CARBAMAZEPINE VERSUS RESPERIDONEIN TREATMENT

OF AUTISTIC SYMPTOMS

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Back ground Autism spectrum disorder (ASD), is a heterogeneous of neuro-developmental syndrome characterized by a wide range of impairments in social interactions, verbal and non-verbal communication and restricted and repetitive behaviors in the first three years of life. There is no curative treatment for ASD, The early and correct diagnosis is important in successful intervention program. Recently Risperidone is used to treat patients with ASD. The children with ASD that show Electro-Encephalo-Graphic (EEG) changes are about 10.3% to 72.4% of patients. The prevalence of epilepsy with Autistic children has been estimated at 7-14%. The management of seizures waves using Anti-Epileptic Drugs such as Carbamazepine in children and adolescents with ASD may cause functional improvement and reduction of autistic symptoms. Although pharmacological treatment is beneficial in decreasing symptoms in ASD, Behavior Modification must associate these pharmacological agents.

Objectives: to assess the effect of Risperidone, Carbamazepine, and Behavioral Modification in decreasing severity of the symptoms of ASD.

Patients and Methods: Sixty patients were diagnosed as having ASD according to Diagnostic and Statistical Manual of Mental Disorders fifth edition (DSM-V) , then the sample is divided into three groups. The first group will be given Risperidone and Behavior Modification. The second group will be given Carbamazepine and Behavior Modification. The third group will be given Behavior Modification only.The duration of the study was six months. Evaluation of symptoms of ASD was done before the study and after the study. Statistical analysis was done.

Results: Clinical and Statistical improvement occurred between before the study and after the study. On the other hand, there are no statistical significant results from comparing the three groups after the study.

Conclusion: Risperidone and Carbamazepine are effective and tolerable agents in the course of treatment of ASD. Behavior Modification is non- pharmacological effective treatment of ASD.

Key words: Autism – Autism Spectrum Disorder- Risperidone - Carbamazepine- Behavior Modification

**دراسة مقارنة بين الكاربامازيبين والريسبريدون فى علاج الاعراض الذاتوية**

مقدمه :اضطراب طيف الذاتوية هو أحد اضطرابات تشوه النمو العصابى التي تتصف بسلوك تكراري محدود ونقص في التكامل الاجتماعي التي يتميز به الأطفال فى الثلاث سنوات الأولى من أعمارهم . لا يوجد عقار بحد ذاتة لعلاج هذه الاضطرابات و لكن التشخيص الصحيح والعلاج المبكر لهذه الاضطرابات يعتبر هاما لعمل البرامج التدخلية المناسبة لكل طفل . حديثا فأننا قد نستعمل بعض العقارات لعلاج الإعراض الموجودة بهذه الاضطرابات مثل عقار الريسبريدون. مرضي الذاتوية يعانون من تغير في القوة الكهربية لرسم المخ   
منهم يعانون من مرض الصرع لذا فإن استخدام مضادات الصرع مثل عقار الكاربامازيبين للأطفال و الشباب الذاتويين قد يحسن أسلوب الحياة ويقلل الأعراض الذاتوية. و بالرغم أن العلاج العقارى يعتبر هاما لتقليل الأعراض الذاتوية فإن تعديل السلوك يعتبر هاما أيضا ولابد منه بجانب العقارات.

الهدف من الدراسة : تقدير فاعلية ريسبريدون بالمقارنة بالكاربامازيبين و العلاج السلوكى في علاج وتقليل الأعراض الذاتوية.

نوع الدراسة : دراسة مقارنة .

وصف الدراسة: ستون طفلاً يعانون من ن اضطرابات طيف الذاتوية بواسطة اختيار الكارز كما تم قياس الذكاء ورسم المخ الكهربائي .تم يقسم هؤلاء الأطفال إلى ثلاث مجموعات متساوية فى العدد : المجموعة الأولي أعطيناهم عقار الريسبريدون مع جلسات التعديل السلوكى .المجموعة الثانية : أعطيناهم عقار الكاربامازيبين مع جلسات التعديل السلوكى . المجموعة الثالثة: أعطيناهم جلسات التعديل السلوكى فقط \ لمدة ستة أشهر ثم أعدنا قياس الأعراض بمقياس الذاتويين ( CARS ) واختبار النضج الإجتماعى و إختبار تقييم العلاج للذاتويين ( ATEC )ثم أعدنا رسم المخ الكهربائي أيضاً .

