Assessment of the utilization of pharmacotherapy for pediatrics with Autism Spectrum Disorder in Jeddah, KSA

Suzan Morsy
Raghad Mohammed Hadi Awaji
Reem Mohammed Bashowair
Tuqa Shaker Alahmadi
Shouq Wahid Alshatifi

Medical Intern, Ibn Sina National College for Medical Studies, Jeddah, Kingdom of Saudi Arabia

Corresponding author:
Dr. Suzan Morsy
Pharm D Clinical pharmacology
Ibn Sina National College for Medical Studies,
Jeddah, Kingdom of Saudi Arabia
Tel: 00966598319174
Email: s_almorsy@outlook.com

Received: November 2019; Accepted: December 2019; Published: January 1, 2020.
Citation: Suzan Morsy, Raghad Mohammed Hadi Awaji, Reem Mohammed Bashowair, Tuqa Shaker Alahmadi, Shouq Wahid Alshatifi. Assessment of the utilization of pharmacotherapy for pediatrics with Autism Spectrum Disorder in Jeddah, KSA. World Family Medicine. 2020; 18(1): 139-149. DOI: 10.5742MEWFM.2020.93744

Abstract

Background: Assessing children with autism and the effect of different modalities in management of autism is a critical issue as the disease is a lifelong disorder that has a negative effect on the social health of the families.

Aim of the work: Evaluate the pharmacotherapy for children with au-tism spectrum disorder in Jeddah.

Method: The current study is a descriptive cross sectional study that was conducted in three private hospitals in Jeddah (KSA); Ibn Sina Hospital, Al Jeddain Gholeel and AlJeddaani AlSafaa. The study included 152 children aged 2-18 years diagnosed with autism according to DSM V criteria. The collected data and the designed questionnaire were filled out by the care giver. Children with concomitant other chronic disease and parents who refused to participate or did not complete the questionnaire were excluded from the study. The collected data were analyzed by SPSS version 20.

Results: The mean age of the children was 4.5±3.2 and the source of the data was mainly from the mother (69.1%). Children were mainly males (75.7%) and the majority of families had only one child with autism (85.5%) and about (45.5%) were diagnosed in the second year of life. The majority of children complained of social withdrawal (85.5%), distraction of attention and repetitive behavior (75%). About (36.2%) of the studied children received combined treatment modalities and the most common pharmacological line used was SSRIs and kebra.

Conclusion: Nowadays management of autism depends on a combination of behavioral management, pharmacotherapy, family and educational therapy for the best outcome. The most common pharmacological line used was SSRIs and kebra and about 75% of children who took drugs complained of side effects.

Key words: Autism, therapeutic, behavior.

Introduction

Autism Spectrum Disorder (ASD) is a neuro-developmental disorder that affects children in the early years of life. It is characterized by lan-guage delay, cognitive, behavior and intellectual impairment and also affects social interaction [1]. Attention deficit hyperactivity disorder (ADHD) and other psychiatric comorbidities like depression, anxiety and behavioral problems are found to be associated with it [2].|

According to DSM-V criteria for diagnosis of (ASD) based on the difficulties in two areas - social communication and restricted, repetitive behavior with difference in ranking of severity [3].

ASD is a complex disorder that reflects the interaction between genetic and environmental factors [4], as many studies revealed a strong genetic hereditability. Hundreds of copy number variants (CNVs) including 16p11.2, 22q11.2, 1q21.1, 7q11.23, and 15q11–q13, have been shown to be strongly associated with it [5], however while genetics is a well-established risk factor it is important to be aware of the contributing environmental factors and other risk factors such as increased maternal and paternal age at time of birth more, than 35 years old, use of hormonal induction and Assisted Reproductive Technologies (ART), exposure to chemical pollutants at critical developmental stages which may affect neural and behavioral development[6] and maternal nutritional status as many micronutrients such as iron contribute to neurotransmitter production, myelination and immune function[7] .

Many studies have demonstrated the prevalence of autism in Saudi Arabia; 42,500 children were diagnosed with autism in 2002, and a study done in 2013 revealed that the prevalence was greater in males than in females [8], however actual prevalence has not been determined up till now as the less-developed child psychiatric services in Saudi Arabia explain the high number of dropped cases [9].

