Psychopharmacological management of binge eating disorder

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Abstract

Binge Eating Disorder (BED) is a common atypical eating disorder. The treatment of BED calls for multi-professional expertise and co-operation between doctors, psychologists and nutritional therapists. Different therapeutic and psychosocial approaches are the primary means in treating BED. Medication may be used as supportive treatment. Selective serotonin reuptake inhibitors (SSRIs) are the most studied drugs in this context. This is a review article on studies examining the efficacy of the psychopharmacological treatment of BED.

Introduction

In Finland, the recently published Current Care Guidelines for the treatment of eating disorders outline that drugs play a minor role in the treatment of BED, stating that medication may temporarily reduce binge eating but is not recommended for routine use (1). Of various drugs, antidepressants have been studied most extensively, and it seems that some patients may benefit from them, especially those who have comorbid disorders, such as depression or anxiety disorders. The aim of this article is to review studies on the efficacy of several antidepressants, two drugs licensed for the treatment of attention-deficit/hyperactivity disorder (ADHD), namely atomoxetine and lisdexamfetamine, and one anti-epileptic, namely topiramate. The focus is on randomized, controlled trials (RCTs).

Antidepressants

Escitalopram and citalopram

Forty-four adult outpatients, with BED and obesity, took part in a 12-week, double-blind, flexible dose (10-30 mg/day) study conducted in the USA. The patients were randomized in two groups: 21 received high-dose escitalopram and 23 placebo. At baseline, the subjects' body mass index (BMI) was 40.1 (SD 6.8) kg/m^2 in the escitalopram group and 40.3 (SD 4.8) kg/m^2 in the placebo group. The outcome measures were: binges/week, binge days/week, BMI, weight, Clinical Global Impression-Severity (CGI-S), Yale-Brown Obsessive-Compulsive Scale Modified for Binge Eating (YBOCS-BE total score) and Hamilton Depression Rating Scale (HAM-D). Escitalopram was associated with significantly greater improvement than placebo in weight, BMI (at week 12 in escitalopram group BMI was 40.4 (SD 7.0) kg/m^2 and 40.5 (SD 5.0) kg/m^2 in placebo group) and CGI-S. High-dose escitalopram was not efficacious in reducing binges (RR = 1.5, 95% CI: 0.2-2.3, χ^2 = 0.45, p = 0.50) or obsessive-compulsive symptoms (2).

In the USA, thirty-eight adult outpatients with BED were enrolled in a study and randomly assigned to receive either citalopram or placebo in a 6-week, double-blind, flexible dose (20-60 mg/day) study. During the course of the study, 7 subjects (3 citalopram and 4 placebo) withdrew prematurely, all after 4 weeks of treatment: 4 for worsening depressive symptoms (1 citalopram, 3 placebo), 1 for non-adherence to the study protocol (placebo), 1 for an adverse event (citalopram - sexual dysfunction) and 1 for personal conflict (citalopram). The outcome measures were the frequency of binge eating episodes, binge days/week, BMI, weight, CGI-S, YBOCS-BE and HAM-D. At the baseline, binges/week amounted to 5.2 (SD 3.6) in the citalopram group and 5.7 (SD 2.6) in the placebo group, and the corresponding figures at week 6 were 1.7 (SD 3.1) and 3.4 (SD 3.0), respectively. Citalopram was efficacious in reducing binge eating frequency, weight and severity of illness. Remission was achieved by 9 of those who completed the study in the citalopram group and by 4 in the placebo group (3).

Fluvoxamine

In the USA, eighty-five adult outpatients with BED were randomly assigned to receive either fluvoxamine (42) or placebo (43) in a 9-week, parallel-group, double-blind, flexible-dose (50-300 mg/day) study. The primary outcome measures were the frequency

of binge eating and CGI-S, and secondary measures included BMI and HAM-D. At the baseline, binges/week amounted to 5.4 (SD 2.9) in the fluvoxamine group and 5.3 (SD 2.5) in the placebo group. When compared with placebo, fluvoxamine was associated with a significantly greater reduction in the frequency of binges, and there was improvement in the CGI-S scores, the level of response for those patients who completed the study and the reduction in BMI. Remission was achieved by 15 in the fluvoxamine group and 11 in the placebo group. During the study course 18 patients withdrew: 10 before the end of 4 weeks, and another eight between weeks 4 and 9. A significantly greater proportion of fluvoxamine-treated patients than placebo patients discontinued treatment because of an adverse medical event (4).

