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A STUDY ON EFFECTIVENESS AND ADVERSE EFFECTS OF RISPERIDONE IN CHILDREN WITH AUTISM SPECTRUM DISORDER IN A TERTIARY CARE HOSPITAL, SOUTH KERALA

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ABSTRACT

Background: Autism spectrum disorders (ASD) are a group of complex neurodevelopment disorders that are characterized by abnormal or delayed speech, poor social communication, repetitive stereotypical behavior/restricted interests, and sensory abnormalities. Although there is no efficient pharmacological treatment for the core symptoms of ASD, atypical antipsychotics, such as Risperidone and Aripiprazole, are U.S. Food and Drug Administration (FDA)- approved for the management of ASD-associated irritability. The aim of this study is to examine the effectiveness and adverse effects of Risperidone in children with Autism Spectrum Disorder.

Methods: A Prospective Observational study was carried out at the Department of Child Developmental Center, Pratheeksha, Pushpagiri Medical College Hospital, Thiruvalla, for a period of six months. Effectivenesss were assessed based on CGI score and adverse effects were assessed based on a structured questionnaire.

Results: This study included 64 patients consisted of 71.9% males (n=46) and 28.1%

females (n=18) with mean age of 5.27 years, reflects a high proportion of males, which is consistent with the typical gender distribution observed in ASD populations and majority of the population (78.1%) falls within the age group of 3-6years, while only a small proportion (12.5%) & (9.4%) falls within the age group of 10- 12years and 7-9 years, respectively. A notable rise in BMI seen in both males and female group but when compared with age group, study suggests more pronounced effect on BMI among age group 3-6 years when compared with 7-9 years and 10-12years of age group. And there is a significant association between severity level and effectiveness. Weight gain and somnolence were the notable adverse effects shown in these patients.

Conclusion: The results of this study indicated that males are most commonly affected than females. Risperidone is moderately effective in both the groups and shows weight gain and somnolence as the notable adverse effects.

Keywords: ASD; Risperidone; Effectiveness; Adverse effects; Severity of ASD; Global Improvement; Efficacy Index

INTRODUCTION

The complex neurodevelopment disorders known as Autism spectrum disorders (ASD) are typified by delayed or aberrant speech, poor social communication, restricted interests and repetitive stereotyped behavior, and abnormal sensory experiences. According to estimates, the incidence of ASD in the industrialized world today is at least 1.5% [1].

Autism is known as "SPECTRUM" because there is a wide variation in type and severity of symptoms people experience [2]. ASD sufferers may exhibit distinct behaviors, modes of communication, interactions, and learning from most other people. Frequently, there is nothing unique about their appearance that makes them stand out from the crowd. People with ASD might have a wide range of talents. For instance, while some ASD sufferers may be nonverbal, others may possess sophisticated conversational abilities. While some ASD sufferers require extensive support in their everyday life, others are able to work and lead normal lives with little to no assistance. ASD can manifest at any point in a person's life, however symptoms may gradually become better. It usually starts before the age of three. Within the first 12 months of life, some children exhibit signs of ASD. Others may not experience symptoms until they are 24 months old or older. Around 18 to 24 months of age, some children with ASD cease learning new abilities or lose the talents they previously have. Until then, they continue to fulfill developmental milestones and acquire new skills [3].

According to the World Health Organization

(WHO), the prevalence of ASD is estimated to be 0.76% worldwide [4]. There is no cure exists for autism spectrum disorder, and there isno one-size-fits- all treatment [5]. The goal of current autism spectrum disorder (ASD)treatments is to lessen symptoms that affect a person's ability to function normally and their quality of life. Since autism affects each individual differently, each person with autism has different strengths and challenges as well as different treatment needs [6].

Typical starting dosage for children weighing less than 44 lb (20 kg) is 0.25 mg taken once per day. For children weighing 44 lb (20 kg) or more 0.5 mg taken once per day [7]. Side effects of Risperidone are Weight gain, Somnolence, Increased appetite, Abdominal pain, Rashes and Constipation.

MATERIALS AND METHODS

A single centred, hospital based, prospective observational study was conducted in the Department of Child Development Centre, Pushpagiri Medical College Hospital, Thiruvalla, Kerala, India for a duration of 6 months including a total of 64 patients.