الخلاصة: إن عقار الريسبريدون و عقار الكاربامازبين هما عقاران فعالان ومحتملان فى علاج الأعراض الذاتوية. و تعديل السلوك هو جزء هام جدا في علاج الذاتوية .

نتائج الدراسة: إن عقار الريسبريدون والكاربامازبين والعلاج السلوكي فعالين في علاج اعراض مرض الذاتوية .

التوصيات:يعتبر الريسبريدون والكاربامازيبين فعالين في اغلب حالات مرض الذاتوية ويعتبر العلاج السلوكي من افضل طرق علاج اعراض مرض الذاتوية.لابد من تطويل مدة العلاج عن مدة الدراسة و اخذ عينة اكبر لتظهر نتائج افضل في المستقبل.

Introduction: Autism spectrum disorder (ASD), is a phenotypically heterogeneous neuro-developmental syndrome with polygenic heritability, characterized by impairments in social interactions, communication and restricted and repetitive behaviors in the first three years of life (Kaplan and Sadock, 2015). The current prevalence of ASD is about 1%-2%. There is male predominance, that male to female ratio is 4~5:1 (CDC., 2016).

There is no curative treatment for ASD, but multimodel intervention programs show significant improvement. The early and correct diagnosis is important in successful intervention program. The goals of treatment are to increase socially acceptable behaviors, to decrease odd behavioral symptoms, and to enhance the verbal and nonverbal communication (Rapin and Tushman, 2017).

Recently, the second generation of antipsychotics (SGA) are used to treat patients with disruptive behaviors, mood disorders and ASD. Evidence-based researches support the benefit of Risperidone for stereotyped behaviors in children with ASD (Stigler and Mc Douglas., 2016).

It was found that, ASD is usually coexisted with different types of epilepsies. This co-occurrence may be due to genetic element and biologic processes of both syndromes The children with ASD that show Electro-Encephalo-Graphic (EEG) changes are about 10.3% to 72.4% of patients. The prevalence of epilepsy with Autistic children has been estimated at 7-14%, whereas the cumulative prevalence by adulthood is estimated at 20% to 35% of patients (Cohen, 2015).

The management of seizures waves using Anti-Epileptic Drugs such as Carbamazepine in individuals with ASD may cause functional improvement and reduction of autistic symptoms. The side effects of Carbamazepine are GI discomfort, Hepatic affection, and skin rash (Yasubara, 2016).

Early Intension Behavioral Intervention (EIBI) has positive outcome among children with ASD. EIBI is used to maximize the effect of pharmacological agents in the management of ASD. It is also used to decrease the mal adaptive behaviors and increase the adaptive ones (Unwin and Ded, 2017).

Objectives: to assess the effect of Risperidone, Carbamazepine, and Behavioral Modification in decreasing severity of the symptoms of ASD.

Patients and Methods: The study was conducted from November, 2011 to May, 2013.This study was conducted on children diagnosed with autistic disorder according to the criteria of (DSM – V), attending as outpatients in clinic of special needs in Institute of Postgraduate Childhood Studies, Ain Shams University. Risperidone and Behavioral Modification Therapy were given for six months to groupI. The drug dose were 0.5mg/ day as initial dose, which could be increased after 4 weeks according to the patient response. Carbamazepine and Behavioral Modification Therapy were given for six months to group II. The drug dose was 50 – 200 mg / day. Behavioral Modification Therapy only (3 sessions per week, each session was 30 – 45 minutes) was given to group III for 6 months. Then all patients were subjected to CARS, ATEC, Vineland Social Maturity Scale, Stanford – Binet IQ tests the fifth edition and EEG before and after 6 months of taking these therapies. Data obtained from the study will be analyzed and the three groups will be compared with each others.

