Efficacy and Tolerability of Ziprasidone Use in Children and Adolescents, a Systemic Review and Meta Analysis

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OBJECTIVE

The aim of this study is to examine the efficacy and tolerability of Ziprasidone in children and adolescents.

METHODS

- Literature search consisting of open label or randomized control trials (RCT) that report on Ziprasidone use in children on the PubMed database.
- Review of the literature found 13 studies (11 open label and 2 RCT) that met inclusion criteria.
- The resulting outcome measures included efficacy measures such as BPRS, YMRS, CGI-S and adverse effects such as weight gain, increase in BMI, QTc prolongation, sedation, dizziness and EPS.
- Random effects meta- analysis and meta-regression of potential moderators including age, gender, race, dosage and study duration was conducted.
- Publication bias was assessed with funnel plots.

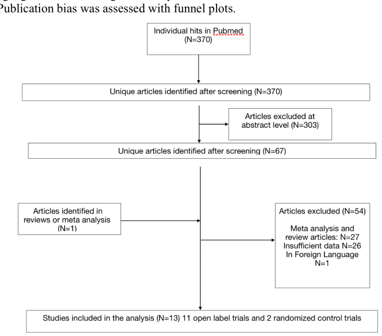
Individual hits in Pubmed (N=370)
Unique articles identified after screening (N=370)
Articles excluded at abstract level (N=303)
Unique articles identified after screening (N=67)
Articles identified in reviews or meta analysis (N=1)
Articles excluded (N=54)
Meta analysis and review articles: N=27
Insufficient data N=26
In Foreign Language N=1
Studies included in the analysis (N=13) 11 open label trials and 2 randomized control trials

Figure 1c.

RESULTS

- Data from thirteen studies was meta-analyzed (Total n= 560, mean age=13.16 years, male= 70.35% that reported the use of Ziprasidone in children and adolescents with Psychosis, Bipolar, Autism spectrum disorders and Tourette's syndrome.
- Mean Ziprasidone dose = 80.76 mg and mean study duration = 3.38 months).
- We found that Ziprasidone was efficacious in children and adolescents in measures of BPRS (-13.493, p<0.05), YMRS (-14.225, p<0.05), CGI-S (-1.430, p<0.05).
- In measures of adverse effects, Ziprasidone was not found to cause any significant weight gain (0.164, p>0.05) or change in BMI (-0.159, p>0.05).
- QTc prolongation was found to be significant (13.122, p<0.05). Most common side effects were sedation (49.3%), followed by EPS (17.9%) and Dizziness (15.5%).

DISCUSSION

- The meta-analysis provides evidence in the efficacy and safety of Ziprasidone use in children and adolescents
- Four studies reported reduction in BPRS scores. Five studies reported reduction in YMRS scores and six studies reported in CGI-S scores. All three parameters were significantly reduced demonstrating that Ziprasidone is an effective treatment option in children and adolescents.
- Six studies reported on weight change, in which four studies showed weight loss and two studies showed weight gain. The meta-analysis did not find any significant change of weight. Ziprasidone appears to be a weight neutral treatment option. Thereby an effective treatment option in children and adolescents who are obese or concerned with gaining weight.
- Five studies reported on BMI change in which two studies reported a reduction in BMI and three studies showed increase in BMI. Overall, there was no significant change in BMI, which also shows that Ziprasidone is neutral in terms of BMI and weight change.

Ziprasidone has demonstrated efficacy and neutral metabolic profile with minimal weight gain in treatment of pediatric populations.

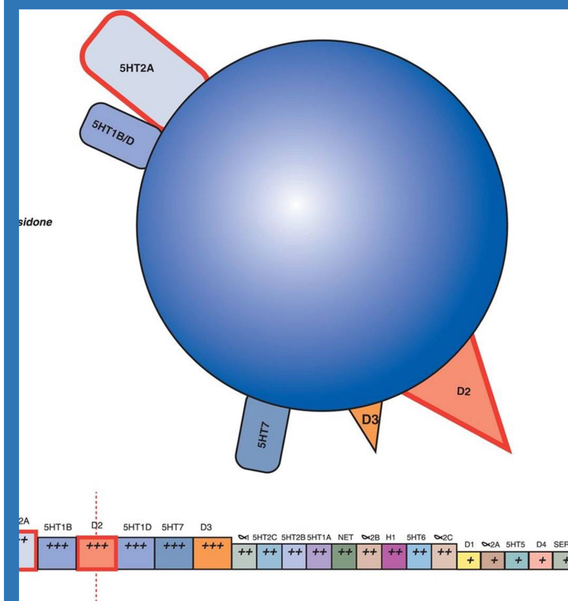

Figure 1a : Pharmacological profile of Ziprasidone

Study	Diagnosis	Age: yrs (mean)	N	Sex: Male (%)	Ethinicity: White (%)	Dosage mean	Study duration (months)
Barzman et al. (2007)	Retrospective	15	59	66	42	85	
Bastiaens et al. (2009)	Open Label	12.1	22	73	91	42.9	2
Bierderman et al. (2007)	Open Label	10.3	21	81		57.3	2
Blair et al. (2005)	Open Label	13.2	20	80	80	30	4.6
Correll et al. (2011)	Open Label	15.3	29	44.8	48.3	112.8	3.31
Delbello et al.(2008)	Open Label	13.61	23	52.17		80	6.75
Delbello et al.(2008)	Open Label	14	40	75		160	6.75
Dominick et al. (2015)	Naturalistic	11.8	42	80.95	71.4	98.7	10.8
Findling et al. (2013) a	Randomized control trial	13.59	149	56.37	81.21		1
Hrdlicka et al. (2009)	Open Label	15.8	6			96.7	0.75
Findling et al. (2013) b	Randomized control trial	15.24	193	56.47	60.1		1.5
Malone et al. (2007)	Open Label	14.5	15	80	73.3	98.3	1.5
Salle at al. (2000)	Open Label	11.3	16	87.5		28.2	1.9
Schneider et al. (2012)	Open Label	14.7	14	64	86	105	1
Mcdougle et al. (2002)	Open Label	11.62	12	83.33		59.23	3.54

Table 1: Demographics of studies

Ziprasidone is an efficacious option for use in the children and adolescent population. It does not cause significant weight gain, however QTc prolongation and sedation were found to be the most significant side effects of Ziprasidone use. Therefore, baseline EKG and thorough history must be obtained before prescribing Ziprasidone in children and adolescents.

References

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- Six studies showed QTc prolongation with Ziprasidone use in children and adolescents ranging from (3.1ms to 22.9ms). The analysis revealed the mean increase in QTc to be 13.12 which was significant. Therefore, it is important to get a baseline EKG and a thorough medical and family history of cardiac disease before starting Ziprasidone.
- Analysis for events of sedation was conducted in 9 studies, dizziness—in 5 studies and EPS—in 7 studies. Most common reported event was sedation (49.3%) followed by EPS (17.9%) and dizziness (15.5%).