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Case Report

Amantadine Treatment of Psychotropic-Induced Weight Gain in Children and Adolescents: Case Series

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ABSTRACT

Objective: **The purpose of this study was to explore whether amantadine would slow or reverse significant weight gain in children and adolescents treated with antipsychotics and/or mood stabilizers that may promote increases in weight.**

Methods: **Eight boys and one girl ages 9–16 years and their parents consented to an open trial of amantadine 100 mg po bid or tid for weight gain in children. Side effects and body mass index were determined at baseline and during amantadine treatment.** *Results:* **A mean weight gain of 10.5 kg (19.9% mean increase in body weight) occurred from baseline to the beginning of amantadine treatment. Amantadine trial length averaged 14.5 weeks (range 4–33 weeks). A planned comparison using repeated measures analysis of variance demonstrated strong support for a "slowing weight gain" mechanism ($p = 0.001$) for weight gain and body mass. Weight loss was strongly correlated with length of amantadine treatment ($p = < 0.05$). One child experienced orthostatic hypotension with concomitant stimulant medication. No other side effects or exacerbation of psychiatric symptoms was reported.**

Conclusions: **Amantadine appears to stabilize weight gain related to psychotropic medications. Decreased weight and body mass index may occur with continued amantadine usage. Controlled trials of amantadine in children and adolescents taking weight-gain-inducing psychotropics are warranted.**

INTRODUCTION

WEIGHT GAIN AND POTENTIAL ADVERSE health effects in child and adolescent psychiatric patients prescribed antipsychotic medications, lithium, and sodium valproate are beginning to be reported, similar to what is described in the adult psychiatric literature. Of 76 child and adolescent patients treated with quetiapine, risperidone, or olanzapine, 68% (52) experienced an increase in body mass index (BMI), with 26% developing a BMI greater than or equal to 2.5 standard deviations from the mean (Courvoisie et al. 2001). Six-month expo-

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sure to risperidone was associated with clinically significant weight gain in 78% of children and adolescents compared to 24% in a comparison group of psychiatric inpatients with no atypical neuroleptic exposure (Martin et al. 2000). Acute onset diabetic ketoacidosis associated with olanzapine use in a 16-year-old girl (Selva 2001) and hypertriglyceridemia associated with olanzapine in a 10-year-old boy (Nguyen and Murphy 2001) have also been described, leading to concerns about both acute and longitudinal medical risks of obesity.

There are no currently proven published pharmacologic treatment strategies for severe weight gain in children and adolescents treated with atypical antipsychotics and/or mood stabilizers that promote weight gain. Standard weight-loss strategies involving diet and exercise appear to be unsuccessful. Medications typically used to treat weight gain in adults, such as stimulants, are not appropriate for use in children due to concerns about side effects, tolerance (including transient anorexia), and dependence. In addition, these medications are only recommended for brief periods of time, which is inadequate for treatment of weight gain in children who are taking maintenance medications. Newer medications such as xenical and sibutramine are now being studied in adolescents. Xenical is a reversible inhibitor of lipases that acts by inhibiting the absorption of dietary fats in the gastrointestinal tract. Sibutramine hydrochloride monohydrate works by inhibiting reuptake of norepinephrine, serotonin, and dopamine. The active ingredient is a reacemic mixture of the (+) and (−) enantiomers of a cyclobutanemethanamine (*Physicians' Desk Reference* 2002). There are no data about their use in children 12 years of age and under. In addition, sibutramine is contraindicated in combination with selective serotonin reuptake inhibitors due to the potential of precipitating a serotonin syndrome.

