

Tolerability of Zeprasidone use in Children and Adolescents: A PRISMA model systematic review and Meta-analysis

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Introduction

- * Ziprasidone is an atypical antipsychotic that has demonstrated efficacy for the treatment of bipolar disorder and schizophrenia in adults .
- * The drug has less propensity for neurological side effects, metabolic side effects and weight gain in adults.
- * Ziprasidone is FDA approved for treatment in adults but not for children and adolescents.
- * There is some preliminary evidence for Ziprasidone use in children and adolescents with several open label studies and two randomized control trials.
- * It is advantageous to understand overall tolerability in children and adolescents.

Methods (see Figure 1 at lower right)

- * We conducted a literature search consisting of open label or randomized control trials (RCT) that report on Ziprasidone use in children on three databases: Embase, PsychInfo and PubMed using the PRISMA guidelines of Systematic review and Meta-analysis.
- * Out of 1690 articles found in these databases, 11 studies (8 open label, 1 retrospective and 2 randomized control trial) met our inclusion criteria.
- * Our outcome measures included adverse effects such as weight gain, increase in BMI, QTc prolongation, changes in metabolic parameters, sedation, dizziness and other side effects.

Studies Selected

* Data from Eleven studies was meta-analyzed (Total n= 474, mean age=12.87 years, male= 68..37%) that reported the use of Ziprasidone in children and adolescents with Psychosis, Bipolar, Autism spectrum disorders and Tourettes syndrome.

Demographics

Table 1.	
Total number of participants	474
Mean Age	12.8 yrs
Mean dose	84.4 mg
Mean study duration	2.85 months
% male	68.37%
% caucasian	68.9%

Weight Change

Studyname			Statistics	s for each	study				_Me	an and 95%	a	
	Mean	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value					
Biederman J. et al (2007)	0.600	0.454	0.206	-0.290	1.490	1.322	0.186			+■		
DelBello, M.P. (2008) - low dos	se 1.000	0.209	0.043	0.591	1.409	4.796	0.000					
DelBello, M.P. (2008) - high do	se1.000	0.158	0.025	0.690	1.310	6.325	0.000					
Findling, R. Letal (2013)	0.700	0.204	0.042	0.300	1.100	3.429	0.001					
Cleson et al	5.700	0.484	0.234	4.752	6.648	11.782	0.000				-■	⊢
Salee et al	0.700	0.375	0.141	-0.035	1.435	1.867	0.062			├		
	1.552	0.469	0.220	0.633	2.472	3.308	0.001	ı			>	- 1
								-8.00	-4.00	0.00	4.00	8.00
									Favours A		Favours B	

BMI

Study name		Statistics	for eac	<u>h stud</u> y				<u>Mea</u>	<u>n and 95%</u>	<u> </u>	
Mean	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value					
Biederman J. et al (2007)0.200	0.131	0.017	-0.057	0.457	1.528	0.127			+-	—I	
Dominick, K. et al (2015)0.690	0.115	0.013	0.464	0.916	5.976	0.000				 -	-1
Findling, R. L et al (2013)0.200	0.031	0.001	0.140	0.260	6.532	0.000					
Oleson et al 1.900	0.169	0.028	1.569	2.231	11.258	0.000					k
0.278	0.028	0.001	0.222	0.334	9.773	0.000				♦	
							-1.00	-0.50	0.00	0.50	1.00
								Favours A		Favours B	

QTc Interval Change

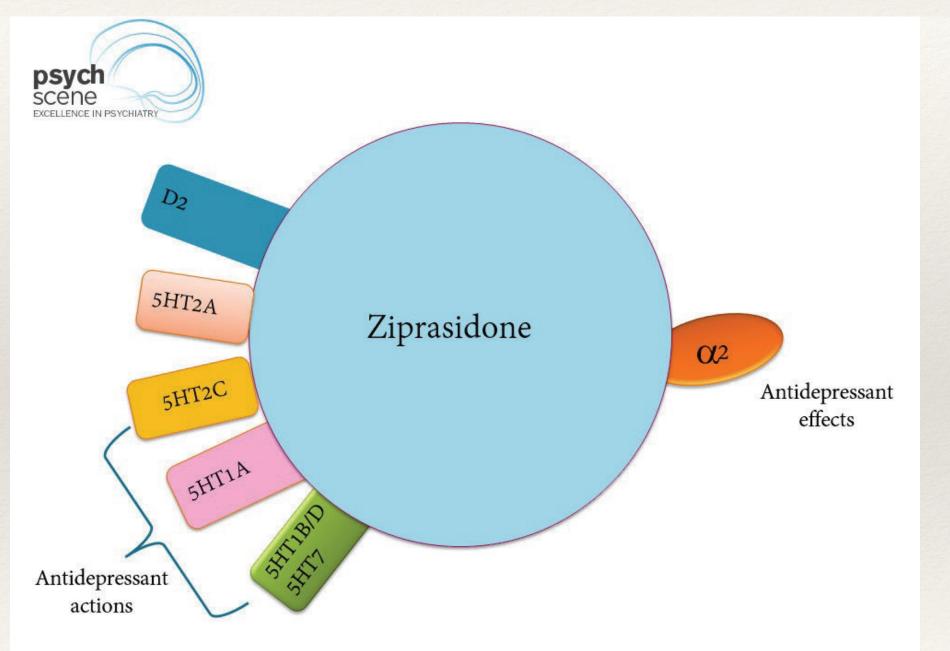
Studyname			Statistics	for each	nstudy.				_Ma	ean and 95%	a	
	Mean	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value					
Biederman J. et al (2007)	-3.100	5.514	30.400	-13.906	7.706	-0.562	0.574			=	-	
Blair, J. et al 2005	28.000	5.814	33.800	16.605	39.395	4.816	0.000		- 1		-	—■
Correll, Cetal	22.900	3.900	15.207	15.257	30.543	5.872	0.000		- 1		—	ightharpoonup
DelBello, M.P. (2008) - low d	ose 1.300	7.508	56.365	-13.415	16.015	0.173	0.863		1—			
DelBello, M.P. (2008) - high o	dosel 1.200	4.338	18.816	2.698	19.702	2.582	0.010		- 1	I —	-	
Findling, R. Let al (2013)	8.300	1.637	2.679	5.092	11.508	5.071	0.000		- 1	-	■-	
Malone et al, 2007	14.700	6.332	40.091	2.290	27.110	2.322	0.020		- 1	1-	-	— I
	12.164	3.618	13.090	5.073	19.255	3.362	0.001	ı	- 1	-		ı
								-30.00	-15.00	0.00	15.00	30.00
									Favours A		Favours B	

