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Positive therapeutic effects of Risperidone drug on autistic children (Trial Study) in Nassiriya city, Iraq

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ABSTRACT

Autism is one of pervasive developmental disorder (PDD), mentioned to a significant disturbance in communication and social interaction, with a poor interest in normal behaviours. Risperidone is frequently the medication used that is licensed by (FDA), it revealed encouraging and favorable initial relief of both communication skill and social interaction through family, teacher impression and clinical interview at scoring levels of severity by downward fluctuation of its drug administration started with low dose from 0.5 mg per day with gradual increase according to tolerability and body weight until reaching 3 mg per day in divided dose that shows no extrapyramidal side effects. They were 5 years ago and above examined in a private clinic in Nassiriya city in Iraq, all cases were presented by their families for odd, aggressive behaviours and communication problems, they were exposed for two scales in first and second session to diagnose autism by ASD assessment scale and severity of the disorder by ASD assessment scale grading and scoring, all patients were treated with Risperidone for one month duration exposed to the same steps in the second interview to reveal the improvement rate, comorbid and probable risk also re-evaluated. Descriptive tables were used to reveal all percentages before and after the treatment. All participating children families gave oral and written consent. All steps, diagnosis and drug side effects were discussed to parents with hotline connection with them. Typical anti-psychotic Risperidone has magic and dramatic effects on controlling children overactivity, relatively verbal improvement and improves his acceptance to settle in the centre of autism and schools.



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INTRODUCTION

Autism is neurodevelopment problem, it is not well revealed underlying pathogenesis, no curative pharmacological treatment is available, but lastly Food and Drug Association (FDA) approved use of Risperidone to treat autism as core and secondary symptoms (Holander *et al.*, 2005) like disruptive

behaviours, instability, aggressive behaviour (ADHD) which disturb behavioural language therapy (Francis, 2005), new study mentions that (31 %) of autistic children use Risperidone, which is well accepted and curative & ADHD, self-injury social isolating (McDougle *et al.*, 1989). Risperidone adheres to different neurotransmitters receptor in brain like serotonin, D2 receptor, and Alpha adrenergic receptor (Ribases *et al.*, 2004), neuroimmune pathology, suggests that inner rather than adjustment neuroimmune response delinquency associate PDD (Pervasive Developmental Disorder) (Pardo *et al.*, 2005) condition was documented with postmortem study of brain tissues which shows cerebral cortex with severe inflammatory reaction (Kumar *et al.*, 2012). All trial studies that used drug therapy of autism mentioned that Risperidone is better than placebo for its less side effects like extra-pyramidal symptoms, epilepsy,

mild sedation but increase generalised weakness, increase food intake, vertigo (Cracken *et al.*, 2002).

Regarding comorbid disorder with autism, about 75 % of ADD have another medical or psychiatric disorders, most common comorbid disorders are anxiety including akathisia, overactivity, sleep disorder, ADHD and autism have similar symptoms like poor attention, 50-60 % of autism child has learning disabilities (CA, 2014).

PATIENTS AND METHODS

(50) children were involved initially in this study, (18) of them did not complete the second step, so (32) children were fulfilled the trial study, all of them were above (5) years age, (19) children of them were males, (13) were females, study was carried out in a private clinic through 6 months' duration from January to the end of July (2018).

Steps of Study

- The detailed history of disorder was expressed by family involving odd behaviours, poor social interaction and communication skills; the physical and psychiatric assessment was thoroughly done to identify the suspected cases.
- All (32) children were submitted for the (ASD) assessment scale/screening questionnaire (Appendix No.1), grading for assessment questions, in general, was done in the following scores:
 - No (0 points): perfectly normal, never had such problem.
 - Resolved (1 point): perfectly normal, but used to belong to one of the below categories.
 - Mild (2 points): features present minimal, whether improved or rarely noted or skill (speech) only minimally impaired must be different from other children.
 - Moderate (3 points): features present frequently or skills significantly impaired.
 - Severe (4 points): features present almost all times or skill almost absent. (no speech or no eye contact)
- The severity of the study sample (32) children were measured by (ASD) screening scale grading and scoring: DSM-IV criteria require onset before 3 years of age; significant impairment referred for severity of dysfunction, at least moderate, severe which involves:
 - Social interaction
 - Language
 - Symbolic or imaginative play

If the mentioned criteria are met, then the following scores may be suggestive of the corresponding definitions:

0-49 = no ASD

50-100 = mild ASD

100-150 = moderate ASD

> 150 = severe ASD

Explanation of ASD assessment scale questionnaire must be achieved by an expert psychiatrist with parents' information.