Sertraline

In the USA, thirty-four adult outpatients with BED were randomly assigned to receive either sertraline or placebo in a 6-week, double-blind, flexible-dose (50-200 mg/day) study. The outcome measures were binges/week, BMI and CGI-S. Eight patients withdrew during the study, 5 in the sertraline group and 3 in the placebo group. No patients withdrew because of an adverse medical event or worsening psychiatric status. When compared with placebo, sertraline was associated with a significantly greater reduction in the frequency of binges and BMI as well as improvement in CGI-S. Sertraline was also associated with a higher degree of response, although the effect was not significant (5).

Fluoxetine

In the USA, sixty adult outpatients with a diagnosed BED were randomly assigned to receive fluoxetine or placebo in a 6-week double-blind, flexible-dose (20-80 mg/day) study. The primary outcome measure of efficacy was binges/week. Secondary measures included BMI, weight, CGI-S and HAM-D. At the baseline, binges/week totalled 6.0±2.5 in fluoxetine group and 6.1±4.8 in the placebo group, and at week 6 the corresponding figures were 1.8±2.9 and 2.7±3.8. There was a significantly greater reduction in the frequency of binge eating ($p = .033$), BMI and weight, and improvement in CGI-S. A significantly greater proportion of placebo-treated subjects (n=17) than fluoxetine-treated subjects (n=7) withdrew from the study (8).

Sertraline and fluoxetine

An Italian study assessed the effectiveness of sertraline and fluoxetine in the treatment of obese patients with BED over a period of 24 weeks. Forty-two adult obese outpatients were randomized and assigned to one of two different drug treatments: 22 were treated with sertraline (dose range 100-200 mg/day) and 20 with fluoxetine (dose range 40-80 mg/day). There was no placebo-group. The outcome measures were binges/week, BMI, weight and Beck's depression scale. At the baseline, there were 4.6±3.2 binges/week in the fluoxetine group and 6.2±7.3 in the sertraline group and, at the end of the study, correspondingly 0.9±1.1 in the fluoxetine group and 1.1±3.3 in the sertraline group. The mean BMI was at baseline 39.3 (SD ±3.5), range 33.3 - 49.5. Weight reduced by at least 5% in 8 patients in the fluoxetine group and in 9 patients in the sertraline group. Depressive symptoms alleviated. There was no significant difference between the two study drugs (7).

Duloxetine

In the USA, a 12-week outpatient, randomized, placebo-controlled, double-blind, parallel-group, flexible-dose study was carried out to evaluate the effect of duloxetine in the treatment of BED with comorbid depressive disorders. A total of 40 adult patients participated in the study. The primary outcome measure was binge days/week. The secondary outcome measures were binges/week, weight, BMI, CGI-S, YBOCS-BE and Hamilton Anxiety Scale (HAM-A). Seven patients in the duloxetine group and six in the placebo group withdrew from the study. At the baseline, binge days/week were 4.5 (SD 1.8) in the duloxetine group and 3.5 (SD 1.5) in the placebo group and, at the end of the study, the corresponding figures were 1.0 (SD 1.7) and 1.3 (SD 1.2). Remission was achieved by 56% of the duloxetine group and 30% of the placebo group: the difference between the groups was not statistically significant. Duloxetine was significantly more effective in terms of reduced weight and improved CGI-S. There were no significant differences between the groups in BMI, depression or anxiety (6).

Psychostimulants

Atomoxetine

In an American 10-week, single-centre, randomized, double-blind, placebo-controlled, flexible-dose (40-120 mg/day) trial, adult outpatients with BED received either atomoxetine or placebo. Altogether 40 patients participated in the study. The primary outcome was binges/week and secondary outcomes included binge days/week, weight, CGI-S, HAM-D and YBOCS-BE. Three patients who received atomoxetine and one with placebo withdrew because of adverse events (constipation, nervousness, depression). This difference was not statistically significantly. In both groups, binge eating reduced, and atomoxetine reduced binges/week statistically significant. At the baseline, there were 4.2 (SD 1.4) binges/week and 3.8 (SD 1.1) binge days/week in the atomoxetine group. In the placebo group, the corresponding figures were 4.9 (SD 2.5) and 3.9 (SD 1.5). At the endpoint, the estimated difference between the groups in binges/week was -0.16 (95% CI -0.29 - -0.01, t = 2.2 and p = .034) and in binge days/week -0.17 (95 % CI -0.30 - 0.03, t = 2.37 and p = .023). The difference between the groups was also significant in weight, BMI and CGI-S (9).

