Olanzapine Use as an Adjunctive Treatment for Hospitalized Children with Anorexia Nervosa: Case Reports

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Abstract: **Objective:** *A recent case report suggested that olanzapine resulted in improved weight gain and maintenance, as well as decreased anxiety and agitation, for two hospitalized inpatients with anorexia nervosa (AN). However, a subsequent larger case study did not show a relationship between the use of olanzapine and rate of weight gain among a primarily adult population. The aim of this case report was to clinically examine the therapeutic benefit and tolerability of olanzapine as an adjunctive treatment for four children with AN in a pediatric inpatient setting.* **Results:** *Olanzapine use was associated with considerable weight gain and maintenance, with an average rate of weight gain during hospitalization of 0.99 kg per week. In addition to weight gain, olanzapine was associated with a clinically notable decrease in levels of agitation and premeal anxiety and almost immediate improvement in sleep, general functioning, and overall compliance with treatment. Olanzapine was also well tolerated in these young patients.* **Discussion:** *These case report findings warrant more controlled research, including randomized controlled studies, to better determine the therapeutic benefits and safety of olanzapine use in children with AN. © 2002 by Wiley Periodicals, Inc.* Int J Eat Disord 33: 98–103, 2003.

Key words: *anorexia nervosa; children; olanzapine; hospitalization*

INTRODUCTION

The current knowledge about anorexia nervosa (AN) indicates that it is a complex, serious, and often chronic condition that may require a variety of treatment modalities at different stages of illness and recovery (Mayer & Walsh, 1998). Typical treatment involves a multidisciplinary approach including nutritional rehabilitation, psychological intervention, and pharmacotherapy (American Psychiatric Association [APA], 2000).

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Because body mass index (BMI) at discharge is predictive of future recurrence (Baran, Weltzin, & Kaye, 1995), a main goal of treating inpatients with AN is weight restoration. However, severely ill patients have a longer hospital stay and the high cost of providing extended treatment to inpatients suggests a need to identify more cost-effective treatments without compromising long-term outcome (Jenkins, 1987).

Several psychotropic medications have been used to treat eating disorder patients either in addition to or instead of psychologically based treatment (Johnson, Tsoh, & Varnado, 1996). Controlled studies have shown no benefits in terms of speed or degree of recovery with the addition of fluoxetine to nutritional and psychological intervention in the treatment of hospitalized malnourished patients with AN when patients were still malnourished (Ferguson, LaVia, Crossan, & Kaye, 1999). However, there is evidence that weight-restored patients may benefit psychologically by the adjunctive use of fluoxetine (Kaye et al., 2001), which highlights the importance of weight gain in the treatment and recovery of AN patients.

Typical neuroleptics have been used to treat AN patients with some evidence of success, but their use may be limited due to severe side effects (Dally & Sargant, 1966). Clinicians are increasingly using low doses of newer novel antipsychotic medications as an alternative because of a more favorable side effect profile (APA, 2000). These medications have been used extensively in children and adolescents with other psychiatric conditions based on clinical evidence (Lavid, Franklin, & Maguire, 1999).

Olanzapine (Zyprexa) (Eli Lilly, Toronto, Canada) is an atypical neuroleptic principally used in the treatment of acute and chronic schizophrenia. However, it has been indicated in other psychiatric conditions (Lavid et al., 1999). There are several reasons to believe that olanzapine may be used effectively as an adjunctive treatment for AN patients. First, it is associated with significant weight gain in child (Potenza, Holmes, Kanes, & McDougle, 1999) and adult (Ganguli, Brar, & Ayrton, 2001) psychiatric patients. One study reported greater weight gain in younger patients and those with below-average BMI at initiation of treatment (Sachs & Guille, 1999). Second, it has a sedating effect and relieves agitation and negative affect (Chang & Ketter, 2000; McElroy et al., 1998). Third, it has a more favorable side effect profile than other atypical neuroleptics (Zarate, 2000). Finally, there are some case report data to support the use of olanzapine as an adjunctive treatment of AN in adults (La Via, Gray, & Kaye, 2000), although another case study did not find olanzapine use to be associated with a greater rate of weight gain (Gaskill, Treat, McCabe, & Marcus, 2001).

