A Retrospective Naturalistic Study of Ziprasidone for Irritability in Youth with Autism Spectrum Disorder

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Abstract

Objective: The purpose of this study was to assess the impact of ziprasidone monoantipsychotic treatment targeting irritability in a naturalistic outpatient autism spectrum disorder (ASD) clinical setting.

Methods: We examined the use of ziprasidone, predominantly in combination with other psychotropic agents, targeting irritability in 42 youth with ASD in a large ASD-specific treatment database. Mean age at start of treatment, treatment duration, final dose, body mass index (BMI), BMI Z score, and Clinical Global Impressions-Improvement Scale (CGI-I) score at final visit were determined, and changes with treatment were analyzed using paired *t* tests. Cardiac corrected QT (QTc) interval data were extracted from electrocardiograms when available.

Results: Mean age at start of treatment was 11.8 years. And final mean dose of ziprasidone was 98.7 mg/day or 1.7 mg/kg/day. Seventeen (40%) participants were considered treatment responders based on the CGI-I. No changes in QTc (although only examined in nine participants), weight, BMI, or other vital signs were noted, with ziprasidone use. The rate of treatment response was less than what has been reported for the two atypical antipsychotics, risperidone and aripiprazole, approved by the Food and Drug Administration (FDA) for the treatment of irritability in autistic disorder. The response rate with ziprasidone may be more consistent with response rates for other atypical antipsychotics, although none of these agents has been studied in larger-scale double-blind, placebo-controlled trials. The lower rate of response to ziprasidone in this open-label trial is likely influenced by the treatment-refractory nature of the population studied.

Conclusions: The weight neutrality of ziprasidone appears favorable compared with other second generation antipsychotics in this population. The response rate to ziprasidone targeting irritability may be lower than response rates associated with FDA-approved agents for this indication. Overall, ziprasidone use appeared well tolerated in youth with ASD.

Introduction

AUTISM SPECTRUM DISORDER (ASD) IS CHARACTERIZED by marked impairment in social and communicative functioning combined with restricted interests and repetitive behaviors (American Psychiatric Association 2013). In addition to the core features of ASD, a number of associated behaviors occur in many, but not all, individuals with the disorder. Among interfering associated behaviors, irritability marked by aggression, self-injury, and severe tantrums cause serious distress for both the child and the family, and this behavior cluster includes the most frequently reported coexisting conditions in ASD (Mills and Wing 2005). Irritability has been the focus of significant pharmacotherapy research in ASD. The United States Food and Drug Administration (FDA) has approved risperidone and aripiprazole for irritability in youth with ASD. However, given the tolerability issues with these drugs, particularly in youth (primarily weight gain), and given cases refractory to the use of first-line agents (Adler et al. 2015),

other psychotropic drugs, including ziprasidone, are frequently used off-label for this indication, with limited available safety or efficacy data.

One of the most-cited advantages of ziprasidone is its reported weight neutrality (De Hert et al. 2011). In a meta-analysis of randomized placebo-controlled trials (RCTs) examining the metabolic effects of second generation antipsychotics in youth regardless of diagnosis, De Hert and colleagues (2011) found the average weight gain in trials of risperidone and aripiprazole to be 1.04 kg and 2.37 kg, respectively. The average weight gain for ziprasidone in the analysis was 0.49 kg, and was not significantly different from placebo. There were, by far, more studies examining the use of risperidone (15 total, 5 in participants with ASD, with ages ranging from 2.5 to 62 years, and with durations of treatment ranging from 4 to 24 weeks) in the analysis. There were five RCTs of aripiprazole in total, with two completed in the ASD population (ages 5–18 years, treatment durations 4–8 weeks) and only three for ziprasidone (ages 7–19 years, treatment durations 3–8 weeks). No RCTs

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for ziprasidone in autism have been completed. In ASD, Wink and colleagues (2014) found that body mass index (BMI) Z score change per year of treatment was 0.56 and 0.53 for aripiprazole and risperidone, respectively. This weight gain carries with it significant risks for metabolic complications. BMI Z score may be a better measure of weight effects in youth by controlling for age and gender, in addition to height (Must and Anderson 2006).