Preliminary studies in animals and in adult human subjects provide evidence of potential efficacy of amantadine for psychotropic-induced weight-gain treatment. Correa et al. (1987) reported weight loss with amantadine in patients using typical antipsychotics; they suggested that the results were due to the ability of amantadine to reverse neuroleptic-induced hyperprolactinemia. Baptista et al. (1997) documented successful reversal of weight gain during amantadine treatment of obese rats administered atypical antipsychotics. Floris et al. (2001) described a case series of 12 adults (mean age 37) taking olanzapine, approximately 10 mg/day, for mood instability and/ or psychotic symptoms. Subjects were given 100 to 300 mg/day of amantadine in divided doses. In all subjects, weight gain stopped when amantadine was begun, and in all but one patient, body weight gradually decreased with a mean weight loss of 3.5 kg over a mean of 21 weeks. No deterioration of psychiatric symptoms and no adverse effects were documented.

A clinically practical pharmacologic agent for the treatment or prevention of psychotropic-induced weight gain in children should have a low abuse potential, a relatively slow onset of action (to observe for possible side effects), a high safety profile including documented use in children and adolescents, and wide availability at a reasonable cost. Amantadine hydrochloride, a dopamine agonist primarily used for the treatment of Parkinson's disease and neuroleptic-induced Parkinsonism, possesses characteristics of an ideal agent. Amantadine may have weight-minimizing properties for individuals treated with weight-gain-inducing psychotropics, which include the atypical antipsychotics, sodium valproate, and lithium. The mechanism of action is unknown but may be due to improving the balance between fats and carbohydrates metabolized for energy production (Heiman et al. 2001). As measured by the criteria above, it is reasonably safe, as suggested by its long history, broad range of uses, and the wide age range of administration in humans for indications such as prophylaxis of influenza type A in children as young as newborns (Munoz et al. 1999). It also has relatively few reported interactions with other drugs (central nervous system stimulants, antihistamines, and anticholinergics increase the incidence of adverse central nervous system reactions as per Schnack et al. 1969), does not require laboratory monitoring, and (as an older generic product) is inexpensive.

Amantadine has been used safely in pediatric populations 1 year of age and older for influenza type A treatment and prophylaxis since 1976

(Advisory Committee on Immunization Practices 2000; Atkinson et al. 1986; Dolin et al. 1982). The U.S. Food and Drug Administration-approved dosage for children ages 1–9 years is 4.4–8.8 mg/kg/day, not to exceed 150 mg/day, and for children ages 10 years and up the approved dosage is 200 mg/day (100 mg bid). More than 90% of amantadine is excreted unchanged into the urine by glomerular filtration and tubular secretion. Thus, dosage needs to be reduced or possibly discontinued in patients with renal insufficiency. Patients with liver disease have no reported increase in adverse reactions to amantadine (Schnack et al. 1969). Rare cases of reversible elevated liver enzymes have been reported, but without an established causal relation to amantadine use. There is an increased incidence of seizures reported in patients with a known seizure disorder taking amantadine, but this report is contraindicated by King et al. (2001b) as outlined below. Most side effects associated with amantadine are mild and spontaneously disappear with continued usage. The most common side effects are nausea and anorexia (1–3% compared to 1% taking placebo) and central nervous system effects such as nervousness, lightheadedness, and difficulty concentrating (13% in one study compared to 4% taking placebo). One case of amantadine-associated peripheral neuropathy has been reported, but the treating neurologists in the case disagree with the hypothesis that amantadine was the cause of the neuropathy (Shulman et al. 1999; Swerdloff and Tarras 2000). Serious side effects are rare and can include marked behavioral changes, delirium, hallucinations, and seizures. Most articles, including a double-blind crossover study in 26 patients with schizophrenia (Silver and Geraisy 1996), indicate that amantadine does not potentially worsen psychosis; however, the review article by Stanton (1995) cited four studies that reported an increased risk of worsening psychosis. Amantadine has also been preferable to anticholinergics for some patients in managing antipsychotic-induced extrapyramidal side effects, as it may be less likely to cause memory impairment in adults with chronic schizophrenia (Silver and Geraisy 1996).