Other Side Effects

Side effect	%
Sedation	42.44
EPS	5.47
Dizziness	16.96
Headache	22.92
Nausea	19.32
Fatigue	16.76
Vomiting	12.27

Conclusion

- * Results from the current analysis demonstrate that Ziprasidone cause minimal weight gain or change in BMI.
- * QTc prolongation and sedation were found to be the most significant side effects of Ziprasidone use.
- * Therefore, baseline EKG and thorough history may be beneficial before prescribing Ziprasidone in children and adolescents



Ziprasidone Receptor profile

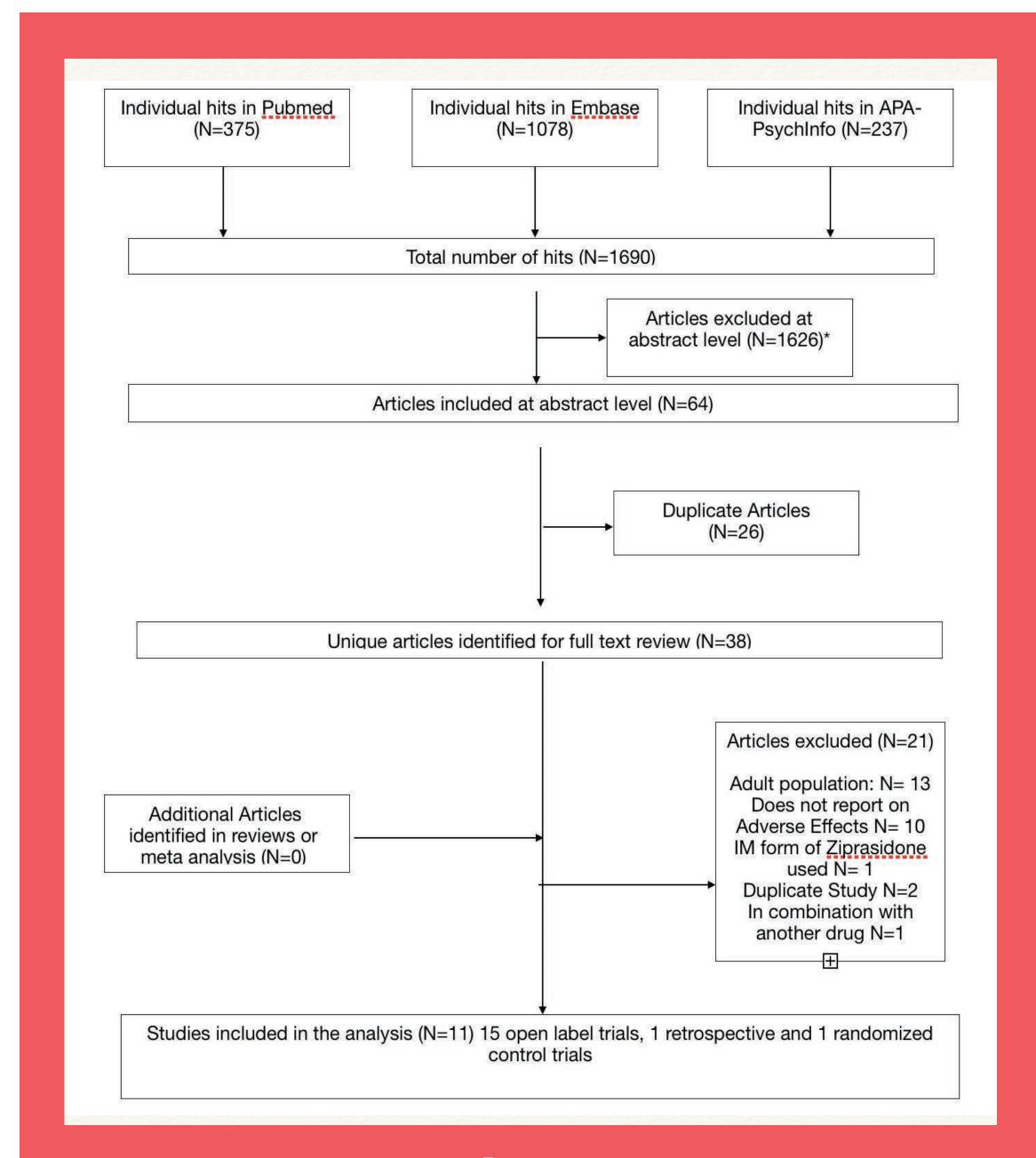


Figure 1