Inclusion Criteria: Patients are in good general condition and able to take oral medicine. Male and female patients are included. Age 3 - 10 years old. CARS Score from 31 to 39. Medication free for one month.

Exclusion Criteria:The presence of epileptic fits. The presence of any other co-morbid psychiatric disorder.The IQ below 50. Hearing or visual, Motor disabilities such as hemiplegia or paraplegia.

Ethical consent: Written informed consent will be obtained from each child parents after explanation of the aim of the study and its benefits for their children and other children who might have the same disease. The study is not sponsored by any pharmaceutical company.

All children will be subjected to: (1) Full Psychiatric history and examination to diagnose ASD according to (DSM-V) criteria (APA, 2013). (2) Complete Medical History and clinical examination to exclude any co-morid disorder. (3) Psychological Assessment by Childhood Autism Rating Scale (CARS), which is the most widely used to determine symptoms and severity of autistic disorder. It is done by ( Schoppler et al ., 1980) and the Arabic version translated by ( El Dafrawi, 1998 ). It covers social, emotional, and communication skills and repetitive behaviors, play routines and unusual sensory interests. The scale subjectively rate 15 items, ( Relationship to people, Imitation, Emotional response, body use, Adaptation to change, Visual response, Listening response, Taste-smell-touch response and use, Fear or nervousness, Verbal communication, Non-verbal communication, Activity level, General impressions (Rellini et al., 2015).

(4) The Vineland Social Maturity Scale : which measures social competence, self-help skills, and adaptive behavior from infancy to adulthood. It is used in planning for therapy and/or individualized instruction for persons with mental retardation or emotional disorders. The Vineland scale, which can be used from birth up to the age of 30, consists of a 117-item interview with a parent or other primary caregiver. (There is also a classroom version for ages 3-12 that can be completed by a teacher.) Personal and social skills are evaluated in the following areas: daily living skills (general self-help, eating, dressing); communication (listening, speaking, writing); motor skills (fine and gross, including locomotion); socialization (interpersonal relationships, play and leisure, and coping skills); occupational skills; and self-direction. (An optional Maladaptive Behavior scale is also available.) The test is untimed and takes 20-30 minutes. Raw scores are converted to an age equivalent score (expressed as social age) and a social quotient (McCullough, 1992).

(5) The Autism Treatment Evaluation Checklist (ATEC): it was developed in 1999 to help researchers evaluate the effectiveness of various treatments for autistic children and adults and to help parents determine if their children benefit from a specific treatment. Parents and teachers use the ATEC to monitor or track how well their children are progressing over time, even without the introduction of a new treatment (Magiati et al ., 2015).

(6) Assessment of Intelligence Quotient (IQ) by Stanford Binet Scale 5th edition (APA,2013), Arabic version translated by (Abu Elneil, 2013). The test is scored manually from which verbal and performance score and intelligent quotient were obtained.

(7)Electroencephalogram (EEG), it will be recorded using twenty-one electrodes placed according to the International 10-20 system with sixteen channels subset. The impedance of the silver-silver chloride electrodes, which were glued to the scalp coildion (Chadwick et al., 2016).

Statistical analysis: Data will be obtained from research will be tabulated and analyzed using the SPSS program on PC software (Rapin and Tushman, 2017).

Results: Table I: Group I: The effect of Risperidone + Behavioral Modification on EEG