American Academy of Child and Adolescent Psychiatry [10], recommended sets of parameters for best assessment and treatment practices for ASD according to the strength of the underlying clinical state. Psychiatric assessment of young children should routinely include questions about ASD symptomatology; if it indicates significant ASD, diagnostic evaluation should be performed and the clinician should help the family to obtain appropriate structured educational and behavioral interventions for their children with ASD; pharmacotherapy may also be offered to them especially those with comorbid conditions.

The National Institute for Mental Health and Research Units on Pediatric Psychopharmacology assesses the safety and efficacy of pharmacological interventions used in behavioral management of autism, based on pharmaceuticals that has an effect for ameliorating behavioral symptoms with other disorders such as attention deficit hyperactivity disorder (ADHD). They can reduce symptoms such as aggression, irritability and hyperactivity [11].

ASD is a lifelong disorder that has negative effects on the Quality of life (QoL) of parents or caregivers as well as patients. For this reason management of autism is not for eliminating the disorder but improvement of the individual's QoL [12]. Studies have revealed that caregivers of children with different developmental disorders especially ASD were more stressful, tired or exhausted and it impaired their QoL [13].

The aim of this study was to assess aims to evaluate the effect of pharmacotherapy and different therapeutic modalities on the children with autism spectrum disorder and their family in Jeddah.

Patients and methods

Type and site of the study:
Convenient sample of ASD patients was collected from Pediatrics and Psychiatric Clinics in three private hospitals in Jeddah (KSA), Ibn Sina Hospital, AlJeddain Gholeel and AlJeddaani AlSafaa, in a four month duration from July 2019 till October 2019.

Study population:
The study included 152 children diagnosed with autism according to DSM V criteria [3]. The questionnaire was filled out by one of the parents or the care giver.
Inclusion criteria were: children aged 2-18 years diagnosed with autism treated by either drugs only or either combined therapeutic modalities. Children with concomitant other chronic disease and parents who refused to participate or did not complete the questionnaire were excluded from the study.

Data collection:
Upon receiving ethics approval the caregiver of children diagnosed with autism were contacted to participate in a survey by filling out the questionnaire. Basic characteristics were collected including age, sex, and age of diagnosis and the source of information. The care giver was asked about the investigations done and if the child had abnormal EEG, and the received therapeutic modalities.

The questionnaire used was designed to evaluate the effect of different therapeutic modalities (Behavioral, educational and different pharmacotherapy) for the autistic child and family.

The first section: included child basic characteristics (age, gender, age of diagnosis, previous EEG done and any abnormalities) and source of information from the caregiver.

The second section involved the patient's experience of the following symptoms (seizures, anxiety, violence, social withdrawal, repeat behavior, hyperactivity, distraction, sleep disturbance and any abnormalities in cognitive behavior).

The third section included the following items: Drug therapy, Behavioral therapy and Educational therapy (duration of therapy, its effect on the child's behavior and if there was a side effect).

The fourth section included parent awareness and attitude toward having an autistic child.

The questionnaire was translated to Arabic language and a pilot study was carried out (10% of the sample size, 15 subjects) who were excluded from the final analysis, to evaluate the questionnaire in its Arabic version. Feedback was positive and we provided help to participants and aided those facing any difficulty in completing the questionnaire. Validation of the questionnaire was made as follows: the questionnaires were translated using a back-translation technique. An expert translated the original questionnaire from English into Arabic. Arabic version of the questionnaires was translated back into English by a bilingual individual. The back-translated and original versions of the questionnaire were compared with attention given to the meaning and grammar.

Data management:
The collected data were coded, entered, presented, and analyzed by computer using a data base software program, Statistical Package for Social Science (version 20, SPSS Inc., Chicago, IL). Quantitative variables were expressed as the mean ± standard deviation (SD) while the qualitative variables were expressed as a number and percentage.

Ethical considerations:
Ethical approval for the study was obtained from the ethical review committee of the college. The nature of the study was fully explained to the study participants and informed written consent was signed by a care-giver of each child. The study was compliant with the World Medical Association Declaration of Helsinki regarding ethical conduct of research involving human subjects.