The use of amantadine medically has also been explored in chronic fatigue syndrome (Bowman et al. 1997), tardive dyskinesia (Angus et al. 1997), attention deficit hyperactivity disorder (Masters 1997), chronic hepatitis C (Goff et al. 2000), febrile catatonia and nonfebrile catatonia (Northoff et al, 1997, 1999), cerebellar dysfunction in chronic toluene abuse (Deleu and Hanssens 2000), human Borna disease (in a bipolar patient; Bode et al. 1997), heredodegenerative ataxias (Friedreich's ataxia and olivopontocerebellar atrophy; Botez et al. 1996), and sexual dysfunction associated with selective serotonin reuptake inhibitors (Shrivastava et al. 1995). Two recent studies have examined the role of amantadine in treating psychopathology in children and adolescents. The first study (King et al. 2001b) administered 150–300 mg/day openly to eight inpatients ages 5–12 years for treatment of significant disorders of impulse control, aggression, and hyperactivity. All but one subject had neurodevelopmental disorders, including mental retardation, tuberous sclerosis, autism, and seizures. All subjects were considered to have moderate to marked clinical response to amantadine, although the duration of the trials is unclear. Transient sedation, early morning awakening, and nightmares were reported as possible adverse reactions. One patient was administered three times the prescribed dose inadvertently, which resulted in temporary hallucinations.

King et al. (2001a) also reported a 4-week, double-blind, placebo-controlled study of amantadine in 39 autistic children ages 5–19 years with IQs greater than 35. No statistically significant changes were noted in the parent-rated Aberrant Behavior Checklists–Community Version (ABC-CV); however, clinician-rated ABC-CVs showed significant improvements in hyperactivity and inappropriate speech. Side effects included insomnia (21%) and somnolence (10%).

METHODS

Subjects

Eight boys and one girl ages 9–16 years (mean age = 11.8 years) and their parents gave verbal consent to a clinical open trial of amantadine after being informed that use for psychotropic-induced weight gain was not a Food

and Drug Administration-approved indication and that this medication trial was an open clinical trial. Parents were informed that amantadine has been prescribed safely in psychiatric patients and children for the indications described above. No specific dietary or exercise instructions were given. In addition, all children and their parents were told that the results of this trial might be submitted for publication. Due to the exploratory nature of the data, known safety of amantadine administration to psychiatric patients and children, and series of the primary author's own clinical patients, formal Institutional Review Board approval was not required by the University Hospitals of Cleveland Institutional Review Board. Subject details including diagnosis and concurrent medications are provided in Table 1. The amantadine trials began in April 2000. End date for analysis of data was January 2001.

Dosing

Amantadine doses were started at 100 mg daily for the first week and increased to 100 mg twice daily at week 2 if no side effects were identified. Two patients' doses were increased to 100 mg three times daily after no significant change in appetite reduction or weight was noted. The length of amantadine trials ranged from 4–33 weeks, with a mean of 14.2 weeks.

Measurements

All children had a baseline weight and height recorded in the clinical chart prior to onset of or continued significant weight gain on the psychotropics described above. Weight and height were recorded at all clinical follow-up visits. Parents and children were separately asked about any possible side effects since beginning amantadine at each visit as well.

RESULTS

Group results are presented in Table 2. The data were normally distributed. Individual data are presented in Table 3. Data were again roughly normal in distribution. Paired-samples,