There is some suggestion in the literature that ziprasidone may effectively target irritability in individuals with ASD (for review see Polite and McDougale 2014). To date, no placebo-controlled trials of ziprasidone have been conducted in ASD. Reports of open-label ziprasidone use in ASD have included 36 individuals: 24 children and adolescents and 12 adults. There has been one study looking exclusively at adults. Cohen and colleagues (2004) completed a retrospective chart review of 10 adults with ASD treated with ziprasidone for at least 6 months, the majority of which (90%) had profound intellectual disability. Six adults demonstrated improvement in maladaptive behavior as measured by the Maladaptive Behavior Scale at a mean daily dose of ziprasidone of 128 ± 41 mg. Eight of the participants demonstrated weight loss on ziprasidone, probably because of losing weight gained while previously taking other atypical antipsychotics prior to use of ziprasidone.

There have been two case reports of the use of ziprasidone in youth with ASD (Goforth and Rao 2003; Duggal 2007). The first (Goforth and Rao 2003) was of a 7-year-old boy with ASD, intellectual disability, severe agitation, irritability, and impulsivity who had not responded to amphetamine salts, guanfacine, sertraline, and valproic acid. The child responded to a very low dose (10 mg) of ziprasidone, and his improvement was sustained over an 8 month follow-up using the Clinical Global Impressions Improvement (CGI-I) (Guy, 1976) scale. Duggal (2007) reported a case of a 15-year-old boy with comorbid attention-deficit/hyperactivity disorder (ADHD) and moderate intellectual disability, who had not improved with trials of risperidone (no effect) and quetiapine (weight gain). The patient demonstrated improvement based on parental report and CGI-I, with rapid titration of ziprasidone to 60 mg twice daily.

McDougale et al. (2002) reported a case series of 10 children and adolescents and 2 young adults with ASD (11 of whom had comorbid intellectual disability) who were treated with ziprasidone at doses ranging from 20 to 120 mg/day (mean dose 59.23 ± 34.76 mg/day) with dose increases based on tolerability and effect. Six (50%) were considered treatment responders, meaning that they received a rating of "much improved" or "very much improved" on the CGI-I. Five participants lost weight, five had no change, and one gained weight. Again, weight loss was likely associated with loss of weight previously gained while taking other atypical antipsychotics. Sedation was the most common side effect (4 of 12), and no cardiovascular side effects were noted.

In the most recent report on ziprasidone use in ASD, Malone et al. (2007) conducted a 6 week prospective open-label trial of ziprasidone in 12 individuals with ASD using a slow titration (over 4 weeks) of the medication with final dosing ranging from 40 to 160 mg per day (mean dose 98.3 ± 40.4 mg/day). Nine (75%) subjects were deemed treatment responders, which was determined using the CGI-I, and there was no weight gain with treatment.

A commonly reported potential disadvantage of ziprasidone use is the risk for prolongation of the cardiac corrected QT (QTc) interval (see Taylor 2003). Significant QTc interval prolongation is associated with heightened risk of developing torsade de

pointes, a potentially fatal ventricular arrhythmia. Changes in heart rate along with PR and QTc intervals have been reported in children, with relatively low doses of ziprasidone (Blair et al. 2005). Blair and colleagues (2005) completed a prospective, open-label trial in adolescents using a mean ziprasidone dose of 30 ± 13 mg/day over an average of 4.6 ± 2 months. The mean QTc prolongation was 28 ± 26 msec. In the trial of ziprasidone in ASD by Malone et al. (2007) that has been described, the mean increase in the QTc interval was 14.7 msec (ranging from -13 to 52 msec), and no participant had a QTc > 450 msec (QTcs measured 381–443 at 6 weeks).

This body of literature suggests that ziprasidone may provide a more weight-neutral option in targeting irritability in individuals with ASD than the more commonly used FDA-approved agents. This evidence base remains limited by small subject numbers, limited duration of treatment, and lack of placebo control. We sought to build upon the evidence base by describing ziprasidone use targeting irritability in youth with ASD, given the frequent use of this drug off-label for this indication. We describe aspects of ziprasidone dosing, associated vital sign and weight change, and potential clinical treatment response in a naturalistic longitudinal treatment setting.

Methods

Data were collected (longitudinal) as part of an ongoing comprehensive assessment of medication management in ASD. Data were drawn from individuals with idiopathic ASD, evaluated and treated at the Christian Sarkine Autism Treatment Center from 2004 to 2012. Data were prospectively collected during clinical treatment and retrospectively reviewed, extracted, and coded into a RedCap database. This project was approved by the local institutional review board (IRB).