Results

This study was a cross sectional study that included 152 children diagnosed with autism. The mean age of the children was 4.5±3.2. The source of the data was mainly from the mother (69.1%) and father (19.7%). Most of the children were males (75.7%) and the majority of families had only one child with autism (85.5%). About (45.5%) were diagnosed in the second year of life. [Table1]

It was noticed that about (69.1%) of parents had previous knowledge about autism and (44.7%) had taken courses about autism. [Table 1]

The majority of children complained of social withdrawal (85.5%), distraction of attention and repetitive behavior (75%). [Table 2]

About (36.2%) of the studied children received combined treatment modalities and the most common pharmacological line used was SSRIs and kebra and about 75% of children who took drugs complained of side effects and the parent either waited for improvement or consulted a doctor. [Table 3]

Regarding different modalities in management of children with autism, it was noticed that about 78.95% reported that their children had started the behavioural therapy and also family therapy since they had been diagnosed and showed no problem with these types of therapy and about 32 of the children out of 76 changed their modalities. [Table 4&6]

While 81 autistic children had received educational therapy, 61.73% of them had started it since they had been diagnosed and 25.93% had problems with this and about 19.75% changed this type of therapy. [Table 5]

Table 1: Basic characteristics of the studied group (n=152)

Characteristics	Value	
Age (years):		
Mean± SD	4.5±3.2	
(minimum-maximum)	(2-10)	
Items	No	%
Source of information:		+
Mother	105	69.1
Father	30	19.7
Others (care giver)	17	11.2
Total	**152**	**100**
Gender of child:		
Male	115	75.7
Female	37	24.3
Total	**152**	**100**
Number of family members with autism		
One	130	85.5
More than one	22	14.5
Total	**152**	**100**
Previous knowledge about autism		
Yes	105	69.1
No	47	30.1
Total	**152**	**100**
Had previous courses about autism		
Yes	68	44.7
No	84	55.3
Total	152	**100**
Age of diagnosis:		
Second year of life	69	45.5
Third year	12	7.9
Fourth year	35	23.0
Fifth year	25	16.4
Sixth to ninth year	11	7.2
Total	**152**	**100**

Table 2: Distribution of different symptoms among the studied group (n=152)

Items	No (n=152)	%
Seizures	60	39.5
Anxiety	76	50
Violence	53	43.9
Social withdrawal	132	85.5
Repetitive behaviour	114	75
Hyperactivity	92	60.5
Distraction	114	75
Sleep disturbance	71	46.7
Cognitive behavior	41	27

Table 3: Distribution of investigation and different treatment modalities among the studied group (n=152)

Items	No (n=152)	%
EEG		
Yes	94	61.8
No	58	38.2
Total	**152**	**100.0**
Abnormal EEG (n=94)		
Yes	32	34.1
No	62	65.9
Total	**94**	**100**
Type of therapy received		
Behavioural therapy	21	13.8
Educational therapy	26	17.1
Family education	25	16.4
Pharmacological therapy	25	16.4
Combined treatment	55	36.2
Total	**152**	**100**
Type of pharmacological treatment		
Buspar	5	6.25
SSRIS	30	37.5
Ritalin	5	6.25
Tegretol	10	12.5
Kebra	20	25
Lithium	5	6.25
Pexidrin	5	6.25
Total	**80**	**100**
Side effects of the drugs		
Yes	60	75
No	20	25
Total	**80**	**100**
Dealing with side effects		
Ignore	8	13.3
Wait for improvement	32	53.4
Doctor consultation	20	33.3
Total	**60**	100
Stop drugs		
Yes	26	32.5
No	54	67.5
Total	**80**	100

Table 4: Distribution of behavioral therapy among the studied group (n=76)

Items	No	%
Start of behavioural therapy		
Since diagnosis	60	78.95
Period after diagnosis	16	20.05
Total	**76**	**100**
Any problems with behavioural therapy (n=76)		
Yes	6	7.89
No	70	92.10
Total	**76**	**100**
Dealing with problems (n=6)		
Ignore	0	0
Wait for improvement	2	33.33
Doctor consultation	4	66.67
Total	**6**	**100**
Stop behavioural therapy		
Yes	5	6.58
No	71	93.42
Total	**76**	**100**
Change modality of therapy		
Yes	32	42.10
No	44	57.9
Total	**76**	**100**