TABLE 1. SUBJECT CHARACTERISTICS

Subject no.	*Age (years)*	*Sex*	*Race*	*DSM-IV diagnosis*	*Concomitant medications*
1	16	Female	Caucasian	Schizoaffective disorder, bipolar type	Pimozide, fish oil, sodium valproate
2	11	Male	Hispanic	Bipolar disorder, type I; manic, with psychotic features	Olanzapine, sodium valproate, lithium
3	9	Male	Caucasian	Pervasive developmental disorder NOS, moderate mental retardation	Thioridazine, molindone hydrochloride, guanfacine hydrochloride, lithium carbonate
4	10	Male	Caucasian	Bipolar disorder, type I; ADHD; conduct disorder, childhood onset	Adderall, olanzapine, gabapentin
5	10	Male	Caucasian	Bipolar disorder, type I; ADHD	Risperidone, sodium valproate, lithium carbonate
6	16	Male	Caucasian	Bipolar disorder, type I; ADHD	Risperidone, sodium valproate, lithium carbonate
7	12	Male	Caucasian	Bipolar disorder, type I; manic, with psychotic features	Clozapine
8	11	Male	Caucasian	Bipolar disorder, type I; ADHD	Risperidone, quetiapine, sodium valproate, dextroamphetamine, buspirone
9	13	Male	Caucasian	Bipolar disorder, type I	Quetiapine, sodium valproate, fluoxetine

ADHD = attention deficit hyperactivity disorder; DSM-IV = *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition; NOS = not otherwise specified.

TABLE 2. GROUP RESULTS FOR THE NINE SUBJECTS

	Minimum	*Maximum*	*Mean*
Age (years)	9	16	12
Baseline weight	25.2	81.8	51.5
Baseline to AMT (time in weeks)	5	58	33
Weight at AMT start	40.1	93.4	62.1
Change in weight (baseline–AMT start)	1.8	22.5	10.5
Weight at AMT end	41.4	86.9	61.4
Change in weight (AMT start–end)	−6.5	7.1	−0.689
Weeks on AMT	4	33	14.2
Baseline BMI	14.7	32.7	23.1
BMI at AMT start	20.7	35.9	27.4
BMI at AMT end	21	32.5	26.7
Change in BMI (AMT start–end)	−3.4	3.1	−0.733

All weights are expressed in kilograms; BMIs are expressed in kg/m^2.
AMT = amantadine; BMI = body mass index.

two-tailed t tests showed significant increases in group weight and BMI from baseline to the start of amantadine at the $p = 0.001$ level. Two planned comparisons were made using repeated measures within-subject analysis of variance. The first comparison tested a "slowing" hypothesis, whereby the means at baseline and follow-up of the amantadine regimen were expected to be approximately equal, and both would be higher than the initial weight at outset of treatment. The data strongly support a slowing hypothesis, $F(1, 8) = 24.28$, $p = 0.001$. The slowing hypothesis also was supported when examining BMI instead of weight in kilograms, $F(1, 8) = 22.64$, $p = 0.001$.

In the second comparison, we examined whether weight actually decreased across subjects when the amantadine baseline weight was compared to the termination weight (Fig. 1). On average, there was no significant decrease between the beginning and end of the amantadine regimen in terms of weight, $F(1, 8) = 0.31$, $p = 0.591$, or BMI, $F(1, 8) = 1.20$, $p = 0.305$. There was no significant increase in weight during the amantadine trial according to paired t tests. However, weight change was strongly correlated with the length of amantadine treatment, $r = -0.63$, $p < 0.05$. Scatterplots (Fig. 2) clearly reveal that the subject on clozapine was an outlier in the direction of continued significant weight gain (7.1 kg). The association between length of time taking amantadine and weight change becomes even stronger when clozapine is excluded from the analysis, $r = -0.93$, $p < 0.001$.

Weight loss of more than 2 kg was observed in 44% (4/9) of patients without reported side effects. Of the remaining five patients, one