Lisdexamfetamine

To examine the efficacy and safety of lisdexamfetamine dimesylate for the treatment of moderate to severe BED, a multicentre, randomized, double-blind, parallel-group, forced-dose titration, placebo-controlled trial was conducted in the USA. The study duration was 14 weeks, and 31 sites were involved. The participants were adults, aged 18-55 years, and they were randomized (1:1:1:1) to receive 30, 50, or 70 mg/day of lisdexamfetamine dimesylate or placebo. The primary efficacy measure was the number of binge days/week. Secondary efficacy measures included the number of binge episodes per week, 1-week binge episode response status, and 4-week cessation of binge episodes and CGI-S. When compared with the placebo, lisdexamfetamine dimesylate treatment with 50 and 70 mg/day, but not with 30 mg/day, demonstrated a significant decrease in the number of weekly binge days at week 11. Similarly, binge episodes decreased in the 50 and 70 mg/day treatment groups, and a greater proportion of participants achieved 4-week cessation of binge episodes and improvement in CGI-S. The incidence of any treatment-emergent adverse effects was 84.7% for the treatment groups versus 58.7% for the placebo group. With lisdexamfetamine treatment, elevated mean heart rates were observed. One participant died during the study. Post-mortem toxicology analysis reported that methamphetamine/amphetamine levels were consistent with a methamphetamine overdose (12).

Table 1. The reviewed studies in summary.

Study	Study design	Study drug, average dose mg/day	Number of patients F/M	Mean age of patients
Guerdjikova et al. (2008)	Randomized, double-blind, placebo-controlled	Escitalopram 26.5	44 43/1	36.9 in escitalopram group, 41.0 in placebo group
McElroy et al. (2003)	Randomized, double-blind, placebo-controlled	Citalopram 56.9	38 36/2	42.0 in citalopram group, 39.2 in placebo group
Hudson et al. (1998)	Randomized, double-blind, parallel-group, placebo-controlled	Fluvoxamine 260	85 77/8	42.2 in fluvoxamine group, 43.0 in placebo group
McElroy et al. (2000)	Randomized, double-blind, placebo-controlled	Sertraline 50-200	34 32/2	43.1 in sertraline group, 35.8 in placebo group
Leombruni et al. (2008)	Randomized, double-blind	Sertraline 100-200 Fluoxetine 40-80	42 All females	39.6
Arnold et al. (2002)	Randomized, double-blind, placebo-controlled	Fluoxetine 71.3	60 56/4	41.9 in fluoxetine group, 40.8 in placebo group
Guerdjikova et al. (2012)	Randomized, double-blind, placebo-controlled	Duloxetine 78.7	40 35/5	40.1
McElroy et al. (2007)	Randomized, double-blind, placebo-controlled	Atomoxetine 106	40 33/7	43.1 in atomoxetine group, 39.2 in placebo group
McElroyet al. (2015)	Randomized, double-blind, placebo-controlled, parallel-group	Lisdexamfetamine 30/50/70	724	18 - 55
McElroy et al. (2004)	Randomized, double-blind, placebo-controlled	Topiramate 250	61	41
McElroy et al. (2007)	Randomized, double-blind, placebo-controlled	Topiramate 300	404 340/64	44 in topiramate group, 45 in placebo group

Abbreviations: BMI=Body Mass Index, CGI-S=Clinical Global Impression-Severity, YBOCS-BE=Yale-Brown Obsessive-Compulsive Scale Modified for Binge Eating, HAM-D=Hamilton Depression Rating Scale.