Table 5: Distribution of educational therapy among the studied group (n=81)

Items	No	%
Start of educational therapy (n=81)		
Since diagnosis	50	61.73
Period after diagnosis	31	38.27
Total	**81**	**100**
Any problems with educational therapy (n=81)		
YES	21	25.93
NO	60	74.07
Total	**81**	**100**
Dealing with problems (n=81)		
Ignore	1	4.76
Wait for improvement	18	85.71
Doctor consultation	2	9.52
Total	**21**	**100**
Stop educational therapy (n=81)		
Yes	5	6.17
No	76	93.83
Total	**81**	**100**
Change modality of therapy		
Yes	16	19.75
No	65	80.25
Total	**81**	**100**

Table 6: Distribution of family therapy among the studied group (n=76)

Items	No	%
Start of family therapy		
Since diagnosis	60	78.95
Period after diagnosis	16	21.05
Total	**76**	**100**
Any side effects of family therapy (n=76)		
Yes	8	10.53
No	68	89.47
Total	76	**100**
Dealing with side effects (n=8)		
Ignore	2	25
Wait for improvement	2	25
Doctor consultation	4	50
Total	**8**	**100**
Stop family therapy		
Yes	5	6.6
No	71	93.42
Total	**76**	**100**
Change modality of therapy		
Yes	32	42.10
No	44	57.9
Total	**76**	**100**

Discussion

Autism spectrum disorder is one of the neurodevelopmental disorders that needs very specific and unique care of caregiver or family because it has no specific biological marker and this gives no ideas about the prognosis of this disorder [14].

This was descriptive cross sectional study done on 152 children diag-nosed with autism from three different hospitals. One of the most re-markable finding in this study was that ASD is more common in males than females (75.5% & 24.3% respectively). Also studies done in Stockholm, Sweden stated the distribution of cases of ASD in males and female were 8,033 to 3,297 [15]. One of the theories that explained the decrease in prevalence among females is the presence of female protective effect (FPE) which delays and protects them from some symptoms of autism[16]. However other epidemiological studies supposed the inherited risk factors transmitted to the siblings, showed that the higher rate of ASD siblings is more from the affected female than the affected male. This results in increasing the burden and the rate of sibling ASD recurrence [17].

Diagnosis of ASD in early childhood provides a broad scope in good parent-child relationship which consequently has a great impact in the prognosis of autism[18]; about 45.5% of the studied patients were diagnosed in the first two years however Oswald et al[18] reported that children with ASD were diagnosed at age more than five years old despite early parental concerns but contributed this to late intervention and health care professionals were more likely to explain their concerns as it was too early to tell if anything was wrong.

Systematic review has been done by Spain et al [19], on 24 cross-sectional studies on children diagnosed with ASD; most of them were associated with poor social skills and it showed a link between core diagnosis of ASD and social anxiety. This is found in the present result as more than 85.5% of children had social withdrawal and 75% presented with distraction of attention and repetitive behavior. In a study done in India on 21 children diagnosed with autism, 95.2% of them had little interest in other children and 28.6% presented with repetitive behavior [20].

As seizures affect a high proportion of children with ASD [21], Viscidi et al [22] reported average prevalence of seizures was 12.5% among children with ASD, 2-17 years old. In this study, about 39.5% of ASD children had

seizures and 34.1% had abnormal EEG findings, 37.5% of them received medical treatment (tegretol 12.5% and kebra 25%).

In meta-analysis of randomized, ASD and placebo-controlled trials to assess the efficacy of AED drugs in children diagnosed with autism, from five studies, three studies found no significant difference with placebo while one study showed significant difference in Child Yale-Brown Obsessive Compulsive Scale (CY-BOCS) while the last study showed significant difference regarding irritability, repetitive behavior and agitation [23].