INCLUSION CRITERIA

All children aged 3 to 12 years attending Child Developmental Centre with the diagnosis of Autism and being prescribed with Risperidone.

EXCLUSION CRITERIA

Children with comorbid epilepsy and those on anticonvulsants, as well as those prescribed with any other psychotropic medications.

The sample size obtained was n=64 using the formula Sample size,

$$n= \frac{(Z\alpha/2)^2 \times PQ}{d^2}$$

STUDY PROCEDURE

The study involved Autism Spectrum Disorder patients, identified through specific inclusion and exclusion criteria. All caregivers of the subjects participating were given a brief introduction regarding the study and confidentiality of data. A written informed consent was obtained from the caregivers in care of the subjects. A well-designed data collection form was used to collect the necessary information such as demographic details of the patient, diagnosis and treatment of the patient. A structured questionnaire was prepared which was used to collect the side effect details of the subjects regarding the intake of Risperidone. Improvement, Severity and effectiveness were assessed based on CGI score which was based on the clinicians note. Pretreatment and post treatment BMI were analyzed, as a marker for weight gain.

STATISTICAL ANALYSIS

The information collected on the proforma were uploaded in an excel sheet and data was analyzed using IBM SPSS v29. For obtaining the continuous variables, the

results are either given in Mean ±SD and for categorical variables as percentage. To obtain the association between categorical variables, Chi Square Test, Mann-Whitney and Kruskal Wallis Test were applied. T test is used for pre and post treatment analysis of BMI among age group and gender. A P value of <0.05 is considered as statistically significant.

RESULTS AND DISCUSSION

1. Effectiveness of Risperidone in children with ASD

Clinical Global Impression (CGI) is a 3-item observer-rated scale that measure Severity of illness, Global improvement and Efficacy index. Based on the CGI-score, 64 patients were assessed, out of which majority of the patients were markedly ill before the treatment and minimally improved and showed marked efficacy index after the treatment. According to CGI- S scale majority of participants exhibited marked severity levels before the treatment followed by of severe, moderate and mild severity, levels, and after the treatment majority of them showed marked efficacy index followed by moderate and minimal. In this study majority of individual experienced minimal improvement in their conditions.

2. Adverse effects of Risperidone in children with ASD

In this study, most of the patients experienced side effects (78.1%). This is due to the drugs interaction with various neurotransmitter systems of brain such as serotonin, histamine, dopamine. The most commonly reported adverse effects was weight gain (42.2%) followed by somnolence (32.8%). Weight gain occurs because Risperidone can affect the appetite centers in brain, leading to increased food intake. The drugs antagonism of histamine H1 receptors contributes to sedation and drowsiness. Most commonly reported adverse effects is weight gain followed by somnolence, increased appetite, irritability, constipation, skin rash and abdominal pain.

3. Gender related differences in effectiveness and adverse effects of Risperidone in children with ASD

Distribution of study population based on gender reveals majority of participants were males than females. This was because of a combination of genetic, hormonal, and neurological factor. Gender related differences in adverse effects were more common in females than in male.

4. Age related differences in effectiveness and adverse effects of Risperidone in children with ASD

Majority of the patients were in the age group of 3-6years, mean age of the study population was 5.27years. This is consistent with the typical age of onset of diagnosis of ASD which often occurs in early childhood. age related differences

were more common among younger children age 3 to 6 years (80.0%), followed by 10 to 12 years (75.0%) and 7 to 9 years (66.7%). The study shows that the distribution of the study population based on age groups and the presence or absence of adverse effects from Risperidone reveals that the majority of reported adverse effects occurred among younger children aged 3 to 6 years (80.0%), followed by 10 to 12 years (75.0%) and 7 to 9 years (66.7%).