Study duration weeks	Outcome measures	Results	Adverse effects
12	Binges/week, binge days/week, BMI, weight, CGI-S, YBOCS-BE, HAM-D	Escitalopram was associated with a significantly greater improvement than placebo for weight, BMI and CGI-S.	Dry mouth, diarrhoea, fatigue, all differences between groups were non-significant.
6	Binges/week, binge days/week, BMI, weight, CGI-S, YBOCS-BE, HAM-D	The citalopram group showed a significantly greater reduction in binges/week, binge days/week, weight and CGI-S.	Sweating and fatigue were significantly more common in the citalopram group.
9	Binges/week, CGI-S, HAM-D	The fluvoxamine group showed a significantly greater reduction in binges/week and CGI-S.	Insomnia, nausea, abnormal dreams were significantly more common in the fluvoxamine group.
6	Binges/week, BMI, CGI-S	Sertraline was significantly more efficient for all outcome measures.	Insomnia was significantly more common in the sertraline group.
24	Binges/week, weight, BMI, Beck's depression scale	No significant differences between the groups. Significant improvement in binges/week and weight loss.	Nausea, headache, anxiety, no significant differences between the groups.
6	Binges/week, weight, BMI, CGI-S, HAM-D	Fluoxetine was significantly more efficient in reducing binges/week, BMI, weight and severity of CGI-S.	Dry mouth, headache, nausea, no significant differences between groups.
12	Binge days/week, binges/week, depressive and anxiety disorders, CGI-S, weight, BMI,	No significant differences between groups, except for weight.	Nausea, dry mouth, constipation, no significant differences between groups.
10	Binges/week, binge days/week, weight, BMI, CGI-S	Atomoxetine was significantly more efficient in reducing binges/week, binge days/week, weight, BMI, and CGI-S.	Dry mouth occurred significantly more frequently in the atomoxetine group.
14	Binge days/week, binge cessation for 4 week, CGI-S	Doses of 50 and 70 mg/day demonstrated efficacy, when compared to placebo group in decreased binge days/week, binge cessation, and improved CGI-S.	Dry mouth, insomnia, mean heart rate tended to increase in the treatment group.
14 followed by open-label trial	Binges/week, binge days/week, weight	In topiramate group, binges/week and weight reduced to a significantly larger extent.	Paraesthesias, dry mouth and headache were common in the topiramate group.
16	Binges/week, binge days/week, weight, BMI	Topiramate was significantly more efficient in reducing binges/week, binge days/weeks, weight, and BMI.	Paraesthesias, upper respiratory tract infection, somnolence, nausea were common in the topiramate group.

Antiepileptics

Topiramate

In the USA, sixty-one adult patients with BED and obesity enrolled in a 14-week, single-centre, randomized, double-blind, placebo-controlled study on topiramate. The completers were offered an opportunity to continue in a 42-week, open-label extension trial to assess the long-term effectiveness and tolerability of topiramate. At first, 31 patients received topiramate (25-600 mg/day) and 30 received placebo. Fifteen patients receiving topiramate and 16 patients receiving placebo entered the open-label extension trial.

The primary outcome measure was binges/week, and the secondary outcome measures were binge days/week and weight. At the baseline, binges/week were 5.0 (SD 2.93) in the topiramate group and 4.1 (SD 4.48) in the placebo group. At week 14, the mean number of binges/week reduced by -3.2 from the baseline. At the endpoint of the open trial, at week 56, the average change was -5.0 (10 patients completed the study). At the baseline, there were 4.1 (SD 1.72) binge days/week in the topiramate group and 2.6 (SD 2.72) in the placebo group. In the topiramate group, the mean change was -1.2 at week 14 and -2.0 at week 56. The mean weight loss in the topiramate group was -6.0 kg at week 14 and -14.2 kg at week 56 (11). Fourteen (32%), of the 44 patients, discontinued topiramate due to adverse events. The most common adverse event was paraesthesia, 75% of patients receiving topiramate reported symptoms.

In the USA, a total of 407 adult patients with BED and obesity were enrolled in a single-centre, placebo-controlled study comparing topiramate and placebo over a period of 16 weeks. Thirteen failed to meet the inclusion criteria, thus resulting in 195 patients receiving topiramate and 199 patients receiving placebo. The primary outcome measure was binge days/week. The secondary outcome measures were binges/week, weight and BMI. Remission was achieved by 58% of patients in the topiramate group and 29% of patients in the placebo group. When compared to placebo, topiramate reduced significantly ($p < 0.001$) binge days/week (-3.5 ± 1.9 vs. -2.5 ± 2.1), binges/week (-5.0 ± 4.3 vs. -3.4 ± 3.8), weight (-4.5 ± 5.1 kg vs. 0.2 ± 3.2 kg) and BMI (-1.6 ± 1.8 kg/m^2 vs 0.1 ± 1.2 kg/m^2). In both groups, 30% of patients withdrew from the study. Adverse effects were the cause for discontinuity of 16% for patients in the topiramate group and 8% in the placebo group (10).

The contents of reviewed studies are summarized in Table 1.

Conclusions

The accumulating evidence of the effect of drugs in the treatment of BED is not very strong. There are only a few repeated studies and the number of patients is small in most studies. Further studies are needed, especially to evaluate long-term safety issues.

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