

Psychopharmacology Update:

A Review of Medication Use for Children and Adolescents with Eating Disorders

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Abstract

Objective: This paper aims to review the research literature on the use of medication for eating disorders in children and adolescents. **Method:** The literature was reviewed on the pharmacotherapy of anorexia nervosa (AN), bulimia nervosa (BN) and eating disorder not otherwise specified (EDNOS). The PubMed database was searched for all articles on medication use in the child and adolescent population using the terms medication, antipsychotic, antidepressant, child, adolescent, eating disorders, anorexia nervosa and bulimia nervosa. **Results:** Very little literature exists on the use of medication for the treatment of eating disorders in children and adolescents. There is one retrospective study on the use of SSRIs and some case reports on atypical antipsychotics for children and adolescents with AN, and one small open trial on SSRIs for adolescent BN. **Conclusions:** Evidence-based pharmacological treatment for children and adolescents with eating disorders is not yet possible due to the limited number of studies available. It appears that olanzapine and other atypical antipsychotics may prove to be promising for AN at low body weights. It remains uncertain whether SSRIs are helpful in preventing relapse in AN. For children and adolescents with BN, the first line pharmacological option is fluoxetine given the large evidence base of this drug with the adult population and a small open trial of adolescents with BN.

Key words: anorexia nervosa, bulimia nervosa, medication, children, adolescents

Résumé

Objectif: L'objectif de cet article est de passer en revue la littérature sur la médication prescrite aux enfants et adolescents qui souffrent de troubles du comportement alimentaire. **Méthodologie:** L'examen a porté sur la pharmacothérapie de l'anorexie, de la boulimie et d'autres troubles du comportement alimentaire non précisés. **Résultats:** Très peu d'articles portent sur la médication utilisée pour traiter les troubles du comportement alimentaire chez les enfants et les adolescents. Il existe une étude rétrospective sur l'utilisation des ISRS, quelques études de cas sur les antipsychotiques atypiques pour les enfants et adolescents anorexiques, et une étude de petite envergure sur les ISRS prescrits aux adolescents boulimiques. **Conclusions:** Le traitement pharmacologique factuel des enfants et adolescents souffrant de troubles du comportement alimentaire n'est pas encore possible en raison du nombre limité d'études sur ce sujet. L'olanzapine et les autres antipsychotiques atypiques semblent avoir un avenir prometteur pour les patients dont le poids est très inférieur à la normale. On ne sait pas avec certitude si les ISRS aident à éviter les rechutes chez les anorexiques. La fluoxétine est la principale option pharmacologique pour les enfants et adolescents atteints de boulimie, comme l'attestent les résultats de nombreuses études auprès de la population adulte et l'essai mené auprès d'une population réduite d'adolescents.

Mots clés: anorexie, boulimie, médication, enfants, adolescents

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Although clinicians often use medications to treat children and adolescents suffering from eating disorders, there is little research literature supporting medication use in this population. This makes evidence-based practice nearly impossible in this area. This paper reviews the literature on medication treatments for children and adolescents with eating disorders, first focusing on Anorexia Nervosa (AN) and then on Bulimia Nervosa (BN), followed by a short comment on Eating Disorder Not Otherwise Specified (ED NOS). The literature was reviewed by searching the PubMed database for all articles on medication use in the child and adolescent population using the terms medication, antipsychotic, antidepressant, child, adolescent, eating disorders,

anorexia nervosa and bulimia nervosa. Due to the scant literature in the child and adolescent area, some literature on adult treatments will be discussed. Our review focuses on the two major classes of drugs used to treat eating disorders – antidepressants, mainly consisting of selective serotonin reuptake inhibitors (SSRIs), and atypical antipsychotics.

Systematic research on antidepressant treatment for AN in children and adolescents is almost non-existent. There is one retrospective study that compared 19 adolescent patients with AN taking SSRIs to 13 patients with AN not treated with SSRIs (Holtkamp et al, 2005). These authors found that there were no differences between these groups in terms of BMI, eating disorder psychopathology, or depressive

and obsessive-compulsive symptoms after evaluating patients on admission, discharge and up to one-year follow-up. In terms of non-SSRI antidepressant treatment, there is one case report on the use of mirtazapine in a 16 year old female with AN and depression (Jaafar, Daud, Rahman, & Baharudin, 2007). These authors found positive results and suggest that further study on this medication is needed.