Mayer and Walsh (1998) noted that although the onset of AN occurs before or during adolescence or early adulthood, the overwhelming majority of pharmacologic research has been conducted among patients 18 years of age and older. Therefore, results may not be generalizable to the pediatric population. The aim of this case study was to clinically examine the therapeutic benefits and tolerability of olanzapine as an adjunctive treatment for children with AN in a pediatric inpatient, hospitalized setting.

CASE STUDIES

Case 1

Patient 1 was a 10-year-old Caucasian female with a 6-month history of AN-restricting type. She also had a 2-year history of obsessive-compulsive disorder (OCD). At the time of admission, she met criteria for major depressive disorder as defined in the 4th edition

of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; APA, 1994). This was her first admission for eating problems. Her weight at admission was 26 kg with a height of 138 cm (BMI 13.6). Her expected BMI based on her ideal body weight for height was 17.7 (Rosner, Prineas, Loggie, & Daniels, 1998). She also reported poor sleep and had severe premeal and postmeal anxiety.

She was immediately started on nasogastric tube (NGT) feeding and gained 3.9 kg within 12 days. However, when NGT feeding was replaced by oral nutrition, she experienced increased premeal and postmeal anxiety, increased agitation, poor sleep, and preoccupation with thoughts of being fat. As a result, olanzapine was administered and titrated to 2.5 mg daily. Her weight increased to 31.7 kg within 21 days of admission, with a BMI of 17.6 (expected BMI 17.7). Overall, she gained 5.7 kg within 5 weeks (an average of 1.1 kg per week) and was discharged home. She was also sleeping better, was less anxious, had fewer compulsive rituals, and fewer food preoccupations. She continued to take olanzapine 2.5 mg daily, which was discontinued successfully 3 ½ months after discharge. Her weight at that time was 34.9 kg and she was enjoying normalized eating. There was no significant side effect of olanzapine.

Case 2

Patient 2 was a 12-year-old Caucasian boy admitted to the inpatient unit with a DSM-IV diagnosis of eating disorder not otherwise specified (EDNOS) characterized by functional dysphagia, with comorbid depression and anxiety. He had a previous admission to the unit 1 month earlier with minimal weight gain, but was discharged because of extreme hospital anxiety. He gave a history of having choked on a piece of meat 2 years previously, and had since refused to eat solid food, especially at home where he would only drink a liquid meal replacement. His work at school had suffered, his sleep was poor, and parents and teachers considered him stubborn and defiant.

His admission weight was 29.8 kg, with a height of 142 cm (BMI 14.5). He had already been started on olanzapine 2.5 mg daily a week before this admission with no significant change in weight. His total duration of admission was 36 days. At the time of discharge, his weight had increased to 35.2 kg, with a BMI of 17.4. His average weight gain was 1 kg per week. During this admission, his sleep and anxiety levels were markedly improved and he was not irritable or defiant. He was able to take solids with minimal worries. He continued on olanzapine for 4 months after discharge and was reintroduced successfully to school. His weight was 40.8 kg when olanzapine was discontinued and he was not depressed or anxious.

Case 3

Patient 3 was a 12-year-old Caucasian female admitted with a diagnosis of AN-restricting type. This was her first admission. Admission weight was 27.4 kg, with a height of 149.4 cm and BMI of 12.2. She was severely emaciated. A decision to start olanzapine 2.5 mg was made at the time of admission because she was very agitated, had severe premeal anxiety, and suffered from poor sleep and selective mutism. Her admission lasted 10 weeks.

Her weight at discharge was 39.8 kg, for an average weight gain of 1.2 kg per week, with a BMI of 17.8, which approximated her expected BMI. At discharge, she was not agitated, was sleeping well, was talking to almost everyone, and was enjoying improved relationships with her family. Olanzapine was discontinued 2 weeks after discharge. She

has continued to eat well and has maintained her weight 4 months postdischarge without purging or using laxatives.