TABLE 3. INDIVIDUAL RESULTS

Subject	*Baseline weight (kg)*	*Time (weeks)*	*Weight at AMT start (kg)*	*Weight gain (kg/week)*	*Weight at AMT end (kg)*	*Weight change (kg)*	*Weeks on AMT*	*BMI 1*	*BMI 2*	*BMI 3*
1	80.1	32	93.4	0.4	86.9	−6.5	33	28.5	35.9	32.5
2	40.7	41	63.2	0.55	60.3	−2.9	20	20.7	28.9	27.3
3	36	48	42.8	0.14	42.2	−0.6	13	21.5	24.1	23.3
4	25.2	58	40.1	0.26	41.4	+1.3	5	14.7	20.7	21.0
5	46.8	9	48.6	0.2	50.5	+1.9	4	21.6	22.8	24.0
6	77.7	29	87.3	0.33	85.2	−2.1	13	27.8	30.2	28.3
7[a]	42.1	25	52.7	0.42	59.6	+7.1	12	20.6	25.2	28.3
8	33.9	51	45.7	0.23	44.7	−1.0	4	20.2	24.2	23.3
9	81.8	5	85.2	0.68	81.8	−3.4	24	32.7	34.8	32.2

AMT = amantadine; BMI = body mass index (in kg/m^2); BMI 1 = BMI at baseline; BMI 2 = BMI at start of AMT; BMI 3 = BMI at AMT end.
[a]Patient on clozaril.

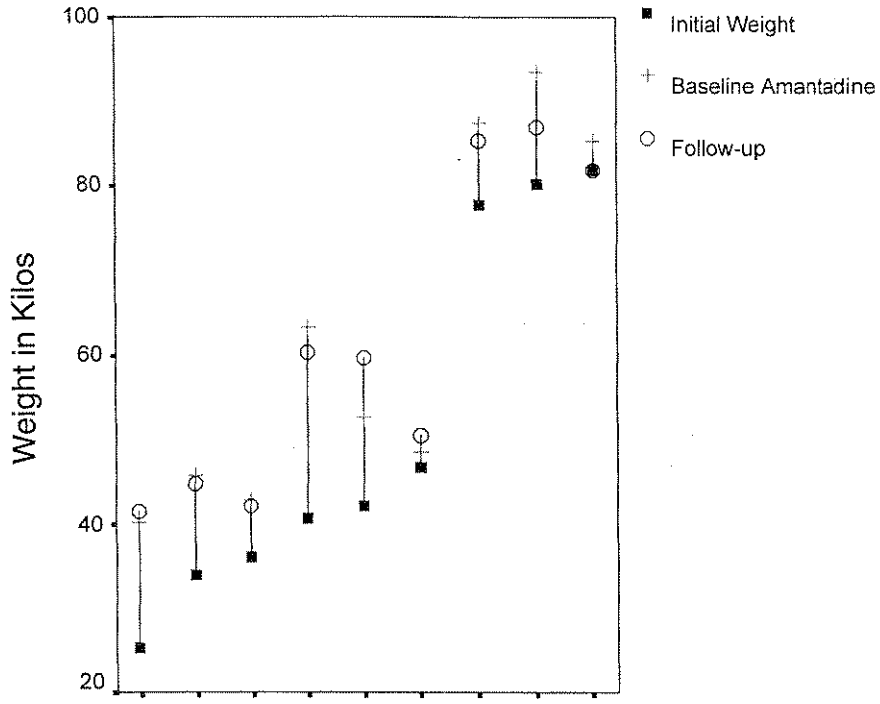

FIG. 1. Weight change in kilos over course of treatment.

could not tolerate the trial due to orthostatic changes in blood pressure and tachycardia associated with complaints of dizziness and palpitations while taking concomitant stimulant medication. No patient experienced exacerbation of psychiatric symptoms while taking amantadine.

Of the patients who lost weight, average BMI decreased by 3.4 kg/m^2 over the mean course of 14.2 weeks. In addition to these objective results, several patients and their parents reported noticeable decreases in appetite as well as the frequency of eating and amount of food consumed while taking amantadine. One par-

