

## Effect of Antipsychotics on Bone Mineral Density in Autistic children

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### Abstract

**Background:** The prevalence of fractures in autism spectrum disorder (ASD) appear to be on the rise, we assessed variables as Antipsychotics used in ASD treatment which may have an effect on bone mineral density. BMD is measured with dual energy X- ray absorptiometry (DEXA).

**Objective:** The present study investigates the effect of Antipsychotics on bone mineral density in ASD children.

**Patients and methods:** 44 Participants were randomly chosen 36 boys and 8 girls, age ranged 3- 9 years old, and they were classified into 3 groups. First group: 20 Autistic children under Antipsychotic. Second group: 16 Autistic children didn't receive medication. Third group: 8 Normal children.

**Result:** The study revealed that in Group 1: 65% had no osteopenia and 35% had osteopenia. Group 2: 50% had no osteopenia and 50% had osteopenia. Group 3: 75% had no osteopenia and 25% had osteopenia.

**Conclusion:** Antipsychotics had minimal effect on bone mineral density.

**Keywords:** Bone mineral density, Dexa

### تأثير مضادات الذهان على كثافة عظام أطفال اضطراب التوحد الطيفي

**المقدمة:** هناك ارتفاع في نسبة كسور العظم لدى أطفال اضطراب التوحد الطيفي، ولقد قمنا بتقييم المتغيرات كمضادات الذهان المستخدمة في العلاج والتي قد تكون لها تأثير على كثافة المعادن في العظم، تقاس الكثافة المعدنية للعظام باستخدام الأشعة السينية ثنائية الطاقة.

**هدف الدراسة:** تبحث الدراسة عن تأثير مضادات الذهان على كثافة المعادن في العظم.

**المنهجية:** اشترك في الدراسة 44 طفل 36 أولاد و 8 بنات وقسموا الى ثلاث مجموعات: المجموعة الأولى: 20 طفل من أطفال اضطراب التوحد وبأخذون الدواء، المجموعة الثانية: 16 طفل من أطفال اضطراب التوحد ولا يأخذون الدواء، المجموعة الثالثة: أطفال أسوياء.

**نتيجة الدراسة:** 65% من المجموعة الأولى ليس لديهم هشاشة و 35% لديهم هشاشة و 50% من المجموعة الثانية ليس لديهم هشاشة و 50% لديهم هشاشة و 75% من المجموعة الثالثة ليس لديهم هشاشة و 25% لديهم هشاشة.

**استنتاج الدراسة:** مضادات الذهان له تأثير طفيف على كثافة المعادن في العظم.

## Introduction

Autism spectrum disorder (ASD) is a long life set of complex neurodevelopment disorder, characterized by impaired social interaction, verbal and non verbal communication, with stereotyped repetitive behavior. (American Psychiatric Association, 2000)

Bone development begins in childhood, and then continues on into young adulthood, this is considered the most critical timing for bone development (international food information council website, 2009).

Bone remodeling is known to be the sustainable process of bone formation and bone resorption, and this occurs throughout an individual's life, it continuous until skeletal maturity (Halbreich, 2007; Parfilit, 1979; Plgozzi et.al., 2009; Prentice, 1997).

Bone remodeling is going fast at first, bone formation lends to dominate bone resorption, this results in an increase in skeletal mass (Van der Sluis et.al., 2002), it happens between the ages 25 to 35, bone mass reaches its peak point (Plgozzi et.al., 2009).

Autistic children are reported to have low bone mineral density and thus decreased bone cortical thickness (Molley et.al., 2010) for many reasons, these factors food refusal, food selectivity, lack of calcium and vitamins rich food, digestive problems diet that exclude Casein (Hediger et.al., 2008), the use of medications that suppress appetite or interfere with bone metabolism (Pack et.al., 2004; Aman et.al., 2005) or decreased or limited physical activity and exposure to sunlight.

Antipsychotic medication could affect bone metabolism due to its effect on bone modeling, this is done because bone resorption is more stimulated than bone formation therefore, it leads to osteoporosis (Leslie et.al., 2009).

## Aim of the Study:

To decrease the fracture at the E. R. in autism spectrum disorder children due to low bone mass and low bone mineral density as these fractures may represent a source of disability and morbidity.

## Methodology:

Study design: the study used a cross- sectional study design. The main aim of the study is to investigate the effect of medication medical supplements on bone mineral density in autism spectrum disorder.

The participants were chosen from the outpatient clinic of the special need center in the faculty of postgraduate childhood studies, Ain Shams University, 44 participants were chosen for this study, 36 boys and 8 girls, they were classified into three groups:

- ✧ 1st group: 20 Autistic children under Antipsychotic treatment
- ✧ 2nd group: 16 Autistic children, they didn't receive medication.
- ✧ 3rd Group: Normal Children

The 3 groups of included samples of boys and girls with a range of age from (3- 9) years, 36 of the sample were diagnosed with ASD according to DSM V

Exclusion Criteria: The children who suffered from chronic medical condition or psychiatric disorder, or children who are under dietary restriction of gluten or casein

Research Ethical Consideration: the study proposal was approved by the local ethical committee of the faculty of postgraduate childhood studies and it was conducted according to the guidelines of Helsinki, the guidelines for the ethical conduct of medical research involving children, revised by the royal college of pediatrics and child health ethics advisory committee (IPGC, 2014) an informed consent was obtained from the parents.