The studies on antidepressants in adult patients with AN have shown mixed results. Historically, the tricyclic antidepressants have been studied in controlled trials with no benefit in terms of weight gain in hospitalized patients (Biederman et al, 1985; Halmi, Eckert, LaDu, & Cohen, 1986). These medications also had significant side effects. The SSRIs have also been studied but showed little promise in adults. Fluoxetine showed no benefit compared to placebo in hospitalized patients (Attia, Haiman, Walsh, & Flater, 1998), even with the addition of tryptophan which was used in an effort to increase serotonin substrate (Barbarich, McConaha, Halmi et al, 2004). One study has shown an increased time to relapse with fluoxetine treatment compared to placebo in 35 patients who were weight restored, however results must be interpreted with caution given the high drop-out rate (Kaye et al, 2001). Furthermore, a recently completed, well-designed, large randomized controlled trial comparing fluoxetine to placebo in 93 adult patients with AN following weight restoration, showed no significant difference in the time to relapse (Walsh et al, 2006). However, attrition rates in this study were also over 50% making definitive conclusions problematic. Despite these discouraging findings, some suggest that children and adolescents may be more responsive than adults to SSRIs because parents would ensure compliance with medication use and these patients are less chronically ill. However, given recent concerns about the safety of SSRIs in adolescents and children, it is prudent to advise caution in using this class of medications with children and adolescents with AN (Lock, Walker, Rickert, & Katzman, 2005).

A few case reports suggest that atypical antipsychotics may be useful for AN. In one case series, olanzapine was used to treat children and adolescents with AN at low body weights (Boachie, Goldfield, & Spettigue,

2003). These authors report improvement in compliance and weight gain, as well as decreases in agitation, and anxiety in four patients aged 10 to 12 years at a dose of 2.5 mg of olanzapine. In adult patients with AN, there have been several open trials of olanzapine (Barbarich, McConaha, Gaskill et al, 2004; Malina et al, 2003; Powers, Santana, & Bannon, 2002) and one randomized trial in which olanzapine (10mg average dose) was compared with chlorpromazine (50mg average dose) (Mondraty et al, 2005). This study demonstrated that although the group treated with olanzapine experienced decreases in rumination, no differences in weight gain were seen.

There is even less literature on the other atypical antipsychotics. There have been two adolescent cases described in which risperidone was added to antidepressant treatment and improvements in anxiety and weight gain were noted (Newman-Toker, 2000). The safety of the atypical agents in terms of cardiac conduction problems is yet to be determined, although they are thought to be safer than the typical agents.

Treatment guidelines suggest that medication should not be used as the primary treatment of children and adolescents with AN (National Institute for Clinical Excellence, 2004). Generally, family-based psychological treatments are gaining the most evidence-base for children and adolescents with AN. Medication should only be used to treat comorbid conditions, however caution should be used when treating depressive or obsessive-compulsive symptoms, especially those associated with eating and weight control at low weights, as these symptoms often resolve with weight gain. In these cases, a good longitudinal history is important in determining whether the co-morbid symptoms preceded the eating disorder, in which case treatment of these co-morbidities would more likely be indicated. There is currently no evidence that medication is effective in the starved state, although the atypical antipsychotics appear promising in the limited case reports that are available particularly in agitated patients. When using medication, side effects should be closely monitored including cardiac conduction problems.

For BN there have been many studies confirming the effectiveness of SSRIs, particularly fluoxetine in adults. In terms of SSRI treat-

ment for adolescents with BN, there is one open trial of fluoxetine in ten adolescents aged 12 to 18 years (Kotler, Devlin, Davies, & Walsh, 2003). These adolescents received 8 weeks of fluoxetine at a daily dose of 60 mg along with supportive psychotherapy. Frequencies of weekly binge episodes decreased significantly from about 4 to zero, and weekly purges decreased from about 6 to almost none. Seventy percent were rated as improved or much improved on the clinical global impressions-improvement scale. If patients maintained these benefits over the long term is unknown.

Fluoxetine has received approval from the FDA for treatment of adults with BN. It has been shown to be effective in reducing bulimic symptoms in two 8-week double blind trials (Fichter et al, 1991; "Fluoxetine in the treatment of bulimia nervosa. A multicenter, placebo-controlled, double-blind trial. Fluoxetine Bulimia Nervosa Collaborative Study Group," 1992), and in one 16-week double blind trial (Goldstein, Wilson, Thompson, Potvin, & Rampey, 1995) at a dose of 60mg per day. In a long-term follow-up study over a one year period, those who had responded to fluoxetine acutely at a dose of 60mg daily were treated with a maintenance dose of 60mg daily. An increased time to relapse was found compared to those acute responders who were switched to a placebo leading investigators to conclude that fluoxetine should be continued for a period of at least one year. A Cochrane Review concluded that fluoxetine is the most systematically studied antidepressant agent and its better side effect profile makes it superior to other drugs in treating BN. The reviewers suggest that fluoxetine should be the first line agent for BN and that a daily dose of 60 mg is more effective than a dose of 20 mg (Bacaltchuk & Hay, 2003). Eight weeks appears to be an appropriate period to determine effectiveness. Other authors have indicated that medication treatment decreases binge frequency by an average of 56% compared to 11% in placebo treatment. Decreases in purging frequencies are similar (Jimerson, Herzog, & Brotman, 1993). The effect of fluoxetine in treating BN does not appear to be related to the presence of a co-morbid depression with both those with depression and those without depression doing equally well (Goldstein, Wilson, Ascroft, & al-Banna, 1999).