|  |  |  |
| --- | --- | --- |
| Case # | Before | After |
| 1 | increased activity of left hemi sphere (all lobes) | increased activity of left hemi sphere (all lobes) |
| 2 | biparietal epileptogenic discharge | biparietal epileptogenic discharge |
| 3 | bitemporal and left occipital epileptogenic discharge | bitemporal and left occipital epileptogenic discharge |
| 4 | left temporal epileptogenic - abnormal slap records | left tempro - occipital epileptogenic activity - abnormal sleep records |
| 5 | left occipital epileplpgenic discharge | left occipital epileplpgenic discharge |
| 6 | left frontal epileptogenic discharge | bilateral frontal epileplogenic discharge |
| 7 | left temporal epileplogenic discharge | left tempro occipital epileptogenic |
| 8 | left frontal epileplogenic discharge | bilateral frontal |
| 9 | left occipital epileplogenic discharge | bilateral occipital |
| 10 | abnormal sleep record | abnormal sleep record |
| 11 | left frontal epileplogenic discharge | bilateral frontal |
| 12 | left temporal epiteplogenic discharge | left temporal epiteplogenic discharge |
| 13 | left temporal epiteplogenic discharge | bilateral temporal |
| 14 | left temporal - left occipital | bilateral - lateral occipital |
| 15 | left occipital | left occipital - left temporal |
| 16 | left frontal epiteplogenic | left frontal, left occipital |
| 17 | abnormal sleep record left frontal epileptogenic discharge | abnormal sleep record left frontal epileptogenic discharge |
| 18 | left temproccipital epiteplogenic discharge | bilateral tempro occipital |
| 19 | left temporal epiteplogenic discharge | bilateral temporal |
| 20 | abnormal sleep record | abnormal sleep record |

Risperidone may cause increase in the electrical activity and the EEG changes.

Table II:Group II: The effect of Carbamazepine + Behavioral Modification on EEG

|  |  |  |
| --- | --- | --- |
| Case # | Before | After |
| 21 | bilateral occipital bilateral parietal | left occipital – left parietal |
| 22 | bilateral temporal | bilateral temporal |
| 23 | left temporal | Normal |
| 24 | bilateral occipital and left temporal epiteplogenic discharge | Right occipital and left temporal |
| 25 | bilateral temporal epiteplogenic discharge | left temporal epiteplogenic discharge |
| 26 | right occipital epiteplogenic discharge | normal |
| 27 | abnormal sleep record left parietal epiteplogenic discharge | left parietal epiteplogenic discharge |
| 28 | right frontal epiteplogenic discharge | normal |
| 29 | bilateral occipital epiteplogenic discharge and right frontal | left occipital epiteplogenic discharge |
| 30 | left temporal epiteplogenic discharge | left temporal epiteplogenic discharge |
| 31 | bilateral occipital and right temporal epiteplogenic discharge | bilateral occipital epiteplogenic discharge |
| 32 | right occipital epiteplogenic discharge | Normal |
| 33 | right temporal epiteplogenic discharge | normal |
| 34 | right temporal and left frontal epiteplogenic discharge | left frontal epiteplogenic discharge |
| 35 | bilateral tempro occipital epiteplogenic discharge | left temporal epiteplogenic discharge |
| 36 | left temporal epiteplogenic discharge | Normal |
| 37 | bilateral occipital epiteplogenic discharge | right occipital epiteplogenic discharge |
| 38 | bilateral frontal epiteplogenic discharge | left frontal epiteplogenic discharge |
| 39 | right occipital epiteplogenic discharge | normal |
| 40 | right temporal epiteplogenic discharge | normal |

Carbamazepine is an antiepileptic agent so, it cause decrease in the electrical activity and the EEG changes.

Table III: Group III: The effect of Behavior Modification Only (Without Drugs) on EEG

|  |  |  |
| --- | --- | --- |
| Case # | Before | After |
| 41 | Left temporal - right occipital epileptogenic discharge | Left temporal - right occipital epileptogenic discharge |
| 42 | Right temporal epileplogenic discharge | Normal |
| 43 | Left tempro occipital epileptogenic discharge | Left tempro occipital epileptogenic discharge |
| 44 | Right frontal epileplogenic discharge | Normal EEG |
| 45 | Right parietal epileptogenic discharge | Right parietal epileptogenic discharge |
| 46 | Abnormal sleep record | Abnormal sleep record |
| 47 | Left temporal epileptogenic discharge | Left tempro occipital epileptogenic discharge |
| 48 | Bilateral frontal epileptogenic discharge | Bilateral frontal epileptogenic discharge |
| 49 | Right temporal epileptogenic discharge | Right tempro occipital discharge |
| 50 | Left occipital epileptogenic discharge | Left occipital epileptogenic discharge |
| 51 | Bilateral frontal epileptogenic discharge | Bilateral fronto - temprol epileptogenic discharge |
| 52 | (Decreased connectivity) x left occipital | (Decreased connectivity) x left occipital |
| 53 | Right temporal epileptogenic discharge | Bilateral temporal epileptogenic discharge |
| 54 | Left tempro occipital epileptogenic discharge | Left tempro occipital epileptogenic discharge |
| 55 | Right frontal epileptogenic discharge | Right frontal epileptogenic discharge |
| 56 | Right parietal epileptogenic discharge | Right parieto occipital epileplogenic discharge |