## Methods and Tools:

Datasheet: Statistical presentation and analysis of the present study was conducted, using the mean standard deviation, student t- test- chi-square- linear correlation, coefficient and analysis of variance (ANOVA) tests by SPSS V20.

## Data Collection:

1. Full medical history was taken from the participant children including the nutritional history and food intake pattern.
2. Full psychiatric assesment was taken. All information were taken from the parents.
3. Anthropometric Measurements:
  - a. The weight: all participants were assessed using a kilogram weight, the balance ranged from 1- 140 Kgms. The participants were assessed while standing.
  - b. The height: the height was measured using a calibrated portable pediatric height rod, while the participant was barefooted.
  - c. Body mass index: was calculated from weight and height taken by Using This Equation
 
$$\text{Body mass index} = (\text{Weight in Kg})^2 / (\text{Height in m})^2$$
4. Assessment Of The Child: Childhood Autism Rating Scale (CARS) and Intelligence Quotient (IQ) both were assessed by the psychologist working at the outpatient clinic of special need center in the faculty of postgraduate childhood studies Ain Shams University.
5. Dual Energy X- Ray Absorptiometry: Were done to all the three group participants investigating the children at high risk fracture of low bone mineral density fractures or osteoporosis.
6. A DEXA scan is a non invasive x- ray in which two different low x- ray were used (two to double the accuracy) in measuring the bone density.
7. The whole body, hip joint and the spine are the main areas to be scanned.
8. The autistic patient was sedated with chloral hydrate according to the weight of the patient and then he was placed on the DEXA.
9. The child was instructed not to wear clothes with zippers, buttons or any metal object.
10. The scan usually takes 10 minutes and the amount of radiation is very low.
11. The results are reported in Z score and T score.
  - a. T- score compares patient's bone to the mean peak body density of young healthy adult of 30 years old.
  - b. Z- score compares bone density to the mean peak density for

someone of the same age, sex and weight.

12. As for pediatrics, we take the reading of Z score.

- a. For T- score of 1 to -1: No Osteoporosis
- b. For T- score of -1 to -2.5: Osteopenia
- c. For T- score below -2.5: Osteoporosis

**Results:**

Table (1) Correlation between Antipsychotics medications and DEXA whole body scan

		Dexa Whole Body		T- Test Or Anova	
		N	Mean± SD	T Or F	P- Value
Risperidal/ Apixodone	Yes	17	- 0.771±1.426	-0.320	0.753
	No	3	- 0.500± 0.436		
Aripiprex	Yes	6	- 0.167± 0.497	1.270	0.220
	No	14	- 0.971±1.497		
Atomox	Yes	6	- 0.717±1.262	0.029	0.977
	No	14	- 0.736±1.390		
Cerebrolysin	Yes	4	- 0.325± 1.014	0.676	0.507
	No	16	- 0.831± 1.395		
Stimulan	Yes	4	- 1.125± 1.408	-0.659	0.518
	No	16	- 0.631± 1.326		
Combination Of Antipsychotics	One Antipsychotic	9	- 0.722± 1.568	0.116	0.891
	Two Antipsychotic	1	- 0.100± 0.000		
	Antipsychotic And Others	10	- 0.800± 1.200		

Table (2) Correlation between Antipsychotics and the DEXA spine scan

		Dexa Spine Scan		T- Test Or Anova	
		N	Mean ± SD	T Or F	P- Value
Risperidal/ Apixodone	Yes	17	- 0.547 ± 1.265	-0.195	0.847
	No	3	- 0.400 ± 0.436		
Aripiprex	Yes	6	- 0.200 ± 0.984	0.805	0.431
	No	14	- 0.664 ± 1.249		
Atomox	Yes	6	- 0.950 ± 0.638	-1.067	0.300
	No	14	- 0.343 ± 1.314		
Cerebrolysin	Yes	4	- 0.750 ± 0.545	-0.420	0.679
	No	16	- 0.469 ± 1.288		
Stimulan	Yes	4	- 1.350 ± 0.640	-1.645	0.117
	No	16	- 0.319 ± 1.195		
Combination Of Antipsychotics	One Antipsychotic	9	- 0.211 ± 1.405	3.337	0.060
	Two Antipsychotic	1	1.500 ± 0.000		
	Antipsychotic And Others	10	- 1.010 ± 0.569		

Table (3) Correlation between Antipsychotics and the DEXA Hip scan

		Dexa Hip Scan		T- Test Or Anova	
		N	Mean±SD	T Or F	P- Value
Risperidal/ Apixodone	Yes	15	- 0.213±1.394	-0.355	0.727
	No	3	0.100±1.400		
Aripiprex	Yes	6	- 0.050±1.537	0.238	0.815
	No	12	- 0.217±1.330		
Atomox	Yes	5	- 0.220±0.259	-0.111	0.913
	No	13	- 0.138±1.610		
Cerebrolysin	Yes	4	- 0.275±1.846	-0.185	0.856
	No	14	- 0.129±1.274		
Stimulan	Yes	3	0.033±0.757	0.264	0.795
	No	15	- 0.200±1.466		
Combination Of Antipsychotics	One Antipsychotic	8	- 0.425±1.547	0.801	0.467
	Two Antipsychotic	1	1.400±0.000		
	Antipsychotic and Others	9	- 0.100±1.204		

Correlation between Antipsychotic medication Risperidal and DEXA of whole body scan of 17 children.