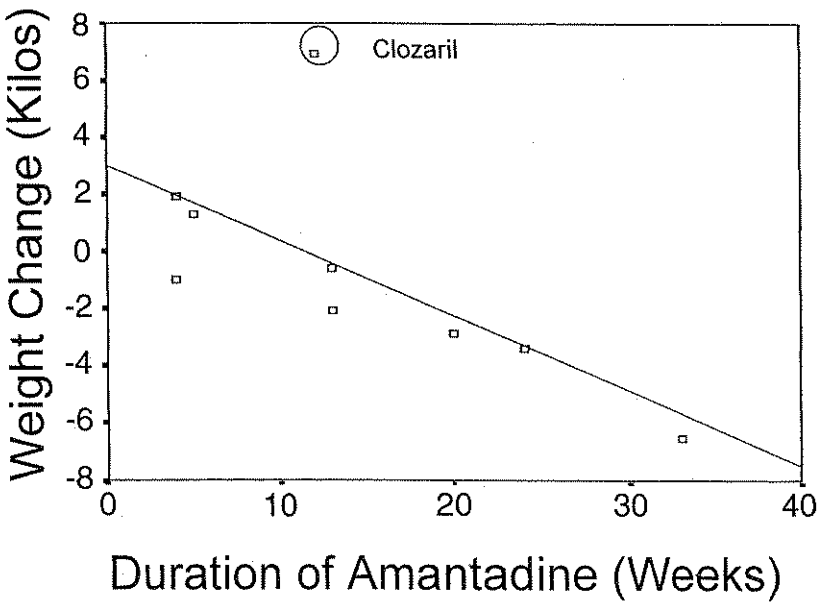

FIG. 2. Weight change as a function of duration of amantadine regimen.

ent described the anorectic effect as short-lasting; if the child missed or took the second dose late in the day, an increase in appetite similar to that at baseline was experienced. No negative effects were noted on growth for any subject.

DISCUSSION

Weight gain on antipsychotics and mood stabilizers is a significant problem both for the overall health of pediatric patients and their long-term compliance with treatment. The mechanisms of this weight gain are poorly understood. Reversal of weight gain has been shown recently with the use of metformin, an oral hypoglycemic medication primarily used for type 2 diabetes mellitus. In seven adolescents, concurrent metformin use at doses of 500–1,500 mg/day was shown to result in significant weight loss while being well tolerated, without serious adverse events or changes in liver function (Cottingham et al. 2000). However, there are drawbacks to metformin, which include the need for periodic bloodwork to monitor liver functions and the possibility of precipitating hypoglycemia in patients who are not hyperglycemic/insulin resistant. Because of these concerns, amantadine is preferable to metformin.

Our results demonstrate significant weight gain prior to the beginning of the amantadine trial, with weight on average then stabilized during administration of amantadine. Our findings also suggest that amantadine may be associated with decreases in weight and BMI with continued use. Three children participated in the trial for 5 weeks or less: one due to orthostatic hypotension and tachycardia associated with stimulant use as mentioned above and the other two due to lack of compliance. They were included in the analysis. This may skew the data toward actually showing less effectiveness than may be present. Additionally, the child taking clozaril continued to gain a significant amount of weight, although a cursory review of the pattern of his weight gain once amantadine was discontinued suggested that amantadine may have slowed weight gain. His mother later asked to resume amantadine. Clozaril appears to be different from the other weight-gain-inducing psychotropics in both the magnitude of weight gain as well as the limited effectiveness of amantadine for this subject. Descriptions by some of the subjects' families of acute onset of appetite suppression suggest that the mechanism of action of amantadine may also have a central component at the level of the appetite regulatory center in the hypothalamus.

Limitations of this study include its open and uncontrolled nature as well as the short time of follow-up in several noncompliant patients, which could indicate potential lack of benefit. Subjects who began to experience weight loss or attenuation may have been able to put other weight-reducing strategies into place more successfully. The attenuation hypothesis may be crucial in enhancing compliance in future subjects; during a discussion of potential benefits of amantadine, parents and children should understand that the intervention may not prevent weight gain but slow it.