We gathered data on newly initiated cases of longitudinal (two or more data points) ziprasidone monoantipsychotic treatment in youth (≤ 18 years of age at time of ziprasidone initiation) with idiopathic ASD, found in the database. ASD diagnoses were made by clinicians with experience in ASD using diagnostic criteria from the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV-TR) (American Psychiatric Association 2000). Given the use of DSM-IV-TR criteria in this report, for reporting purposes we consider ASD to be a collective term encompassing the diagnoses of autistic disorder, pervasive developmental disorder not otherwise specified (PDD-NOS), and Asperger's disorder. Intellectual disability diagnosis was based upon review of neuropsychological testing and school reports when available.

Mean age at start of treatment, treatment duration, final dose, CGI-I score at final visit, along with baseline and final BMI and BMI Z score, were determined. CGI-I scores anchored to change in irritability were assigned at the time of the visit, and were prospectively collected in medical records. Change in BMI Z score per year of treatment, change in systolic and diastolic blood pressure (BP), and changes in pulse during treatment were additionally calculated and compared using paired *t* tests. QTc interval data were extracted from electrocardiograms (ECGs) recorded in our data set if available during the time of ziprasidone treatment. In addition, we comment on concomitant medication use and reasons for ziprasidone discontinuation, when applicable.

Results

Eighty-two participants were prescribed ziprasidone during the 2004–2012 treatment period (8.2% of all treated patients). Fifty-three

TABLE 1. PARTICIPANT DEMOGRAPHICS

Demographics		ASD diagnosis		Comorbidities	
Age at Initiation (years) 11.8±3.9 (5.97–18.67)		Autistic disorder	27 (64.3%)	<i>In utero</i> drug exposure	10 (23.8%)
Sex 8 Female (19.1%) 34 Male (81.0%)		PDD-NOS	9 (21.4%)	Prematurity (<37 weeks gestation)	6 (14.3%)
Race		Asperger's disorder	6 (14.3%)	Attention-deficit/hyperactivity disorder	2 (4.8%)
Caucasian	30 (71.4%)	Intellectual disability (ID)		Anxiety disorder	1 (2.4%)
African American	3 (7.1%)	Mild ID/borderline intellectual functioning	4 (9.5%)	Bipolar disorder	
More than one race	1 (2.4%)				
Unknown/Not answered				Type 1	0
Ethnicity				Type 2	0
Hispanic	1 (2.4%)			NOS	4 (9.5%)
		Moderate ID	5 (11.9%)	Conduct disorder	0
		Severe ID	1 (2.4%)	ODD	4 (9.5%)
		ID, unspecified	8 (19.1%)	Psychotic disorder (schizophrenia, schizoaffective disorder, psychosis NOS)	0
Not Hispanic	33 (78.57%)	Unknown	5 (11.9%)	Major depressive disorder	1 (2.4%)
Unknown/not answered	8 (19.05%)	No ID	19 (45.2%)	Victim of neglect or abuse	3 (7.1%)

ASD, autism spectrum disorder; PDD-NOS, pervasive developmental disorder- not otherwise specified; ODD, oppositional defiant disorder.

received longitudinal (two or more data points) ziprasidone monoantipsychotic treatment. Of those, 42 were ≤ 18 years at time of treatment initiation (34 male, 8 female). See Table 1 for participant demographics, including comorbid diagnoses. For the group of 42 youth, the mean age at start of treatment was 11.8 years (age range 5.97–18.67 years) and the mean recorded treatment duration was 10.8 months. There were 17 subjects who remained on ziprasidone at the time data collection stopped. Doses ranged from 20 to 240 mg per day (see Table 2). Reasons for treatment cessation are outlined in Table 3.

Among the 42 participants, the majority (39 or 92.86%) had received a trial of either risperidone or aripiprazole prior to ziprasidone. Twenty-four (57.14%) children had previously received a trial of both risperidone and aripiprazole, thus meeting a definition

of having drug-refractory irritability (Adler et al. 2015). There were only three participants who had not had a documented trial with either risperidone or aripiprazole. On average, there were two prior antipsychotic drug trials before initiating treatment with ziprasidone. Antidepressants were the most commonly used concomitant drug treatment, followed by α -2 agonists (see Table 4). There were only 8 (19%) participants who were not treated with concomitant psychotropic medication while being treated with ziprasidone.