Regarding ASD assessment scale grading and scoring (Appendix II).

Scoring of the bolded question of, (social interaction difficulties, speech and language delay, abnormal symbolic play), must be calculated in both interviews measured in the following:

- No (0 points): Normal
- Resolved: (0 points)
- Mild: (8 points)
- Moderate: (12 points)
- Severe: (16 points)

Details interpretation of each grade is present in (Appendix II).

- The study sample was exposed for above (3) steps in the first interview, which takes one hour, all (32) children were treated with atypical antipsychotic (Risperidone) which is approved by FDA in gradually building dose starting 0.5 per day up to 3 mg in divided dose daily according to tolerance to treatment and rarely occurring extrapyramidal symptoms, which can be overcome by reducing the dose or adding antihistamine syrup.
- One-month duration on treatment with organized case record and a file containing all data about a child with mobile connection for the second interview (after one month of treatment), the same first (3) steps were repeated for each child to compare the difference in severity before and after treatment.

Statistical analysis

Data were analysed by descriptive methods. Severity percentage of autism before and after treatment, other tables describe comorbid disorders and risk factors. No analytic tests like (X^2 , p-value, Fisher exact test) were used, because of a limited number of the study sample.

RESULTS

Table 1 – shows the severity of autism before treatment as the following (low, mild, moderate, severe) (28.1 %, 15.6 %, 25 %, 31.2 %), successively. After treatment with Risperidone, the results dramatically reduced in the following (low, mild, moderate) were (9.3 %, 6.2 %, 12.5 %, 21.8) successively. 16 (50 %) of patients show negative (ASD screening scale grading and scoring) ADHD (62.5%), and epilepsy (15.4%) were the most common. Neonatal jaundice was (9.3), other comorbidities are less prevalent as (delayed speech, brain atrophy, ptrysis).

Table 1: Severity of Autism before and after treatment according to the modified checklist for autism (ASD screening scale grading and scoring)

Severity	Low	Mild	Moderate	Severe	Total
Before treatment	9(28.1 %)	5(15.6%)	8(25%)	10(31.2%)	32 (100%)
After treatment	3(9.3%)	2(6.2%)	4(12.5%)	7(21.8%)	16 (32%)

*half of the patients shows improvement through (ASD screening scale grading and scoring) (16 patients = (50 %)

Table 2: shows comorbid disorders Comorbid diseases with autism

No.	Type of disease	No. and percentage
1	ADHD	20 (62.5%)
2	Epilepsy	5 (15.4 %)
3	Obsession	1 (3.1%)
4	Neonatal Jaundice	3 (9.3%)
5	Delayed speech	2 (6.16 %)
6	Brain Atrophy	1 (3.1%)
7	Ptrysis	1 (3.1%)

Table 3: Relative associated risk factors

No	Relative Risk Factor	No & Percentage %
	Sex	
1	Male:	19 (59.3 %)
	Female :	13(40.6 %)
	Family history	
2	Positive:	15(46.8%)
	Negative:	18(65.2%)
	Social class	
3	High:	13(40.6%)
	Moderate:	10(31.2%)
	Low:	9(28.1%)

Table 3: Shows indirect relative risk factors like (males, females) were (59.3%, 40.6%) successively, positive family history (46.8) which is very important, most of the cases were mentioned in high and moderate social class (40.6%, 31.2%) successively.

DISCUSSION

(32) Children (19 males, 13 females) were interviewed clinically with a detailed history from parents about odd behaviours like social withdrawal, repetitive behaviour, abnormal movement and overactivity in most of the cases, verbal communication disturbance is a strong leading symptom for consultation especially at (6) year age of school attendance. All study sample children were exposed for autism (ASD screening scale grading and scoring), it is a good tool for simple diagnosis (Appendix No.1), severity of autism was measured by (ASD screening scale grading and scoring) (Appendix 2), in the first interview each positive case was submitted for severity scale and label its score before starting them on atypical antipsychotic Risperidone in dose range from (0.5 mg-3mg), according to tolerability of child to side effects, majority of cases was ranged from moderate (25%) to

severe (31.2%) who express poor social interaction, poor response to external stimuli, restrict communication, these symptoms goes with level 2, level3 severity of autism when behavioural and language therapy are less advantageous (Temothy, 2018).