This study examines a new role for amantadine in prevention of weight gain and mediation of weight loss in children and adolescents treated with weight-inducing psychotropic agents. Significant weight gain is a critical side effect to address in young psychiatric patients for several reasons that encompass overall quality of life. Large weight gain typically results in a negative body image and lowered self-esteem, which are already fragile in the child and adolescent with mental illness. Overweight patients also may experience an increase in dysphoria and a sense of hopelessness, resulting in increased depressive symptomatology. (Our patient taking clozapine expressed a wish to die associated with futility over his loss of control over regulation of body weight.) Amantadine may be of benefit in the prevention of morbidity associated with obesity, such as hypertension, hypercholesterolemia and hyperlipidemia, and diabetes, which would positively influence the future overall health of the individual child/adolescent, decreasing economic costs and suffering associated with chronic systemic illnesses in young patients.

As our results are uncontrolled preliminary data, further prospective randomized controlled studies are needed to establish efficacy and determine potential long-term applicability of this novel use for amantadine. Addi-

tional research should be directed toward establishing a mechanism of action and determining whether weight changes are associated with changes in metabolic parameters in the child and adolescent population.

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REFERENCES

Advisory Committee on Immunization Practices: Prevention and control of influenza. MMWR Morb Mortal Wkly Rep 49;(RR-3):16–29, 2000.

Angus S, Sugars J, Boltezar R, Koskewich S, Schneider NM: A controlled trial of amantadine hydrochloride and neuroleptics in the treatment of tardive dyskinesia. J Clin Psychopharmacol 17:88–91, 1997.

Atkinson WL, Arden NH, Patriarca PA, Leslie N, Lui KJ, Gohd R: Amantadine prophylaxis during an institutional outbreak of type A (H1N1) influenza. Arch Int Med 146:1751–1756, 1986.

Baptista T, Lopez ME, Teneud L, Contreras Q, Alastre T, de Quijada M, Araujo de Baptista E, Alternus M, Weiss SR, Musseo E, Paez X, Hernandez L: Amantadine in the treatment of neuroleptic-induced obesity in rats: Behavioral, endocrine, and neurochemical correlates. Pharmacopsychiatry 30:43–54, 1997.

Bode L, Dietrich DE, Stoyloff R, Emrich HM, Ludwig H: Amantadine and human Borna disease virus in vitro and in vivo in an infected patient with bipolar depression. Lancet 349:178–179, 1997.

Botez MI, Botez-Marquard T, Elie R, Pedraza OL, Goyette K, Lalonde R: Amantadine hydrochloride treatment in heredodegenerative ataxias: A double blind study. J Neurol Neurosurg Psychiatry 61:259–264, 1996.

Bowman MA, Kirk JK, Michielutte R, Priesser JS: Use of amantadine in chronic fatigue syndrome. Arch Int Med June 157:1264–1265, 1997.

Correa N, Opler LA, Kay SR, Birmaher B: Amantadine in the treatment of neuroendocrine side effects of neuroleptics. J Clin Psychopharmacol 7:91–95, 1987.

Cottingham EM, Morrison JA, Barton BA: Metformin leads to weight loss in adolescents who gained weight on psychotropic drugs. Chicago, American Psychiatric Association Annual Meeting, May 17, 2000 (poster).

Courvoisie HE, Koo H, Horrigan JP, Barnhill LJ. A review of weight gain in a pediatric population treated with atypical antipsychotics. National Clinical Drug Evaluation Unit Annual Meeting, Phoenix, Arizona, June 2001 (research poster).

Deleu D, Hanssens Y: Cerebellar dysfunction in chronic toluene abuse: Beneficial response to amantadine hydrochloride. J Toxicol Clin Toxicol 38:37–41, 2000.

Dolin R, Reichman RC, Madore HP, Maynard R, Linton PN, Webber-Jones J: A controlled trial of amantadine and rimantadine in the prophylaxis of influenza A infection. N Engl J Med 307:580–584, 1982.

