

Olanzapine in the Treatment of Children and Adolescents with Anorexia Nervosa- A Systematic Review

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Objective: Olanzapine is a commonly used antipsychotic drug in the treatment of children and adolescents under the age of 18 years with Anorexia Nervosa (AN) to promote weight restoration. This systematic review aims to assess the effectiveness of Olanzapine in influencing weight gain; its effect on eating disorder symptoms, comorbid anxiety and depressive symptoms and its safety for use in children and adolescents with AN.

Method: A Systematic search of the databases MEDLINE, EMBASE, PsycINFO, PubMed, Cochrane was conducted for the period between 1996 and September 2019 for all study designs except reviews, published in English, focussing on olanzapine use for the treatment of Anorexia Nervosa in children and adolescents.

Inclusion Criteria

Population: Children and Adolescents under 18 years of age with a diagnosis of Anorexia Nervosa or Eating Disorder not otherwise specified(EDNOS) / Other Specified Feeding or Eating Disorder(OSFED) according to Diagnostic and Statistical Manual of Mental Disorders(DSM IV, IV TR or V)or an ICD 10 diagnosis of Anorexia Nervosa or Atypical anorexia nervosa. AN could be a clinical or research diagnosis.

Intervention: Olanzapine used as a treatment of Anorexia Nervosa either alone or in combination with other interventions (except antipsychotics) in both outpatient and inpatient settings.

Outcomes: Weight gain and BMI, Eating disorder (ED) symptoms including ED cognitions and Behaviours, anxiety, depression and adverse effects.

Study design: All studies (including case reports and case series) in English language published between the years 1996 and 2019, except reviews.

Exclusion Criteria

1. Concurrent use of any other antipsychotic medication.
2. Anorexia Nervosa Comorbid with severe neurological disorder or medical conditions that would be considered to significantly impact treatment or recovery from the eating disorder.
3. Co-morbid mental disorders like Schizophrenia, Bipolar Affective Disorder, Psychosis Not Otherwise Specified.

Results: From the pool of 246 potentially eligible references, 28 studies were included (2 randomised controlled trials, 10 before and after studies, 3 case series and 13 case reports).

- ❑ Overall, these studies suggest that, albeit small, there is evidence that olanzapine use promotes weight restoration and improves eating disorder symptoms, especially in patients with low baseline body mass index (BMI).
- ❑ Initiation of olanzapine at low doses and slow titration minimises likelihood of adverse effects. Longer duration of treatment (10 weeks and more) appears to have potentially sustainable benefits on improving eating disorder symptoms.

Clinical Implications:

- ❑ For those on the higher range (BMI more than 17.5) a smaller dose and slow titration needs to be considered to avoid rapid and excess weight gain. Small doses between 2.5 to 10mg were found to be effective.
- ❑ Low doses at initiation and slow titration avoids emergence of adverse effects.
- ❑ Though duration of treatment as early as 5 weeks has shown benefit with weight restoration, durations longer than 10 weeks show sustainable improvements with weight and other associated eating disorder symptoms.

Research/Methodological implications:

- ❑ A major difficulty with recruiting patients with Anorexia nervosa for randomized controlled research trials and high dropout rates has been mentioned in published articles (Norris et al 2007) as the objective of weight restoration can be contrary to the belief held by the patients with AN.
- ❑ As studies with longer duration of follow up show promising benefits with improvement in eating disorder symptoms, it is important for future research to design trials with longer follow-up durations to truly understand the effectiveness of Olanzapine in improving the eating disorder symptoms including ED cognitions and behaviours measured by standardized rating scales.
- ❑ Future trials must consider the challenges associated and hence develop innovative study designs with larger sample size, consider longer duration of follow up, use weight measures and rating scales which are comparable and evaluate the impact on comorbidities like depression and anxiety of olanzapine treatment.

Conclusion:

- ❑ There is emerging evidence of the potentially beneficial role of Olanzapine treatment in children and adolescents with anorexia nervosa.
- ❑ Due to the difficulties in recruitment of cases for Randomized controlled trials (RCTs) in this population innovative study designs are needed to expand the evidence base for the use of olanzapine treatment in AN.
- ❑ Longer term studies are important to understand the role of olanzapine in improving eating disorder symptoms and other comorbidities including its effect on weight restoration.