Mean ziprasidone dose at final visit was 98.7±52.0 mg/day (1.74±1.14 mg/kg; see Table 2). There was a significant increase in BMI from baseline to end-point; however, there was no significant change in participant BMI Z score from treatment initiation to final visit (see Table 2 and Table 5). The mean subject BMI Z score change per year of treatment was 0.07±0.69. There were no significant vital sign changes (Table 5). The mean CGI-I score at final visit was 3.14±1.4 (“minimally improved”). Six subjects did not have CGI-I data available for the final visit at which they were prescribed ziprasidone. Using a positive treatment response definition of a CGI-I score of 1 “very much improved” or 2 “much improved,” 17 participants (40.5%) were deemed treatment responders at the final recorded visit.

Regarding vital sign changes (Table 5), the mean QTc interval measurement for nine participants with available ECG data during ziprasidone treatment was 414 ms. No cases of prolonged

TABLE 2. CHARACTERISTICS OF ZIPRASIDONE TREATMENT

Treatment duration (months; mean±SD)	10.8±9.2 (0.4–43.7 months)
Dosage range (mean±SD)	20–240 mg/day
Final dose (mean±SD)	98.7±52.0 mg/day
	1.7±1.1 mg/kg/day
Final CGI-I (mean±SD)	3.14±1.40
	(“minimally improved”)
Treatment outcome	17 (42.7%) responders
Responders final CGI-I=1 “very much improved” or 2 “much improved”	19 (52.8%) nonresponders
QTc interval during ziprasidone treatment (mean±SD)	414±19.88 msec
BMI change per treatment year (mean±SD)	3.33±11.91
BMI Z score change per treatment year (mean±SD)	0.07±0.69

CGI-I, Clinical Global Impressions – Improvement; QTc, cardiac corrected QT; BMI, body mass index.

TABLE 3. REASONS ZIPRASIDONE MONOTHERAPY ENDED

Reason	n (%)
Added another antipsychotic	8 (19.05%)
Ineffective/lost effectiveness	8 (19.05%)
Weight gain	2 (4.76%)
Increased appetite	1 (2.38%)
Dystonia	1 (2.38%)
No reason given	4 (9.52%)
Other (unwilling to adjust dose)	1 (2.38%)

TABLE 4. CONCOMITANT PSYCHOTROPIC MEDICATION USE

Antidepressant	
Selective serotonin reuptake inhibitor (SSRI) (citalopram, fluoxetine, paroxetine, sertraline)	12 (28.6%)
Tricyclic antidepressant	1 (2.4%)
Other	6 (14.3%)
α -2 agonist	13 (31.0%)
Stimulant/ADHD medication	12 (28.6%)
Mood stabilizer	
Valproic acid	2 (4.8%)
Lamotrigine	1 (2.4%)
Topiramate	1 (2.4%)
Oxcarbazepine	1 (2.4%)
Sleep aid	
Melatonin	7 (16.7%)
Trazodone	2 (4.8%)
Free of concomitant medication	8 (19.0%)

ADHD, attention-deficit/hyperactivity disorder.

QTc interval or cardiac events were noted in our analysis. There was only one patient with a repeat ECG. This patient was placed on ziprasidone at two different times and once ECG was completed during each course of treatment with ziprasidone. No changes in systolic or diastolic BP or heart rate were noted with treatment. Mean subject BMI did increase with treatment, but a more accurate assessment of true BMI change with treatment, BMI Z score, which controls for subject age and gender, did not change with treatment.

Discussion

This report is based on the largest sample of youth with ASD treated with ziprasidone to date. It offers insight into how ziprasidone is used in a long-term naturalistic clinical setting, specifically a tertiary care center. Ziprasidone appears to be rather commonly used, most often as a third-line agent. Overall, ziprasidone appeared well tolerated. The most common reasons for ending ziprasidone monoantipsychotic therapy were addition of another antipsychotic agent or ineffectiveness. In three of the cases in which another antipsychotic was added, the medication was prescribed on an as-needed basis only, most commonly for agitation. The other additions were the result of cross-tapers or transitions to a different antipsychotic medication, and are, therefore, likely indicative of ineffectiveness; however, this was not explicitly stated. In addition, there were a number of patients prescribed ziprasidone who received the medication for only one clinic visit. It is likely that a portion of those patients who stopped ziprasidone prior to the subsequent visit did so because of ineffectiveness, meaning that the nonresponder rate to ziprasidone

may be higher than reported here. However, one may question whether an adequate trial to determine efficacy was completed if the patient was only taking the medication at one visit. Other patients may have experienced side effects leading to discontinuation, which would indicate that ziprasidone may not be as tolerable as was seen in this subset of patients.