Case 4

Patient 4 was a 10-year-old Caucasian female. She was admitted with a diagnosis of AN-restricting type and comorbid OCD. At admission, her weight was 23.8 kg, height was 132.5 cm, and BMI was 13.6. She demonstrated high premeal anxiety, inability to sit down for meals, and irritability. She was treated initially with 75 mg of Luvox (Fluvoxamine) (Solvay Pharmaceuticals Inc., Scarborough, Canada) with minimal change in her symptoms of anxiety. She had gained 5 kg during 4 weeks of hospitalization, but was administered 2.5 mg of olanzapine due to her elevated anxiety and agitation. She gained an additional 2.4 kg over 3 weeks after olanzapine was initiated. More significantly, however, there was a clinical improvement in her general and premeal anxiety levels, as well as a reduction in agitation. By this time, her weight of 31.3 kg (BMI 17.5) was appropriate for her age. This was maintained during the rest of her admission, which lasted for 80 days mainly because of severe noneating or non−weight-related OCD symptoms that interfered with her school attendance before admission. At the time of discharge, she had gained 7.5 kg, her height was 134.3 cm, and BMI was 17.6. Two and a half months after discharge, she continued to maintain her weight on olanzapine 2.5 mg and Luvox 75 mg daily. She has minimal problems with meals but continues to exhibit some OCD symptoms. An attempt to increase the dosage of Luvox to control the OCD symptoms resulted in side effects. No side effects of olanzapine were reported.

DISCUSSION

To our knowledge, these four children are among the youngest patients with eating disorders to be treated with olanzapine. They were severely malnourished, agitated, and exhibited severe anxiety and food refusal behaviors. Unlike the treatment-resistant adult cases reported by La Via et al. (2000), we used olanzapine proactively on initial hospital admission and diagnosis. All our patients responded well to low-dose olanzapine (2.5 mg). None of them developed any untoward side effects, indicating that olanzapine was well tolerated in this patient population. Significant weight gain was observed in all patients, irrespective of the time of introduction of olanzapine. The weight gain following introduction of olanzapine was also associated with significant decreases in agitation and premeal and postmeal anxiety and with almost immediate improvement in compliance and sleep. These findings are clinically relevant in light of research indicating that long-term outcome is improved when weight restoration is accompanied by or followed by improved psychological functioning (Kaye et al., 2001).

If controlled clinical trials substantiate the use of olanzapine as a treatment for AN patients, it will be clinically important to determine the mechanisms of action by which the drug may improve recovery with this patient population. La Via et al. (2000) postulated that the effect of olanzapine on weight, appetite, and other behavioral symptoms may be related to 5-HT2 receptor blockade. In addition, olanzapine improved cognition in patients with schizophrenia (Purdon et al., 2000) and Alzheimer's disease (Street et al., 2000) and increased in vivo acetylcholine release greater than resperidone and haloperidol (Meltzer & O'Laughline, 2000). These findings may suggest that olanzapine has

procholinergic activity, rather than anticholinergic activity, as previously reported in in vitro studies (Canadian Pharmacists Association, 2001), due to its blockade of M2 and 5-HT3 and 5-HT6 receptors. It is possible that the improvements in mood, cognition, and agitation that were observed in our patients may be due, in part, to the drug's procholinergic properties.

In summary, olanzapine use was associated with weight gain in children with AN. The weight gain observed in these children may not be wholly attributed to the use of olanzapine. There were definite improvements in other psychological factors that made it easier to treat these individuals, leading to rapid improvements in their illness. These case report findings support the use of low-dose olanzapine as part of the initial treatment plan for younger, severely malnourished hospitalized children with AN. The current findings also warrant more controlled research to better determine the efficacy and tolerability of olanzapine as an adjunctive treatment for children and adolescents with AN.

REFERENCES

American Psychiatric Association. (1994). Diagnostic and statistical manual for mental disorders (4th ed.). Washington, DC: Author.

American Psychiatric Association. (2000). Practice guideline for the treatment of patients with eating disorders. Washington, DC: Author.

Baran, S.A., Weltzin, T.E., & Kaye, W.H. (1995). Low discharge weight and outcome in anorexia nervosa. American Journal of Psychiatry, 152, 1070–1072.

Canadian Pharmacists Association. (2001). Compendium of pharmaceuticals and specialties (36th ed.). Ottawa, Canada: Author.

Chang, K.D., & Ketter, T.A. (2000). Mood stabilizer augmentation with olanzapine in acutely manic children. Journal of Child and Adolescent Psychopharmacology, 10, 45–49.

Dally, P., & Sargant, W. (1966). Treatment and outcome of anorexia nervosa. British Medical Journal, 2, 793–795.

Ferguson, C.P., La Via., M.C., Crossan, P.J., & Kaye, W.H. (1999). Are serotonin selective reuptake inhibitors effective in underweight anorexia nervosa? International Journal of Eating Disorders, 25, 11–17.