|  |  |  |  |
| --- | --- | --- | --- |
| 57 | | Left temporal epileptogenic discharge | Left temporal epileptogenic discharge |
| 58 | Right temporal epileptogenic discharge | Bilateral tempro occipital |
| 59 | Left frontal epileptogenic discharge | Bilateral frontal |
| 60 | Left occipital epileptogenic discharge | Left occipital epileptogenic discharge |

The electrical activity may be increase as the child did not take treatment, or remain as it is, or even there is spontaneous improvement.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Table IV : The gender difference between groups before the study | | | | | | |
|  | | | groups | | | Total |
| Risperidone & BM | Carbamazepine & BM | BM |
| gender | male | Count | 17 | 18 | 17 | 52 |
| % within groups | 85.0% | 90.0% | 85.0% | 86.7% |
| female | Count | 3 | 2 | 3 | 8 |
| % within groups | 15.0% | 10.0% | 15.0% | 13.3% |
| Total | | Count | 20 | 20 | 20 | 60 |
| % within groups | 100.0% | 100.0% | 100.0% | 100.0% |

Group II only has less in girls count than group I and group II.

Table V: The effect of variables ( age and IQ) on groups before the study

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Variables | | N | Mean | SD | F | P value |
|
| age | Risperidone & BM | 20 | 4.89 | 1.50 | 0.017 | .983 |
| Carbamazepine & BM | 20 | 4.95 | 1.46 |
| BM | 20 | 4.97 | 1.34 |
| Total | 60 | 4.93 | 1.41 |
| IQ Before | Risperidone & BM | 20 | 55.75 | 5.34 | 0.116 | .890 |
| Carbamazepine & BM | 20 | 55.60 | 4.59 |
| BM | 20 | 55.05 | 4.52 |
| Total | 60 | 55.47 | 4.76 |

The results were insignificant because there are no significant differences between groups in these variables.

Table VI: Paired t-test between the tests before and after the study in all groups:

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | | Mean | N | Std. Deviation | t | P value |
| Pair 1 | CARS b | 4.7000 | 60 | 1.30579 | 19.309 | 0.000 |
| CARS a | 2.1667 | 60 | 1.20966 |
| Pair 2 | ATEC b | 5.6833 | 60 | .72467 | 12.566 | 0.000 |
| ATEC a | 4.5333 | 60 | 1.01625 |
| Pair 3 | SQ b | 1.3833 | 60 | .58488 | 2.955 | 0.004 |
| SQ a | 2.4333 | 60 | 2.81862 |
| Pair 4 | IQ b | 1.3333 | 60 | .57244 | 6.606 | 0.000 |
| IQ a | 2.1667 | 60 | 1.13745 |

There are significant differences between the results of each test, before and after the study in all groups.

Table VII: Comparison among groups in all tests after the study

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | | N | Mean | SD | F | P value |
| CARS | Risperidone & BM | 20 | 1.9500 | 1.19097 | 0.687 | 0.5 |
| Carbamazepine & BM | 20 | 2.1500 | 1.26803 |
| BM | 20 | 2.4000 | 1.18766 |
| Total | 60 | 2.1667 | 1.20966 |
| ATEC | Risperidone & BM | 20 | 4.5000 | .94591 | 0.904 | 0.4 |
| Carbamazepine & BM | 20 | 7.5000 | 13.81266 |
| BM | 20 | 4.6000 | .99472 |
| Total | 60 | 5.5333 | 8.00099 |
| SQ | Risperidone & BM | 20 | 3.0500 | 4.65069 | 0.714 | 0.5 |
| Carbamazepine & BM | 20 | 1.9500 | .82558 |
| BM | 20 | 3.3000 | 4.58946 |
| Total | 60 | 2.7667 | 3.78385 |
| IQ | Risperidone & BM | 20 | 2.6500 | 1.59852 | 2.892 | 0.06 |
| Carbamazepine & BM | 20 | 1.9500 | .82558 |
| BM | 20 | 1.9000 | .64072 |
| Total | 60 | 2.1667 | 1.13745 |

The results are statistically insignificant may be due to the are small numbered groups and the duration is relatively short.