The P value 0.753 with SD± 1.426 shows no significant effect of

antipsychotic Risperidal on bone mineral density of DEXA whole body scan

The P value 0.847 with SD± 1.265 shows no significant effect of Antipsychotic Risperidal on bone mineral density of DEXA spine scan.

The P value 0.727 with SD± 1.394 shows no significant effect of Antipsychotic Risperidal on bone mineral density of DEXA hip scan.

Correlation between Antipsychotic medication Aripiprex and DEXA of 6 children.

The P value 0.220 with SD± 0.497 shows no significant effect of antipsychotic Aripiprex on bone mineral density of DEXA whole body scan.

The P value 0.431 with SD±0.984 shows no significant effect of antipsychotic Aripiprex on bone mineral density of DEXA spin scan.

The P value 0.815 with SD± 1.537 shows no significant effect of antipsychotic Aripiprex on bone mineral density of DEXA hip scan.

**Discussion:**

The study was carried out on 44 cases, 36 were diagnosed with autism spectrum disorders, and 8 normal children as control. Their age ranged from 3 to 9 years old with a mean age= years old.

The sample of autistic participant included 36 children, 31 were boys (86.1%) and 5 were girls (13.8%) with Boy to girl Ratio 6.2: 1. This means there is a boy predominance in our study. Also (Cohen et.al., 2009) reported a boy predominance, with sex in the ratio Boys to Girls= 4: 1 respectively.

The current study revealed the effect of antipsychotic medication used for the treatment of autistic children.

☒ Group 1: 20 child (45.45%) were using antipsychotic inducing hyperprolactinemia.

☒ Group 2: 16 child (36.36%) did not take medication.

☒ Group 3: 8 normal participant (18.18%).

The result showed that the percentage of no osteopenia to osteopenia is 65%: 35% respectively in the 1st group of autistic children who received medication. Also the percentage of no osteopenia to osteopenia is 50%: 50% in the second group of autistic children who did not receive medication. The percentage of no osteopenia to osteopenia 75%: 25% respectively in the third normal children group.

However, these results are contrasting with (Seriwatanachachai, 2008; Motyl, 2012) who stated that antipsychotics might directly affect bone modulating through stimulating bone resorption relative to bone formation.

Another study stated that antipsychotics produce a change in the energy metabolism and insulin coding, which leads to a decrease in the bone mineral density and the risk of osteoporosis (House Knecht, 2009; Schwelz, 2012).

Two large case control studies showed that antipsychotic medications were associated with increased risk of hip and femur fracture (Hugen Tholz, 2005; Howard, 2007).

A published result reported there was a decrease in the bone mineral

density with autism spectrum disorder children compared to normal children (Hediger et al., 2008).

The present study revealed the effect of antipsychotic risperidone on bone mineral density of autistic children, (85%) of children received risperidone for treatment, and the statistical data showed no significant effect of risperidone on bone mineral density with P- value 0.753 and T- score 0.320 for whole body scan, and P- value 0.727 T- score 0.355 for hip scan.

This result opposed the study which had been carried out on a sample of patients with adequate size and proved that risperidone might induce persistent elevation in prolactin level above the upper limit (Shaw 2001, Staller 2006).

Another study stated that patients who received prolactin raising antipsychotics as risperidone had lower bone mineral density than who received prolactin sparing antipsychotics (Lin Ch et al., 2015).

Also the current study showed the effect of antipsychotic aripiprazole on bone mineral density of autistic children, (30%) of children received aripiprazole for treatment, and the statistical data revealed no significant effect of the medication on bone mineral density

With P- value 0.220 T- score 1.270 for the whole body scan, P- value 0.431 T- score 0.805 for the spin scan and P- value 0.815 T- score 0.238 for the hip scan.

The study stated that there was elevation in the prolactin level, when aripiprazole had been used (Shaw 2001, Staller 2006).

Antipsychotics could affect bone metabolism due to stimulating bone resorption over bone formation causing osteoporosis (Scriwatanachai et al., 2008).

Furthermore the present study showed the effect of combining antipsychotics medication treatment on bone mineral density, 5% of autistic children received combined antipsychotic and the statistical data showed no significant effect with P- value 0.891 and T- score 0.116 for the whole body scan, P- value 0.060 and T- score 3.337 for the spin scan and P- value 0.467 and T- score 0.801 for the hip scan.

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