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 علي كثافة عظام أطفال اضطراب التوحد الطيفى

المقدمة: هناك ارتفاع فى نسبة كسور العظم لدى أطفال اضطراب التوحد الطيفى، ولقد قمنا بتقييم المتغيرات كمضادات الذهان المستخدمة في العلاج والتى قد تكون لها تأثير على كتافة المعادن فى العظم، تقاس الكثافة المعدنية للعظام باستخدام الأشعة السنية ثنائة الطاقة. هدف الدراسة: تبحث الدراسة عن تأثيرمضادات الذهان على كثافة المعادن فى العظم، المنهجية:اشترك فى الدراسة 44 طفل 36 أولاد و 8 بنات وقسموا الى ثلاث مجموعات: المجموعة الأولى:20 طفل من أطفال اضطراب التوحد ويأخذون الدواء، المجموعة الثانية:16 طفل من أطفال اضطراب التوحد ولايأخذون الدواء، المجموعة الثالثة :أطفال أسوياء. نتيجة الدراسة: 65% من المجموعة الأولى ليس لديهم هشاشة و35% لديهم 50% من المجموعة الثانية ليس لديهم هشاشة و50% لديهم 75%من المجموعة الثالثة ليس لديهم هشاشة و25%لديهم. استنتاج الدراسة: مضادات الذهان له تأثير طفيف على كثافة المعادن فى 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; Parfilt, 1979; Plgozzi et al., 2009; Prentrice, 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.

Method and Research tool:

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:

Full medical history was taken from the participant children including the nutritional history and food intake pattern.

Full psychiatric assessement was taken. All information were taken from the parents.

Anthropometric measurements:

The weight: all participants were assessed using a kilogram weight, the balance ranged from 1- 140 Kgms. The participants were assessed while standing.

The height: the height was measured using a calibrated portable pediatric height rod, while the participant was barefooted.

Body mass index: was calculated from weight and height

taken by using this equation

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.

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.

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.

The whole body, hip joint and the spine are the main areas to be scanned.

The autistic patient was sedated with chloral hydrate according to the weight of the patient and then he was placed on the DEXA.

The child was instructed not to wear clothes with zippers, buttons or any metal object.

The scan usually takes 10 minutes and the amount of radiation is very low.

The results are reported in Z score and T score.

T score compares patient’s bone to the mean peak body density of young healthy adult of 30 years old.

Z score compares bone density to the mean peak density for someone of the same age, sex and weight.

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

For T score of 1 to -1: No Osteoporosis

For T score of -1 to -2.5: Osteopenia

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 6children.

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 predominante, 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 Kneckt, 2009; Schwelz, 2012).

Two large case control studies showed that antipsychotic medications were associated with increased risk of hip and fumur 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.

 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.

P-value 0.467 and T-score 0.801 for the hip scan.

References

American Psychiatric Association, 2000. Diagnostic and statistical manual of mental disorders: DSM-IV-TR.

Hediger ML 2008 Dairy-free diets may put boys with autism at risk for thin bones. Available at: http://www.news-medical.net/news/2008/01/29/34760.aspx [Accessed 15 June 2012]

Baron-Cohen, S., Scott, F.J., Allison, C., Williams, J., Bolton, P., Matthews, F.E. and Brayne, C., 2009. Prevalence of autism-spectrum conditions: UK school-based population study. The British Journal of Psychiatry, 194(6), pp.500-509.

International food information council website. <http://www.ific.org/publications/reviews/bonehealthir.cfm> . Accessed 1 April 2009.

Molloy, C.A., Kalkwarf, H.J., Manning-Courtney, P., Mills, J.L. and Hediger, M.L., 2010. Plasma 25 (OH) D concentration in children with autism spectrum disorder. Developmental medicine and child neurology, 52(10), p.969.

Shaw, V. and Lawson, M. eds., 2007. Clinical paediatric dietetics (pp. 3-20). Blackwell Pub.

Parfitt, A.M., 1979. Quantum concept of bone remodeling and turnover: implications for the pathogenesis of osteoporosis. Calcified tissue international, 28(1), pp.1-5.

Pigozzi, F., Rizzo, M., Giombini, A., Parisi, A., Fagnani, F. and Borrione, P., 2009. Bone mineral density and sport: effect of physical activity. Journal of sports medicine and physical fitness, 49(2), p.177.

Prentice, A., 1997. Is nutrition important in osteoporosis?. Proceedings of the Nutrition Society, 56(1B), pp.357-367.

Van der Sluis, I.M., De Ridder, M.A.J., Boot, A.M., Krenning, E.P. and de Muinck Keizer-Schrama, S.M.P.F., 2002. Reference data for bone density and body composition measured with dual energy x ray absorptiometry in white children and young adults. Archives of disease in childhood, 87(4), pp.341-347.