Table VIII: Comparison between tests before and after the study in group I

|  |  |  |  |
| --- | --- | --- | --- |
|  | Mean±SD | T test | P value |
| CARS | | | |
| Before | 37.25±1.83 | 16.808 | 0.000\*\* |
| After | 31.55±2.36 |
| ATEC | | | |
| Before | 109.00±13.53 | 11.204 | 0.000\*\* |
| After | 85.65±17.27 |
| SA | | | |
| Before | 2.87±0.99 | 12.231 | 0.000\*\* |
| After | 3.68±1.06 |
| SQ | | | |
| Before | 55.50±4.46 | 13.183 | 0.000\*\* |
| After | 60.95±4.94 |
| ATEC | | | |
| Before | 55.75±5.34 | 25.354 | 0.000\*\* |
| After | 62.85±5.83 |

There are statistically significant results between tests before and after the study which indicate the improvement of patients.

Table number IX: The correlation

|  |  |  |  |
| --- | --- | --- | --- |
|  | N | Correlation | P value |
| CARSBefore&CARSAfter | 20 | .765 | .000 |
| ATECBefore&ATECAfter | 20 | .844 | .000 |
| SABefore&SAAfter | 20 | .960 | .000 |
| SQBefore&SQAfter | 20 | .927 | .000 |
| IQBefore&IQAfter | 20 | .979 | .000 |

Table X: Comparison between tests before and after the study in group II

|  |  |  |  |
| --- | --- | --- | --- |
|  | Mean±SD | T test | P value |
| CARS | | | |
| Before | 36.25±1.81 | 16.449 | 0.000\*\* |
| After | 32.50±1.96 |
| ATEC | | | |
| Before | 104.95±12.17 | 19.894 | 0.000\*\* |
| After | 92.10±12.06 |
| SA | | | |
| Before | 3.49±1.23 | 2.673 | 0.015\* |
| After | 3.93±1.07 |
| SQ | | | |
| Before | 56.50±4.81 | 26.688 | 0.000\*\* |
| After | 61.35±5.04 |
| ATEC | | | |
| Before | 55.60±4.59 | 16.508 | 0.000\*\* |
| After | 61.15±5.20 |

There are highly significant improvements occurred in this group after the study.

Table XI: Correlation

|  |  |  |  |
| --- | --- | --- | --- |
|  | N | Correlation | P value |
| CARSBefore&CARSAfter | 20 | .765 | .000 |
| ATECBefore&ATECAfter | 20 | .844 | .000 |
| SABefore&SAAfter | 20 | .960 | .000 |
| SQBefore&SQAfter | 20 | .927 | .000 |
| IQBefore&IQAfter | 20 | .979 | .000 |

Table XII: Comparison between tests before and after the study in group III

|  |  |  |  |
| --- | --- | --- | --- |
|  | Mean±SD | T test | P value |
| CARS | | | |
| Before | 36.45±2.04 | 32.484 | 0.000\*\* |
| After | 32.65±2.01 |
| ATEC | | | |
| Before | 102.00±26.47 | 1.743 | 0.097\* |
| After | 93.45±13.79 |
| SA | | | |
| Before | 3.20±0.96 | 20.842 | 0.000\*\* |
| After | 3.79±0.98 |
| SQ | | | |
| Before | 56.55±4.67 | 21.944 | 0.000\*\* |
| After | 61.80±4.79 |
| ATEC | | | |
| Before | 55.05±4.52 | 18.800 | 0.000\*\* |
| After | 60.35±4.76 |

Improvements are statistically recorded from before to after the study.