Table 1: Distribution of study population based on efficacy index

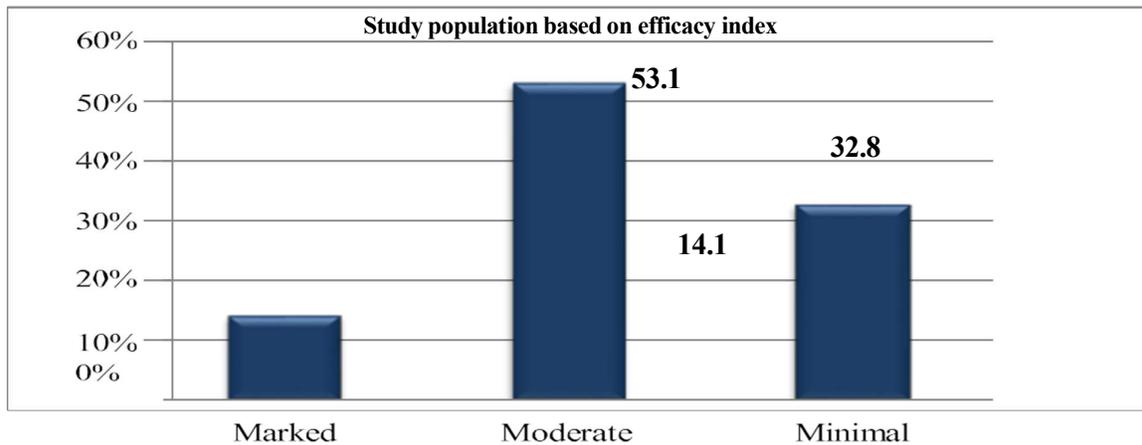| EFFICACY INDEX	FREQUENCY (n=64)	PERCENTAGE (%)
Marked	9	14.1
Moderate	34	53.1
Minimal	21	32.8
Unchanged or worse	0	0
TOTAL	64	100

Figure 1: Distribution of study population based of efficacy index

Table 1.1 Distribution of study population based on severity of illness

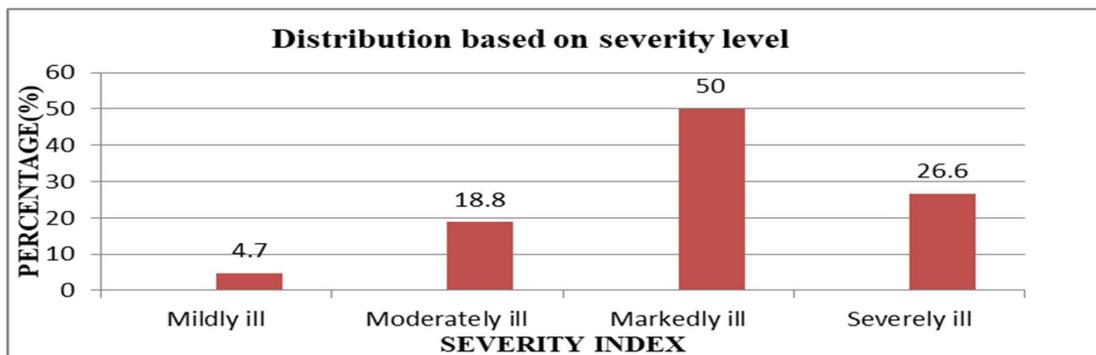| SEVERITY	FREQUENCY	PERCENTAGE (%)
Mildly ill	3	4.7
Moderately ill	12	18.8
Markedly ill	32	50.0
Severely ill	17	26.6
TOTAL	64	100

Figure 1.1: Distribution of study population based on severity of illness

Table 1.2: Distribution of study population based on global improvement

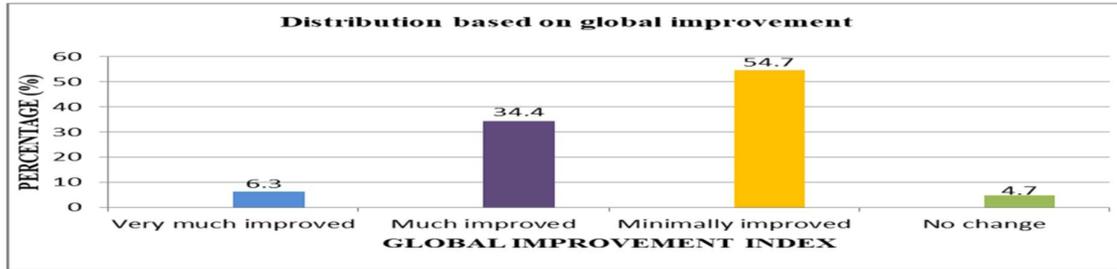| GLOBAL IMPROVEMENT	FREQENCY (n=64)	PERCENTAGE (%)
Very much improved	4	6.3
Much improved	22	34.4
Minimally improved	35	54.7
No change	3	4.7
TOTAL	64	100