General treatment guidelines suggest that Cognitive Behavioural Therapy (CBT) specifically adapted for BN should be offered as a first line treatment with fluoxetine added as adjunctive treatment for adults and for adolescents with BN (National Institute for Clinical Excellence, 2004). Patients should be informed that the long-term effects of treatment with fluoxetine are unknown. No drugs, other than antidepressants are recommended for the treatment of BN, and bupropion is contraindicated due to the risk of seizures in patients with BN.

Often children and adolescents present with a diagnosis of Eating Disorder Not Otherwise Specified (ED NOS) leaving clinicians uncertain of which course of treatment to take. Guidelines suggest that these individuals should be treated with the protocol for the disorder that most closely resembles their eating symptoms (National Institute for Clinical Excellence, 2004). Therefore, if dietary restriction is most prominent, a protocol for AN might be considered, whereas if binge eating or purging is the main problem, a protocol for BN might be most appropriate. For Binge Eating Disorder (BED) psychological treatments such as CBT adapted for BED, dialectical behaviour therapy (DBT) and interpersonal therapy (IPT) are suggested first line treatments with SSRIs as adjunctive treatments for adults with BED. Psychological treatments adapted for adolescents with BED are also suggested as first line treatments, and there are no studies available on SSRI treatment for adolescents with BED.

In conclusion, evidence-based pharmacological treatment for children and adolescents with eating disorders is not yet possible due to the limited number of studies available. Based on studies in adults and some case reports in adolescents, it appears that olanzapine and other atypical antipsychotics may prove to be promising for AN at low body weights to help with eating-related anxiety. It remains uncertain whether SSRIs are helpful in preventing relapse in AN, though the current evidence is not encouraging. Generally, medications for AN should be reserved for co-morbid conditions such as OCD and depression when there is compelling historical evidence that these symptoms preceded the onset of the eating disorder. For children and adolescents with BN, the first line pharmacological option is fluoxetine

given the large evidence base of this drug with the adult population and the small open trial of adolescents with BN. It must be kept in mind that CBT modified for BN is still the first line treatment before a trial of medication, however, this treatment modality is often not available to clinicians and patients. When treating children and adolescents with ED NOS it is best to follow treatment recommendations for the disorder that the symptoms most closely resemble. For example, treatment for restriction might follow treatment guidelines for AN, whereas binge eating or purging behaviour might compel a clinician to follow guidelines for BN. Further medication trials are needed in order to delineate which, if any, pharmacological treatments are efficacious for children and adolescents with eating disorders.

