological implications of weight loss before prescribing topiramate to patients with BN who are generally preoccupied with weight and shape concerns.

BINGE EATING DISORDER (BED)

BED was acknowledged as an independent diagnosis in 2015. As such, the number of studies examining pharmacological approaches for BED is still limited. Main outcome criteria have been reduction of binges and body weight.

Stimulants

The only Health Canada- and FDA-approved drug for the treatment of BED is lisdexamfetamine. It is a drug used to treat attention deficit hyperactivity disorder (ADHD) and has been shown to reduce binge episodes and eating-related obsessions and compulsions in BED. Doses are similar for both ADHD and BED. The long-term efficacy of this medication has not yet been assessed.

Antidepressants

Similar to BN, several antidepressants have shown short-term reductions in binge eating in patients with BED; however, no particular antidepressant has been found to be superior to others. In a meta-analysis evaluating seven studies of SSRIs and the TCA imipramine showed that short-term remission rates from binge eating were significantly higher compared with placebo (Stefano et al. 2008). Long-term studies of the efficacy of antidepressants in BED have yet to be completed.

Antiepileptic drugs

Many patients with BED are large-bodied and seek treatment with weight loss being their primary goal. The anticonvulsants topiramate and zonisamide are known for the side effect of weight loss and have been examined for BED treatment. Topiramate against placebo has shown significantly higher rates of remission in binge eating as well as significantly greater weight loss. Nonetheless, topiramate is associated with significant side effects, which, in turn, hinder treatment adherence. For example, McElroy et al. (2004) conducted a 42-week trial with topiramate, in which 68% of participants dropped out due to adverse events (e.g., abnormal skin sensations, dry mouth, headache, changes in taste, cognitive problems). Similar results were observed with zonisamide; despite significant reductions in binge eating and weight, the drug was associated with intolerable side effects. Additionally, weight loss-focused treatments are ineffective and potentially harmful; BED is a mental health disorder and should as such be primarily treated by means of psychotherapy.

Drugs approved for weight loss

Currently there are two Health Canada-approved medications for weight loss. Of these, only one – orlistat – has been studied in individuals with BED. Orlistat does not appear to be more effective in achieving remission from binge eating compared to placebo and is associated with highly unpleasant side effects such as fatty/oily stools and flatulence.

CONCLUSION

Nutritional rehabilitation and psychotherapy should be considered the primary mode of treatment for eating disorders. Medication may be helpful as add-on to psychotherapy, or when psychotherapy is not accessible, although efficacy data is limited. At present, only fluoxetine for BN and lisdexamfetamine for BED are approved by Health Canada as pharmacological treatments for eating disorders. Many psychiatrists use medications to treat symptoms of depression or anxiety in patients with eating disorders, and to treat eating disorder symptoms in a “off label” manner, which is defined by the FDA as “use of drugs for the indication, dosage form, regimen, patient or other use constraint not mentioned in the approved labeling”. Further research and novel pharmacological approaches for the treatment of eating disorders are warranted.

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