Floris M, Lejeune J, Deberdt W: Effect of amantadine on weight gain during olanzapine treatment. Eur Neuropsychopharmacol 11(2):181–182, 2001.

Goff JS, Reveille RM, Johnson J: Treatment of hepatitis C with amantadine. Dig Dis Sci 45(7):1389–1391, 2000.

Heiman ML, Leader JD, Breier A: Preclinical study on the mechanisms underlying weight gain during olanzapine treatment. Chicago, American Psychiatric Association Annual Meeting, 2001 (poster NR 293).

King BH, Wright DM, Handen BL, Sikich L, Zimmerman AW, McMahon W, Cantwell E, Davanzo PA, Dourish CT, Dykens EM, Hooper SR, Jaselskis CA, Leventhal BL, Levitt J, Lord C, Lubetsky MJ, Myers SM, Ozonoff S, Shah BG, Snape M, Shernoff EW, Williamson K, Cook EH Jr: Double-blind, placebo-controlled study of amantadine hydrochloride in the treatment of children with autistic disorder. J Am Acad Child Adolesc Psychiatry 40:658–665, 2001a.

King BH, Wright DM, Snape M, Dourish CT: Case series: Amantadine open-label treatment of impulsive and aggressive behavior in hospitalized children with developmental disabilities. J Am Acad Child Adolesc Psychiatry 40:654–657, 2001b.

Martin A, Landeau J, Leebens P, Ulizio K, Cicchetti D, Scahill L, Leckman JF: Risperidone-associated weight gain in children and adolescents. A retrospective chart review. J Child Adolesc Psychopharmacol 10:259–268, 2000.

Masters KJ: Alternative medications for ADHD [letter to the editor]. J Am Acad Child Adolesc Psychiatry 36:301–302, 1997.

Munoz FM, Campbell JR, Atmar RL, Garcia-Prats J, Baxter BD, Johnson LE, Englund JA: Influenza A virus outbreak in a neonatal intensive care unit. Pediatr Infect Dis J 18:811–815, 1999.

Nguyen M, Murphy T: Olanzapine and hypertriglyceridemia [letter to the editor]. J Am Acad Child Adolesc Psychiatry 40:133, 2001.

Northoff G, Eckert J, Fritze J: Glutamatergic dysfunction in catatonia? Successful treatment of three acute akinetic catatonic patients with the NMDA antagonist amantadine. J Neurol Neurosurg Psychiatry 62:404–406, 1997.

Northoff G, Lins H, Boker H, Danos P, Bogerts B: Therapeutic efficacy of N-methyl D-aspartate antagonist amantadine in febrile catatonia. J Clin Psychopharmacol 19:484–486, 1999.

Physicians' Desk Reference: Montvale (New Jersey), Medical Economics, 2002.

Selva K, Scott S: Diabetic ketoacidosis associated with olanzapine in an adolescent patient. J Pediatr 138:936–938, 2001.

Schnack H, Wewalka F, Guttmann G: Liver function during amantadine hydrochloride medication in compensated liver disease. Int Z Pharmakol Ther Toxikol 2:185–187, 1969.

Shrivastava RK, Shrivastava S, Overweg N, Schmitt M: Amantadine in the treatment of sexual dysfunction associated with selective serotonin reuptake inhibitors. J Clin Psychopharmacol 15:83–84, 1995.

Shulman LM, Minagar A, Sharma K, Weiner WJ: Amantadine-induced peripheral neuropathy. Neurology 53(8):1862–1865, 1999.

Silver H, Geraisy N: Amantadine does not exacerbate positive symptoms in medicated, chronic schizophrenic patients: Evidence from a double-blind crossover study. J Clin Psychopharmacol 16:463–464, 1996.

Stanton JM: Weight gain associated with neuroleptic medication: A review. Schizophr Bull 21:463–472, 1995.

Swerdloff MA, Tarras SC: Amantadine-induced peripheral neuropathy. Neurology 55:456–457, 2000.

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