Table XIII: Correlation

|  |  |  |  |
| --- | --- | --- | --- |
|  | N | Correlation | P value |
| CARSBefore&CARSAfter | 20 | .967 | .000 |
| ATECBefore&ATECAfter | 20 | .562 | .010 |
| SABefore&SAAfter | 20 | .992 | .000 |
| SQBefore&SQAfter | 20 | .975 | .000 |
| IQBefore&IQAfter | 20 | .964 | .000 |

DISCUSSION

The efficacy of Risperidone: in treating nervousness that associated with autism in 90 autistic individuals, aged 5-17 years. This 8 weeks study compared risperidone to placebo on measurement of nervousness. Response was identified as ≥ 25% decrease in the nervousness and rating of much improved. Result rates were 69% in the Risperidone treatment group and 12% in the placebo group, which was significant difference. Significant side effects in the risperidone group were increased weight (2.7 kg versus 0.8 kg in the risperidone and placebo groups, respectively), raised appetite, fatigue, drowsiness, dizziness and drooling. Among the patients of the risperidone group, about 68% maintained this response at 6 month follow up study. Side effects in the risperidone group included moderate sedation, raised appetite, weight gain (mean 2.8 kg), and mild, temporary dyskinesias. Risperidone is also effective in treating the restricted and repeated behaviors, raising the good behaviors in the areas of communication, socialization, and daily living skills (Stigler and Mc Douglas., 2016).

The management of seizures waves using Anti-Epileptic Drugs such as Carbamazepine in children and adolescents with ASD may cause functional improvement and reduction of autistic symptoms. Carbamazepine is used also in the treatment of bipolar disorder, and in neurogenic pain. The side effects of Carbamazepine are GI discomfort, Hepatic affection, and skin rash (Yasubara, 2016).

Many researches in behavioral therapy was done since 1960.They have shown that, special skills can be taught to autistic children. Specialist must put few points in consideration: First, behavioral therapy should be designed for individual child. Second, autistic children have an impaired ability to generalize from one situation to another, so specialists have to encourage generalization of behaviors. Third, early and intensive behavioral therapy should be done to increase the child's social development (Rapin and Tuchman, 2017).

In table number I there are the EEG changes in group I which had increased in the electric activity of the brain from before to after the research, so Risperidone worsen the electric activity of the brain regions. In table number II The EEG changes in group II had decreased in the electric activity of the brain from before to after the research, as Carbamazepine is an anti- epileptic medication. In table number III The EEG changes in group III, the electric activity of the brain showed no change , or spontaneous improvement, or even worsened as the patient did not take any treatment, so Behavioral Modification does not affect the electric activity of the brain regions. In table number IV, it represents the stability of the sample as regards the gender. In table number V, it also represents the stability of the sample as regards the IQ and the age of the patients. In table number VI, all results are statistically significant in all the 60 patients. In table number VII, it represents comparison between all groups after the study; the results were statistically insignificant as the sample was very small to determine the results and also the duration is relatively short. In tables number from VIII to XIII, they represent comparison between CARS, ATEC, and Vineland Social Maturity Scale before and after the study in group I, II, and III. They show positive results which are statistically significant.

CONCLUSION: This research was done to measure the effect of two different medications (Risperidone and Carbamazepine) besides Behavior Modification Therapy as three different lines of treatment of symptoms of ASD. The results of this research showed statistically significant improvements from before to after the research in the three groups. Risperidone and Carbamazepine are effective and well- tolerated medications. The findings of Risperidone group were more significant in the treatment of autistic symptoms measured by CARS and ATEC, but it may increase the EEG abnormalities. On the other hand, Cabamazepine group show great improvements in EEG abnormalities more than improvements in autistic symptoms. Behavior Modification only group also, showed improvement in autistic symptoms but less than groupI.

RECOMMENDATIONS: Large sample,and long duration studies are preferable to get more statistically significant results. Other atypical antipsychotic drugs such as Aripiprazole should be tried. The pharmacological treatment is important but, other lines of treatment are very important as well.

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