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References

- Attia, E., Haiman, C., Walsh, B. T. & Flater, S. R. (1998). Does fluoxetine augment the inpatient treatment of anorexia nervosa? *American Journal of Psychiatry*, *155*(4), 548-551.
- Bacaltchuk, J. & Hay, P. (2003). Antidepressants versus placebo for people with bulimia nervosa. *Cochrane Database System Review* (4), CD003391.
- Barbarich, N. C., McConaha, C. W., Gaskill, J., La Via, M., Frank, G. K., Achenbach, S., et al (2004). An open trial of olanzapine in anorexia nervosa. *Journal of Clinical Psychiatry*, *65*(11), 1480-1482.
- Barbarich, N. C., McConaha, C. W., Halmi, K. A., Gendall, K., Sunday, S. R., Gaskill, J., et al (2004). Use of nutritional supplements to increase the efficacy of fluoxetine in the treatment of anorexia nervosa. *International Journal of Eating Disorders*, *35*(1), 10-15.
- Biederman, J., Herzog, D. B., Rivinus, T. M., Harper, G. P., Ferber, R. A., Rosenbaum, J. F., et al (1985). Amitriptyline in the treatment of anorexia nervosa: a double-blind, placebo-controlled study. *Journal of Clinical Psychopharmacology*, *5*(1), 10-16.
- Boachie, A., Goldfield, G. S. & Spettigue, W. (2003). Olanzapine use as an adjunctive treatment for hospitalized children with anorexia nervosa: case reports. *International Journal of Eating Disorders*, *33*(1), 98-103.
- Fichter, M. M., Leibl, K., Rief, W., Brunner, E., Schmidt-Auberger, S. & Engel, R. R. (1991). Fluoxetine versus placebo: a double-blind study with bulimic inpatients undergoing intensive psychotherapy. *Pharmacopsychiatry*, *24*(1), 1-7.
- Fluoxetine in the treatment of bulimia nervosa. A multicenter, placebo-controlled, double-blind trial. Fluoxetine Bulimia Nervosa Collaborative Study Group. (1992). *Archives of General Psychiatry*, *49*(2), 139-147.
- Goldstein, D. J., Wilson, M. G., Ascroft, R. C. & al-Banna, M. (1999). Effectiveness of fluoxetine therapy in bulimia nervosa regardless of comorbid depression. *International Journal of Eating Disorders*, *25*(1), 19-27.
- Goldstein, D. J., Wilson, M. G., Thompson, V. L., Potvin, J. H. & Rampey, A. H., Jr. (1995). Long-term fluoxetine treatment of bulimia nervosa. Fluoxetine Bulimia Nervosa Research Group. *British Journal of Psychiatry*, *166*(5), 660-666.
- Halmi, K. A., Eckert, E., LaDu, T. J. & Cohen, J. (1986). Anorexia nervosa. Treatment efficacy of cyproheptadine and amitriptyline. *Archives of General Psychiatry*, *43*(2), 177-181.
- Holtkamp, K., Konrad, K., Kaiser, N., Ploenes, Y., Heussen, N., Grzella, I., et al (2005). A retrospective study of SSRI treatment in adolescent anorexia nervosa: insufficient evidence for efficacy. *Journal of Psychiatric Research*, *39*(3), 303-310.
- Jaafar, N. R., Daud, T. I., Rahman, F. N. & Baharudin, A. (2007). Mirtazapine for anorexia nervosa with depression. *Australia and New Zealand Journal of Psychiatry*, *41*(9), 768-769.
- Jimerson, D. C., Herzog, D. B. & Brotman, A. W. (1993). Pharmacologic approaches in the treatment of eating disorders. *Harvard Review of Psychiatry*, *1*(2), 82-93.
- Kaye, W. H., Nagata, T., Weltzin, T. E., Hsu, L. K., Sokol, M. S., McConaha, C., et al (2001). Double-blind placebo-controlled administration of fluoxetine in restricting- and restricting-purging-type anorexia nervosa. *Biological Psychiatry*, *49*(7), 644-652.
- Kotler, L. A., Devlin, M. J., Davies, M. & Walsh, B. T. (2003). An open trial of fluoxetine for adolescents with bulimia nervosa. *Journal of Child Adolescent Psychopharmacology*, *13*(3), 329-335.
- Lock, J., Walker, L. R., Rickert, V. I. & Katzman, D. K. (2005). Suicidality in adolescents being treated with antidepressant medications and the black box label: position paper of the Society for Adolescent Medicine. *Journal of Adolescent Health*, *36*(1), 92-93.
- Malina, A., Gaskill, J., McConaha, C., Frank, G. K., LaVia, M., Scholar, L., et al (2003). Olanzapine treatment of anorexia nervosa: a retrospective study. *International Journal of Eating Disorders*, *33*(2), 234-237.
- Mondraty, N., Birmingham, C. L., Touyz, S., Sundakov, V., Chapman, L. & Beumont, P. (2005). Randomized controlled trial of olanzapine in the treatment of cognitions in anorexia nervosa. *Australasian Psychiatry*, *13*(1), 72-75.
- National Institute for Clinical Excellence. (2004). *Eating Disorders: Core interventions in the treatment and management of anorexia nervosa, bulimia nervosa and related eating disorders*. London: National Institute for Clinical Excellence.
- Newman-Toker, J. (2000). Risperidone in anorexia nervosa. *Journal of the American Academy of Child and Adolescent Psychiatry*, *39*(8), 941-942.
- Powers, P. S., Santana, C. A. & Bannon, Y. S. (2002). Olanzapine in the treatment of anorexia nervosa: an open label trial. *International Journal of Eating Disorders*, *32*(2), 146-154.
- Walsh, B. T., Kaplan, A. S., Attia, E., Olmsted, M., Parides, M., Carter, J. C., et al (2006). Fluoxetine after weight restoration in anorexia nervosa: a randomized controlled trial. *Journal of the American Medical Association*, *295*(22), 2605-2612.