Al Ameen J Med Sci 2017; 10(3):207-210 ● US National Library of Medicine enlisted journal ● ISSN 0974-1143

ORIGINAL ARTICLE CODEN: AAJMBG

Safety and efficacy of risperidone in children aged less than 5 years - A naturalistic observational study

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Abstract: *Objectives:* To know the safety profile of Risperidone in young children. *Background:* Risperidone is an atypical antipsychotic. It has proven efficacy in treatment of psychotic disorder in adults. Use of risperidone in children and adolescents has been limited. Its usage below 5 years of age is limited mainly due to lack of availability of data. Our study shows safety profile of risperidone in age group below 5 years in treating behavioral problems associated with various childhood disorders. *Material & Methods:* The study was carried out in a tertiary care hospital in the department of Child neurology and Psychiatry. Common childhood disorders were diagnosed according to Diagnostic and Statistical Manual (DSM IV) and those associated with disruptive/behavioral problems were included in the study. Symptom severity and improvement were assessed with Clinical Global Impression- Severity (CGI-S) and Improvement (CGI-I) scales. Risperidone was initiated after taking informed consent from the parent/guardian. *Results:* In our study total 12 (n=12) subjects were included. PDD (n=4), PDD plus ADHD (n=2), PDD plus ADHD plus Intellectual disability (n=2), Cerebral Palsy with Epilepsy (n=2) and Global developmental delay (n=2). Baseline and end point CGI scores were 5-6 and 1-2 respectively. Baseline investigations such as lipid profile, fasting blood sugar levels, Electro cardiogram (ECG) were recorded and compared before and after initiation of risperidone. Dose range of risperidone was 0.5-2mg per day. Common side effects were sedation and weight gain in a few patients only. No life threatening side effects were noted. *Conclusion:* Our study findings suggest that risperidone is well tolerated even in children below 5 years of age over a period of 1 year with improvement in target symptoms. There is significant improvement even in quality of life and reduction in family burden.

Keywords: Risperidone, Young Children, Safety and Efficacy.

Introduction

Risperidone is an atypical antipsychotic. Various indications for usage of risperidone are schizophrenia in adults, acute case of mania in bipolar disorder, short-term use in persistent aggression in Alzheimer's disease and conduct disorder. Its predominant usage is in adults. However risperidone is recently approved by US FDA, in Autistic disorder associated with irritability between age group of 5-16 years [1].

It is found to be effective and safe in this age group. There is very sparse data available on its usage in children below 5 years of age where problems like aggression are seen and there are no effective drugs available. Here we report usage of risperidone in young children (below 5 years of age) for various disorders. This drug was used after discussing in detail about the drug with the parents (indication for use, possible side effects and ensuring regular follow up) and obtaining consent from the parents.

Material and Methods

The study was carried out in a tertiary care hospital in the department of Child neurology and Psychiatry. All children who visited the outpatient department of Child neurology and those referred from department of Psychiatry and who were diagnosed as Pervasive development disorder, ADHD, Cerebral palsy, Intellectual disability according to DSM- IV [2] and others were included in the study. Irritability, aggression and out of control behavior were main reasons for initiating risperidone in these patients. Informed consent was taken from guardians/parents before initiating risperidone.

Risperidone was started at lower doses and gradually titrated according to the clinical response and side effects. Clinical Global Impression-severity (CGI-S) and improvement (CGI-I) [3] scales were applied depending on the parents and treating doctors clinical observation. All the cases were followed up at 4 weeks and assessed for clinical improvement and side effects. Subsequently cases were followed up at the end of 6 months and 1 year respectively. Base line weight, Fasting blood sugar (FBS), Lipid profile, (TC- Total Cholesterol and TG-Triglyceride) and ECG were recorded.

Results

In our study total 12 (n=12) subjects were included. Pervasive developmental disorder (PDD) (n=4), PDD plus Attention deficit hyperactive disorder (ADHD) (n=2), PDD plus ADHD plus Intellectual disability (ID) (n=2), Cerebral Palsy (CP) with Epilepsy (n=2) and Global developmental delay (n=2). Baseline and end point CGI scores were 5-6 and 1-2 respectively. The starting dose of risperidone was 0.25-0.5mg, gradually dosage was increased to the range of 1.5-2mg, reasons for increment in dosage were minimal or non responsive to the lower doses of target symptoms. Dose increment was required in 10 patients. While assessing the side effects 6 patients reported sedation in the initial part of treatment. 2 patients reported weight gain which was more than the expected weight for that particular age. 4 patients did not report any side effects.

None of the subjects in the study developed severe side effects such as extra pyramidal side effects (EPS). Fasting blood sugar levels and Lipid profile (TC- Total Cholesterol, TG-Triglyceride) were recorded before starting medications. There was no significant increase in base line levels of these parameters at the end of one year. Normal fasting blood sugar levels were < 100mg/dl and normal Total Cholesterol levels were <300 mg/dl and normal Triglyceride levels < 150 mg/dl.