Figure 1.3: Distribution of study population based on global improvement

Table 2: Adverse effects of Risperidone in children with ASD

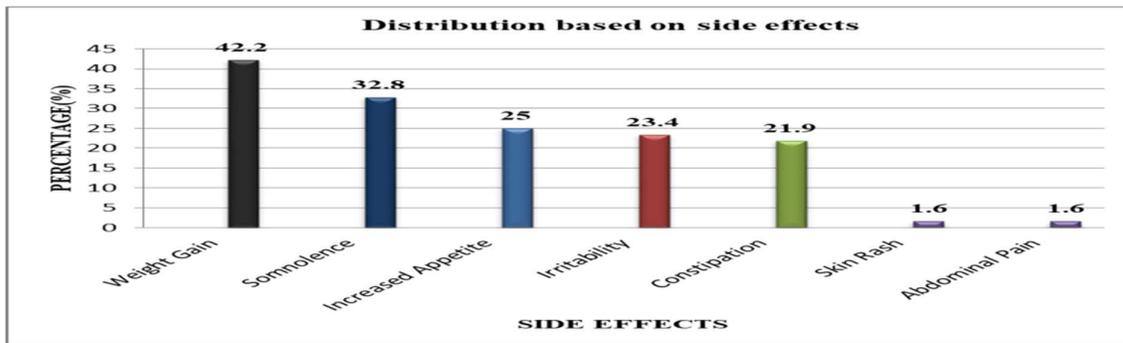| SIDE EFFECTS	FREQUENCY	PERCENTAGE (%)
Weight gain	27	42.2
Somnolence	21	32.8
Increased appetite	16	25
Irritability	15	23.4
Constipation	14	21.9
Skin rash	1	1.6
Abdominal pain	1	1.6

Figure 2: Adverse effects of Risperidone in children with ASD

Table 3: Gender related differences in effectiveness of Risperidone in ASD

PARAMETER	GENDER	MEAN RANK	TEST STATISTICS AND p VALUE
Severity	MALE	33.00	MANN WHITNEY
	FEMALE	31.22	U =391.0, P= 0.709
Global Improvement	MALE	34.14	MANN WHITNEY
	FEMALE	28.31	U=338.5, P=0.206
Efficacy index	MALE	34.6	MANN- WHITNEY
	FEMALE	27.11	U=317, P=0.113

Table 3.1: Gender related difference in adverse effects of Risperidone in ASD

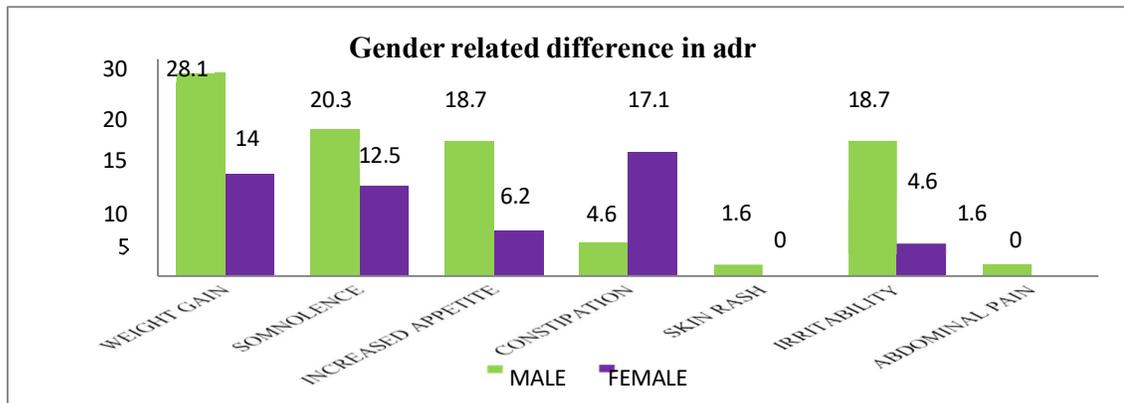| ADVERSE EFFECT	GENDER		PERCENTAGE (%)	
	MALE	FEMALE	MALE	FEMALE
Weight gain	18	9	28.1	14.0
Somnolence	13	8	20.3	12.5
Increased appetite	12	4	18.7	6.2
Constipation	3	11	4.6	17.1
Skin rash	1	0	1.6	0
Irritability	12	3	18.7	4.6
Abdominal pain	1	0	1.6	0