Methylphenidate (Ritalin, Novartis; Concerta, Janssen; and generics) is usually known to be used in Attention Deficit Hyperactive Disorder (ADHD) [24]. In this study 6.25% of the autistic children used Ritalin as 60.5% of the children presented with hyperactivity and 75% with inattention, which are considered the main cardinal symptoms of ADHD. Randomized controlled trials done to assess the effect of methylphenidate on both autistic and ADHD children aged five years old, found improvement in ADHD-like symptoms where hyperactivity as an outcome was rated by both teachers and parents and showed no evidence that it improved social interaction in ASD or worsened symptoms [25].

In the current study the questionnaire used was designed to measure effect of different modalities on the autistic children and their family. One of its domains measured parents as caregivers to a child with autism and expressed some positive aspects (understanding their children, knowing how to help them and working well with therapist); other studies expressed the parents' emotion towards having a child with ASD such as feeling guilty of lack of care, inability to help them and blamed themselves for the inheritance [26].

About 44.7% of the caregivers had previous courses about how to deal with an autistic child. This may be explained by that having a child with a developmental disorder such as autism is a challenge for the family due to the unpredictable behavior that results in increasing levels of stress and also that parents needed both emotional and practical support from the family members and extended family [27].

It was noticed from the previous results that assessing the behavior of children with autism and different therapeutic modalities in addition to their effect on their families is important in determining their needs and their follow up after various interventions, as this will aid in the future care applied to them.

Conclusion

Nowadays management of autism depends on a combination of behavioral management, pharmacotherapy, family and educational therapy for best outcome. The most common pharmacological line used was SSRIs and kebra and about (75%) of children who took drugs complained of side effects.

Recommendation: Further studies are needed with large sample size and screening. A community based study that not only depends on cases taken from hospitals and other interventional programs could be done in future to assess the quality of life of the autistic children's families.

Limitations: The limitations in this study are the small sample size, and needs follow up of the children for the best assessment of behavioral and pharmacotherapy on the autistic child.

References

1. Ferreira X and Oliveira G: Autism and early neurodevelopmental milestones. Acta Med Port. 2016; 29:168–75.
2. Van Steensel F, Bogels S and De Bruin E: Psychiatric Comor-bidity in Children with Autism Spectrum Disorders: A Comparison with Children with ADHD. Journal of child and family studies, 2013; 22(3):368-76.
3. Kent R, Carrington S, Le Couteur A, Gould J, Wing L, Maljaars J, Noens I, Berckelaer-Onnes I nad Leekam S: Diagnosing Autism Spectrum Disorder: Who will get a DSM-5 diagnosis?. J Child Psychol Psychiatry. 2013;54(11):1242-50
4. Chaste P and Leboyer M: Autism risk factors: genes, environ-ment, and gene-environment interactions. Dialogues in Clinical Neuroscience, 2012; Vol 14,(3):281-92
5. Bergbaum A and Ogilvie CM: Autism and chromosome abnormalities-A review. Clin. Anat. 2016; 29: 620–27.
6. Gialloreti L, Mazzone L, Benvenuto A, Fasano A, Alcon A, Kraneveld A, Moavero R, Raz R, Riccio M, Siracusano M, Zachor D, Marini M and Curatolo P: Risk and Protective Environmental Factors Associated with Autism Spectrum Disorder: Evidence-Based Principles and Recommendations. J. Clin. Med. 2019, 8pages, 217; doi:10.3390/jcm8020217
7. Schmidt RJ, Tancredi, DJ, Krakowiak P, Hansen RL and Ozonoff S: Maternal intake of supplemental iron and risk of autism spectrum disorder. Am. J. Epidemiol. 2014, 180, 890–900.
8. Almandil N, Alkuroud D, AbdulAzeez S, AlSulaiman A, Elaissari A and Borgio F: Environmental and Genetic Factors in Autism Spectrum Disorders: Special Emphasis on Data from Arabian Studies. Inter J. of Environmental Research and Public Health. 2019; 16, 658 doi:10.3390/ijerph16040658
9. Kalra V, Seth R and Sapra S: Autism experiences in a tertiary care hospital. Indian journal of pediatrics. 2005;72(3):227-30.
10. Volkmar J, Siegel M, Woodbury-Smith M, King B, McCracken J, State M, and the American Academy of Child and Adolescent Psychiatry (AACAP) Committee on Quality Issues: Practice Parameter for the Assessment and Treatment of Children and Adolescents With Autism Spectrum Disorder. Journal of the American academy of child & adolescent psychiatry 2014;vol 53 no 2: 237-57.
11. Brkanac Z, Raskind W and King B: Pharmacology and genetics of autism: implications for diagnosis and treatment. Per Med. 2008; 5(6): 599–607. doi:10.2217/17410541.5.6.599