Table-1: Shows base line and final assessment of weight and Fasting blood sugar level along with demographic details

Sl. No	Age	Gender	Diagnosis	Weight (kg) before treatment	Weight (kg) after treatment	FBS baseline	FBS at the end of 1 year
1	3 Years 5 months	Male	CP with Epilepsy	13	15	86	79
2	1year 5 months	Male	CP with Epilepsy	9	14	64	84
3	3 Years 4 months	Male	PDD with ADHD	14	16	75	86
4	5Years	Male	PDD with ADHD	15	19	82	78
5	4Years 6 months	Female	PDD with ADHD with ID	16	27	90	88
6	3 Years 2 months	Male	PDD with ADHD with ID	12	16	74	86
7	2 Years 5months	Male	PDD			91	69
8	4 Years 7 months	Female	PDD	17	26	83	80
9	2 years 10 months	Male	PDD	13	16	68	79
10	3 Years 8 months	Male	PDD	15	18	85	92
11	3 Years 3months	Female	GDD	14	17	93	86
12	3Years	Male	GDD	13	16	79	87

CP- Cerebral palsy, PDD- Pervasive developmental disorder, ADHD- Attention deficit hyperactive disorder, ID- Intellectual disability, GDD- Global developmental delay, FBS- Fasting blood sugar level.

Table-2: Shows base line and final lipid profile, CGI scores along with drug side effects								
Lipid profile baseline		Lipid profile at the end of 1 year		Side effects at 4 weeks	Side effects at 6 months	Side effects at the end of 1 year	CGI Score (Initial)	CGI Score at 1year
TC	TG	TC	TG					
114	52	169	63	No SE	No SE	No SE	5	2
145	86	174	74	No SE	No SE	No SE	6	2
117	87	116	43	Sedation	No SE	No SE	6	1
158	98	149	75	No SE	No SE	No SE	6	2
129	49	146	39	Sedation	Sedation	Weight Gain	5	2
159	51	114	62	Sedation	No SE	No SE	5	2
116	69	134	76	No SE	No SE	No SE	4	1
138	97	125	86	Sedation	Sedation	No SE	5	2
187	68	152	77	Sedation	No SE	No SE	6	2
147	56	128	68	Sedation	No SE	Weight Gain	5	1
156	79	140	88	No SE	No SE	No SE	4	2
184	89	142	68	No SE	No SE	No SE	4	2
TC- Total Cholesterol, TG- Triglycerides, CGI- Clinical Global Impression								

Discussion

Behavioral problems often co-occur with developmental disorders. Irritability, aggression, hyperactivity, self injurious behavior are commonly associated with Pervasive developmental disorders, ADHDs and Mental retardation [4]. Disruptive behavior account for 4%- 9% [5] of pediatric population and these are the most common psychiatric disorders of childhood [6]. These behavioral problems interfere with rehabilitative efforts and pose enormous challenges to parents and educators [7].

When behavioral problems interfere with daily activities, general well being and therapeutic programme, pharmacological intervention should be considered. Typical Antipsychotics like haloperidol are used but risk of unwanted extra pyramidal symptoms is high. Atypical antipsychotics score over typicals in these side effects. Risperidone is used and being studied to treat behavioral symptoms. But however the data available is over 5years of age [8]. Also behavioral problems in children if untreated can cause functional impairment and overall deterioration in quality of life. Reports have been published indicating risperidone as effective treatment in these symptoms [9]. Even though psychosocial intervention should be the primary intervention strategy in preschool children, many children still persist to have behavioral problems [10]. Further there are no clear cut guidelines in management of disruptive behaviors in very young children. Psychopharmacological intervention is warranted if symptoms causes significant distress [11].

Risperidone is now more commonly used as effective treatment in disruptive behaviors in preschool children. Risperidone is also shown to be effective in treating autism and related behavioral problems. Some studies have reported that risperidone is effective in treatment of aggressive behavior in preschool children [12]. In fact risperidone was among few medications which was approved for children below 6 years of age [11]. Common diagnosis for which risperidone was used included PDD, ID, ADHD and disruptive behavior disorders [10].

In our study risperidone was initiated in children below 5 years of age group. Common side effects included sedation and weight gain. These findings are generally consistent with other studies. Though these side effects were common none of the study participants

discontinued the treatment. Though the literature suggests that non pharmacological methods should be considered as primary treatment modality, clinically it becomes difficult due to following reasons. Children with behavioral problems pose a significant family burden, generally parents/caregivers want symptom reduction as soon as possible. Further non availability of psychosocial services is also one of the reason. The need to travel long distances and financial constraints are few other reasons. There is hardly any Indian data available regarding usage of risperidone in children below 5 years of age. Considering the above mentioned reasons pharmacological intervention with risperidone in young children would be a better alternative treatment modality.

Conclusions

Study findings suggest that risperidone is well tolerated in children below 5 years of age over a period of 1 year with improvement in target symptoms. Improvement in target symptoms were observed and acknowledged by parents/ guardians and treating doctors. There is significant improvement even in quality of life and reduction in family burden. Limitation of this study would be small sample size. Although these findings are not sufficient to direct treatment, we suggest that larger-scale, double-blind, placebo-controlled investigations of risperidone in children below 5 years may now be conducted.

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