Figure 3.1: Gender related difference in adverse effects of Risperidone in AS

Table 4: Age specific comparison of Severity, Global improvement, and Effectiveness

PARAMETER	AGE GROUP	MEAN RANK	TEST STATISTICS & P
SEVERITY	3-6	30.38	Kruskal Wallis
	7-9	36.00	U= 4.078
	10-12	43.13	P=0.130
GLOBAL IMPROVEMENT	3-6	32.01	Kruskal Wallis
	7-9	37.67	U=0.643
			P=0.725
	10-12	31.69	
EFFECTIVENESS	3-6	33.52	Kruskal Wallis
	7-9	37.00	U=3.230
	10-12	22.75	P=0.199

Table 4.1: Age specific differences in adverse effect of Risperidone in ASD

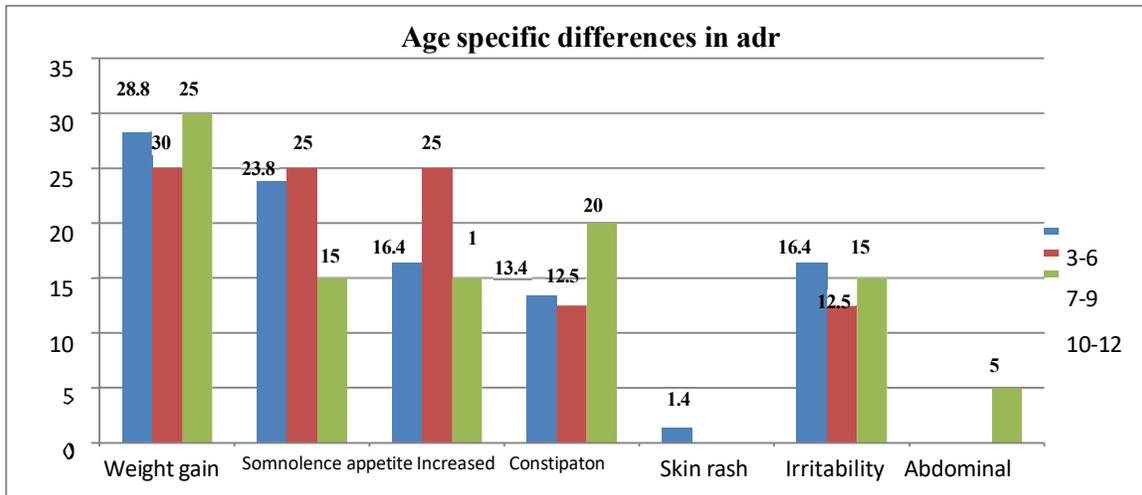| ADVERSE EFFECT	AGE GROUP			PERCENTAGE (%)		
	3-6	7-9	10-12	3-6	7-9	10-12
Weight gain	19	2	6	28.3	25	30
Somnolence	16	2	3	23.8	25	15
Increased appetite	11	2	3	16.4	25	15
Constipation	9	1	4	13.4	12.5	20
Skin rash	1	0	0	1.4	0	0
Irritability	11	1	3	16.4	12.5	15
Abdominal pain	0	0	1	0	0	5

Figure 4: Age specific differences in adverse effect of Risperidone in ASD

CONCLUSION

The study concluded that Risperidone monotherapy is effective and well tolerated in some children with ASD, presenting disruptive behaviour. Weight gain and somnolence were the major adverse effects. Body Mass Index (BMI) is not a diagnostic tool, instead, it is used to screen for potential weight gain. However, rise in BMI was statistically significant in both male and female patients and among the age group of 3-6years. Risperidone is well tolerable and moderately effective in reducing tantrums, aggressiveness and irritability in subjects with ASD. Risperidone would be most judiciously used in those children who fail to make significant gains despite intensive psychosocial and educational treatment.

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CONFLICT OF INTEREST

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