Others were receiving ziprasidone in combination with other antipsychotic medications. Finally, it is important to note that the majority of patients were taking ziprasidone in combination with at least one other psychotropic agent; therefore, it is possible that the improvements seen were not caused by ziprasidone alone. The concomitant use of selective serotonin reuptake inhibitors (SSRIs) may also lead to an overall increase in the effective dose of ziprasidone. However, this is likely reflective of how the medication is used and evaluated in clinical practice.

Previous studies of ziprasidone in ASD have predominantly included participants with comorbid intellectual disability. Our report included a large proportion (45%) of participants who did not have intellectual disability. This differs from previously published reports examining ziprasidone use in ASD; however, it is in keeping with the most recent Centers for Disease Control (CDC) surveillance data (2014), which showed that 46% of children with ASD did not have any intellectual disability. Therefore, these data are likely representative of the general ASD population treated at tertiary care facilities. Our overall treatment response rate was lower than response rates to first-line agents, and was potentially consistent with response rates to other second-line atypical antipsychotics (Polite and McDougle 2014). This response rate, however, must be taken in the context of the drug-refractory nature of many of the subjects, making it difficult to compare this response rate to data from drug-naïve populations.

Overall, ziprasidone was not associated with significant changes in vital signs or body weight. The lack of significant weight gain, as shown with BMI Z scores, is consistent with previous reports. The lack of ziprasidone-associated weight gain is clearly different than the weight gain we have noted in similar analyses from the same database focused on risperidone ($n=70$; mean BMI Z score change per year of treatment = 0.53 ± 1.21) and aripiprazole ($n=72$; mean BMI Z score change per year of treatment = 0.56 ± 2.21) monoantipsychotic treatment (Wink et al. 2014). This is a potential significant benefit of ziprasidone. However, it is notable that the baseline BMI Z score in this study was 1.49 ± 1.41 , which is in the overweight range, whereas the baseline scores in the analyses examining risperidone and aripiprazole were 0.67 ± 1.44 and 0.64 ± 1.94 , respectively. When examining the potential for weight gain in their meta-analysis, De Hert et al. (2011) found that the number needed to harm (NNH) (the number of patients for whom one might prescribe an atypical antipsychotic before having weight gain as a significant side effect) for risperidone was 6, and for aripiprazole was 12, whereas the NNH for ziprasidone was 36, and not significantly different from placebo.

Interpretation of our cardiac QTc interval data is limited by the small sample size. Given that the treatment was completed in a naturalistic clinical setting, there was no set schedule for completing ECGs. The low rate of ECG sampling may relate to potential difficulty in obtaining ECGs from youth with ASD and associated interfering behavior, which may pose a safety problem in the case of long-term ziprasidone use.

Limitations

Our results are subject to several limitations, including the chart review nature of the analysis and potential confounding factors

TABLE 5. TREATMENT RESULTS—VITAL SIGNS

	Baseline	End-point	Two-tailed paired t test
BMI	25.72 $\pm$ 7.32	26.41 $\pm$ 6.98	$t(27)=2.25$, $p=0.03$
BMI Z score	1.49 $\pm$ 1.41	1.44 $\pm$ 1.31	$t(26)=0.71$, $p=0.49$
Systolic BP	111.86 $\pm$ 15.58	114.52 $\pm$ 11.82	$t(26)=1.37$, $p=0.18$
Diastolic BP	63.83 $\pm$ 9.69	65.63 $\pm$ 8.29	$t(26)=0.54$, $p=0.60$
Heart rate	94.29 $\pm$ 18.45	94.70 $\pm$ 16.16	$t(26)=0.68$, $p=0.50$

BMI, body mass index; BP, blood pressure.

associated with concomitant use of nonantipsychotic psychotropic drugs. In addition, diagnosis was based on expert clinical evaluation using DSM-IV-TR diagnostic criteria alone, without corroboration from gold-standard diagnostic measures such as the Autism Diagnostic Interview - Revised or the Autism Diagnostic Observation Schedule. There was also no standardized testing of intellectual functioning. Finally, this study is likely biased toward individuals with more serious psychopathology, given that it was completed at a tertiary care facility, and that many of the subjects would have been considered drug refractory when ziprasidone was initiated. Many of these weaknesses are a function of the naturalistic clinical setting in which the analysis was completed. This setting does offer the significant advantage of providing insight into the effectiveness and tolerability of the drug in real world clinical practice.