One month after treatment, moderate, severe levels showed a clear decline (12.5%, 21.8%) successively, which is related to the efficacy of treatment that improves social interaction and disorganised behaviours, language shows coherent and relevant words (Correia *et al.*, 2010).

Low and mild levels (28.1%, 15.6%) successively revealed the highest level of improvement (9.3 %, 6.2%), successively, due to magic effect of Risperidone in such groups, logically reduction in number and severity of autistic patients after treatment result in half percentage (16)patients shows resolution at clinical and measurement levels, similar significant point of such clinical improvement is that the patients involved were receiving anti-psychotic for the first time, because previous medication result in confounding effect, next medication may alter neurotransmitter receptor (Tarazi *et al.*, 2002).

Common comorbid disorder with autism in the study sample is (ADHD) (62.5%), which is very terrible and bothering both family and teacher, ADHD present in (30% to 80%) of autism core symptoms which may overlap and obscure PDD especially disruptive and aggressive behavior (Belardinelli *et al.*, 2016).

The second comorbid disorder is epilepsy. It constitutes (15.4%), which is common in autistic children, but little is known about how seizure affect PDD. Parent report about the association of seizure and maladaptive behaviours was measured by Poisson regression (Viscide *et al.*, 2014). Epilepsy prevalence in autistic children is 5 % to 4 %. (Spence and Schneider, 2009).

Obsessive-compulsive disorder (OCD) constitute (3.1 %) of comorbidity, OCD shows increase comorbidity with PDD, family study shows the relation between intrusive through urge, the image in adolescent and childhood age, the concurrent diagnosis may be controversial (Lugnegard *et al.*, 2011).

Neonatal Jaundice was (9.3), unconjugated hyperbilirubinemia has toxic effect for the brain, it frequently coexists with autism (Maimburg *et al.*, 2008).

The delayed speech was (6.16 %), this comorbidity makes the severe conflict between ENT specialist and psychiatrist, about the integrity of the hearing system, in many cases, there is overlapping between delayed speech and autism and vice versa. A new study shows poor language abilities at one-year age, who are later on diagnosed as autism and produce muddled speech, a condition related to the size of certain brain structure & speech abilities (Gholipour, 2017).

Brain atrophy presented in (3.1 %) of the study sample, because autism is a neurodevelopmental disorder, patients show excessive neurogenesis, glycogenesis, and synaptogenesis, decrease migration of neurons and low apoptosis, all lead to the pathophysiology of the brain (Palmen *et al.*, 2004).

Regarding relative associated risk factor.

Male: female equal to 3:2, other study shows male to female equal to 3:1, probably due to diagnostic bias, which means that girls that met criteria of autism are at disproportionate risk of being free of clinical implication (Loomes *et al.*, 2017).

A positive family history of autism (46.8 %), which mean half of the children have a genetic loading tendency or experience of the positive family about abnormal behaviour. The family history of ASD probably enhance the risk of autism establishment, autism seems to distribute in families in the presence of one child with autism can enhance another child risk of ASD. Parents with ASD child have a 1 in 20 or 5 % probability of other toddlers with ASD (Rodriguez *et al.*, 2010).

This study shows social class ranked in the following (high, moderate, low) were (40.6 %, 31.2 %, 28.1 %) successively. So, a high percentage of autism among high social class due to their relaxed economic state and their ability to afford, and ignorance of autistic child in low social class for their poor health education and other social obstacles. Our study goes with Michell Diament study, who mentioned patients from low social class with poor financial income usually diagnosed lately, and then shows consistently tied to odd symptoms of ASD, in spite of raised prevalence of PDD for double last years, on controversy Swedish and French study which show no relation between ASD and economic status (Diament, 2017).

CONCLUSION

There were significant effects of atypical antipsychotic Risperidone on children with autism by re-

ducing the severity of social interaction and impairment of communication and relieves of aggressive, stereotyped behaviours. Half of the patients shows negative diagnostic and severity scale, other comorbid disorder like ADHD, or risk factor was clarified and revealed, which give a child a chance to be accepted in family or school or autistic centre.

Limitations: Small size sample due to non-attendance of some children, another point is a one-month period that was given for second evaluation, the condition related for an inadequate sense of disorganized behaviors of children and usual habit of ignorance of disorganized children in study place.

Recommendations: Establishment of academic government centre for persistent contact with the child and his family in scientific updated technique including training multi-disciplinary team on behavioural, language, researches and training of social workers.

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