12. Mugno D, Ruta L, D'Arrigo VG and Mazzone L: Impairment of quality of life in parents of children and adolescents with pervasive developmental disorder. Health Qual Life Outcomes. 2007;5:22.
13. Perumal V, Veeraraghavan V and Lekhra O: Quality of life in families of children with autism spectrum disorder in India. Journal of Pharmacy Research. 2014;8(6),791-7.
14. Gupta A and Singhal N: Psychosocial support for families of children with autism. Asia Pacific Disability Rehabilitation Journal. 2005; 16(2): 62-83.
15. Idring S, Lundberg M, Strum H, Dalman C, Gumpert C, Rai D, Lee BK and Magnusson C: Changes in prevalence of autism spectrum disorders in 2001-2011: Findings from the Stockholm youth cohort. J Autism Dev Disord. 2015;45(6):1766-73.
16. Robinson EB, Lichtenstein P, Anckarsater H, Happe F and Ronald A: Examining and interpreting the female protective effect against autistic behavior. Proc Natl Acad Sci USA. 2013; 110:5258–62.
17. Gronborg TK, Schendel DE and Parner ET: Recurrence of autism spectrum disorders in full- and half-siblings and trends over time: a population-based cohort study. JAMA pediatrics. 2013; 167:947–53
18. Oswald D, Haworth S, Mackenzie B and Willis J: Parental report of the diagnostic process and outcome: ASD compared with other developmental disabilities. Focus on Autism Other Dev Disabilities. 2017;32(2):152–160.
19. Spain D, Sin J, Linder K, MaMahon J and Happe F: Social anxiety in autism spectrum disorder: A systematic review. Research in Autism Spectrum Disorders. 2018;52: 51-68.
20. Malhi P and Singh P: A retrospective study of toddlers with autism spectrum disorder: Clinical and developmental profile. Ann Indian Acad Neurol. 2014; 17(1): 25–9.
21. Frye R, Rossignol D, Casanova M, Brown G, Martin V, Edelson S, Coben R, Lewine J, Slattery J, Lau C, Hardy P, S.] Fatemi H, Folsom T, MacFabe D and Adams J: A review of traditional and novel treatments for seizures in autism spectrum disorder: findings from a systematic review and expert panel. Frontiers in Public Health. 2013; Vol 1, art 31 doi: 10.3389/fpubh.2013.00031
22. Viscidi E, Triche E, Pescosolido M, McLean R, Joseph R, Spence S and Morrow E: Clinical characteristics of children with autism spectrum disorder and co-occurring epilepsy. PLoSOne (2013) 8:e67797.doi:10.1371/ journal. pone.0067797
23. Hirota T, Vander-Weele J, Hollander E and Kishi T: Antiepileptic Medications in Autism Spectrum Disorder: A Systematic Review and Meta-analysis. J Autism Dev Disord. 2014; 44:948-57.
24. Ritalin (methylphenidate) prescribing information. East Hanover, New Jersey: Novartis Pharmaceuticals Corporation; December 2013. Available at: https://www.pharma.us.novartis.com/product/ pi/pdf/ritalin_ritalin-sr.pdf. Accessed October 20, 2019
25. Sturman N, Deckx L and Van Driel M: Methylphenidate for children and adolescents with autism spectrum disorder. Cochrane Database Syst Rev. 2017.21;11 https://doi.org/10.1002/14651858.CD011144.
26. Dale E, Jahoda A and Knott F: Mothers' attributions following their child's diagnosis of autistic spectrum disorder: exploring links with maternal levels of stress, depression and expectations about their child's future. Autism. 2006;10(5):463–79.
27. Myers B, Mackintosh V and Goin-Kochel R: "My greatest joy and my greatest heart ache:" Parents' own words on how having a child in the autism spectrum has affected their lives and their families' lives. Res Autism Spectr Disord. 2009;3(3):670–84.