Conclusions

We believe that our findings warrant future prospective placebo-controlled study of ziprasidone in youth with ASD, particularly given the lack of weight gain associated with this agent. Such studies would benefit from standardized dosing schedules, systematic ECG collection, complete metabolic information, and other laboratory tests performed for safety, as well as use of standardized outcome measures such as the Aberrant Behavior Checklist (Aman et al. 1985). Future work will also require analysis of drug trials prior to ziprasidone use, to determine if our potential response rate is reflective of drug use in a treatment-refractory population.

Clinical Significance

Our report does offer preliminary evidence that ziprasidone is safe and well tolerated by youth with ASD. The overall effectiveness of the drug was limited in this study compared with response rates reported for risperidone and aripiprazole; however, this may be the result of the treatment-refractory nature of the sample.

Disclosures

Dr. Erickson holds equity in Confluence Pharmaceuticals, and has served as a consultant to Confluence Pharmaceuticals, Alcobra Pharmaceuticals, and the Roche Group. Dr. Wink has served as a consultant to Otsuka Pharmaceuticals. Drs. McDougale and Dominick have no potential conflicts of interest to disclose.

References

Adler BA, Wink LK, Early M, Shaffer R, Minshawi N, McDougale CJ, Erickson CA: Drug-refractory aggression, self-injurious behavior, and severe tantrums in autism spectrum disorders: A chart review study. *Autism* 19:102–106, 2015.

Aman MG, Singh NN, Stewart AW, Field CJ: The aberrant behavior checklist: A behavior rating scale for the assessment of treatment effects. *Am J Ment Defic* 5:485–491, 1985.

American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders*, 5th ed. Washington, DC: American Psychiatric Association; 2013.

Blair J, Scahill L, State M, Martin A: Electrocardiographic changes in children and adolescents treated with ziprasidone: A prospective study. *J Am Acad Child Adolesc Psychiatry* 44:73–79, 2005.

Centers for Disease Control and Prevention (CDC): Prevalence of autism spectrum disorder among children aged 8 years – autism and developmental disabilities monitoring network, 11 sites, United States, 2010. *MMWR Surveill Summ* 63:1–21, 2014.

Cohen SA, Fitzgerald BJ, Khan SR, Khan A: The effect of a switch to ziprasidone in an adult population with autistic disorder: Chart review of naturalistic, open-label treatment. *J Clin Psychiatry* 65:110–113, 2004.

De Hert M, Dobbelaere M, Sheridan EM, Cohen D, Correll CU: Metabolic and endocrine adverse effects of second-generation antipsychotics in children and adolescents: A systematic review of randomized, placebo controlled trials and guidelines for clinical practice. *Eur Psychiatry* 26:144–158, 2011.

Duggal HS: Ziprasidone for maladaptive behavior and attention-deficit/hyperactivity disorder symptoms in autistic disorder. *J Child Adolesc Psychopharmacol* 17:261–263, 2007.

Goforth HW, Rao MS: Improvement in behaviour and attention in an autistic patient treated with ziprasidone. *Aust N Z J Psychiatry* 37:775–776, 2003.

Malone RP, Delaney MA, Hyman SB, Cater JR: Ziprasidone in adolescents with autism: An open-label pilot study. *J Child Adolesc Psychopharmacol* 17:779–790, 2007.

Must A, Anderson SE: Body mass index in children and adolescents: Considerations for population-based applications. *Int J Obes* 30:590–594, 2006.

Polite LC, McDougale CJ: Atypical antipsychotics in the treatment of children and adolescents with pervasive developmental disorders. *Psychopharmacology (Berl)* 231:1023–1036, 2014.

Taylor D: Ziprasidone in the management of schizophrenia : The qt interval issue in context. *CNS Drugs* 17:423–430, 2003.

Wink LK, Early M, Schaefer T, Pottenger A, Horn P, McDougale CJ, Erickson CA: Body mass index change in autism spectrum disorders: Comparison of treatment with risperidone and aripiprazole. *J Child Adolesc Psychopharmacol* 24:78–82, 2014.

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