Ganguli, R., Brar, J.S., & Ayrton, Z. (2001). Weight gain over 4 months in schizophrenia patients: A comparison of olanzapine and risperidone. Schizophrenia Research, 49, 261–267.

Gaskill, J.A., Treat, T.A., McCabe, E.B., & Marcus, M.D. (2001, May). Does olanzapine affect the rate of weight gain among inpatients with eating disorders? Paper presented at the International Conference on Eating Disorders and Clinical Teaching Day, Vancouver, Canada.

Jenkins, M.E. (1987). An outcome study of anorexia nervosa in an adolescent unit. Journal of Adolescence, 10, 71–81.

Johnson, W.G., Tsoh, J.Y., & Varnado, P.J. (1996). Eating disorders: Efficacy of pharmacological and psychological interventions. Clinical Psychology Review, 16, 457–478.

Kaye, W.H., Nagata, T., Weltzin, T.E., Hsu, L.K., Sokol, M.S., McConaha, C., Plotnicov, K.H., Weise, J., & Deep, D. (2001). Double-blind placebo-controlled administration of fluoxetine in restricting- and restricting-purging-type anorexia nervosa. Biological Psychiatry, 49, 644–652.

La Via, M.C., Gray, N., & Kaye, W.H. (2000). Case reports of olanzapine treatment of anorexia nervosa. International Journal of Eating Disorders, 27, 363–366.

Lavid, N., Franklin, D.L., & Maguire, G.A. (1999). Management of child and adolescent stuttering with olanzapine: three case reports. Annals of Clinical Psychiatry, 11, 233–236.

Mayer, L.E.S., & Walsh, B.T. (1998). Eating disorders. In B.T. Walsh (Ed.), Child psychopharmacology (pp. 149–174). Washington, DC: American Psychiatric Press.

McElroy, S.L., Frye, M., Denicoff, K., Altshuler, L., Nolen, W., Kupka, R., Suppes, T., Keck, P.E.J., Leverich, G.S., Kmetz, G.F., & Post, R.M. (1998). Olanzapine in treatment-resistant bipolar disorder. Journal of Affective Disorders, 49, 119–122.

Meltzer, H.Y., & O'Laughline, I.A. (1999, October). Atypical antipsychotic drugs (APD) but not atypical APD increased extracellular acetylcholine levels in rat medial prefontal cortex in the absence of acetylcholinesterase inhibition. Paper presented at the Society for Neuroscience 29th Annual Conference, Miami Beach.

Potenza, M.N., Holmes, J.P., Kanes, S.J., & McDougle, C.J. (1999). Olanzapine treatment of children, adolescents, and adults with pervasive developmental disorders: An open-label pilot study. Journal of Clinical Psychopharmacology, 19, 37–44.

Purdon, S.E., Jones, B.D., Stip, E., Labelle, A., Addington, D., David, S.R., Breier, A., & Tollefson, G.D. (2000). Neuropsychological change in early phase schizophrenia during 12 months of treatment with olanzapine, risperidone or haliperidol. The Canadian Collaborative Group for research in schizophrenia. Archives of General Psychiatry, 57 (3), 249–258.

Rosner, B., Prineas, R., Loggie, J., & Daniels, S.R. (1998). Percentiles for body mass index in U.S. children 5 to 17 years of age. Journal of Pediatrics, 132, 211–222.

Sachs, G.S., & Guille, C. (1999). Weight gain associated with use of psychotropic medication. Journal of Clinical Psychiatry, 60, 16–19.

Street, J.S., Clark, W.S., Gannon, K.S., Cummings, J.L., Bymaster, F. P., Tamura, R.N., Mitan, S.J., Kadam, D.L., Sanger, T.M., Feldman, P.D., Tollefson, G.D., & Breier, A. (2000). Olanzapine treatment of psychotic and behavioral symptoms in patients with Alzheimer disease in nursing care facilities: A double-blind, randomized, placebo-controlled trial. The HGEU Study Group. Archives of General Psychiatry, 57 (10), 968–976.

Zarate, C.A.J. (2000). Antipsychotic drug side effect issues in bipolar manic patients. Journal of Clinical Psychiatry, 61 (Suppl. 8), 52–61.