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Potential control of antipsychotic-induced hyperprolactinemia and obesity in children and adolescents by aripiprazole

J Lian

University of Wollongong, jl841@uowmail.edu.au

Xu-Feng Huang

University of Wollongong, xhuang@uow.edu.au

Nagesh Pai

University of Wollongong, nagesh@uow.edu.au

Chao Deng

University of Wollongong, chao@uow.edu.au

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Potential control of antipsychotic-induced hyperprolactinemia and obesity in children and adolescents by aripiprazole

Abstract

The paper published in your journal by Migliardi et al. (2009) reported that increased hyperprolactinemia is a major side-effect of risperidone and olanzapine treatment in children and adolescents. They showed that risperidone could cause 10 times higher prolactin levels than olanzapine treatment in children and adolescents. This was a well-designed study that controlled for dose, gender, and individual differences, as well as response differences to treatment duration (Migliardi et al. 2009). However, another important issue that should be considered, but was not reported in this study, is antipsychotic-induced weight gain/obesity. Clinical data have demonstrated that weight gain is a major side-effect induced by atypical antipsychotics, which may lead to medical and social consequences, such as type II diabetes, cardiovascular disease. It is particularly important that children and adolescents are more sensitive than adults to atypical antipsychotic-induced weight gain/obesity, and other metabolic side-effects (Correll 2008). Clinical studies have shown that olanzapine treatment can cause far greater weight gain than risperidone in both adult and child/adolescent patients (Correll 2008). Therefore, it would be of great value to present body weight data along with prolactin data in Migliardi et al.'s study.

Keywords

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Letter to Editors:

Potential control of antipsychotic-induced hyperprolactinemia and obesity in children and adolescents by aripiprazole

Jiamei Lian¹, Xu-Feng Huang^{1,2}, Nagesh Pai³, Chao Deng^{1,2,*}

1: School of Health Sciences, University of Wollongong, NSW 2522, Australia

2: Schizophrenia Research Institute, NSW 2010, Australia

3: Graduate School of Medicine, University of Wollongong, NSW 2522, Australia

***Corresponding author:**

Dr Chao Deng, School of Health Sciences, University of Wollongong, Wollongong, NSW 2522, Australia

E-mail: chao@uow.edu.au

Tel: (+61 2) 4221 4934

Fax: (+61 2) 4221 4096

Sir,

The paper published in your journal by Migliardi et al. (2009) reported that increased hyperprolactinemia is a major side-effect of risperidone and olanzapine treatment in children and adolescents. They showed that risperidone could cause 10 times higher prolactin levels than olanzapine treatment in children and adolescents. This was a well-designed study that controlled for dose, gender, and individual differences, as well as response differences to treatment duration (Migliardi et al. 2009). However, another important issue that should be considered, but was not reported in this study, is antipsychotic-induced weight gain/obesity. Clinical data have demonstrated that weight gain is a major side-effect induced by atypical antipsychotics, which may lead to medical and social consequences, such as type II diabetes, cardiovascular disease. It is particularly important that children and adolescents are more sensitive than adults to atypical antipsychotic-induced weight gain/obesity, and other metabolic side-effects (Correll 2008). Clinical studies have shown that olanzapine treatment can cause far greater weight gain than risperidone in both adult and child/adolescent patients (Correll 2008). Therefore, it would be of great value to present body weight data along with prolactin data in Migliardi et al.'s study.

One key issue is how to control antipsychotic-induced hyperprolactinemia and weight gain at the same time. Prolactin is secreted from pituitary lactotroph cells and primarily inhibited by dopamine D2 receptors. As D2 receptor antagonists, blockage of D2 receptors in the dopaminergic tubero-infundibular pathway has been suggested as a major mechanism for antipsychotic-induced hyperprolactinemia (Correll 2008). In fact, the relative incidence of hyperprolactinemia (roughly Risperidone > Haloperidol > Olanzapine > Ziprasidone > Quetiapine > Clozapine > Aripiprazole) could be predicted by their potency as D2 antagonists (Correll and Carlson 2006). Aripiprazole has even been reported to decrease prolactin

secretion in adults (Hoffer et al. 2009). On the other hand, H1 receptor antagonist properties are the main predictor for the development of antipsychotic-induced weight gain (approximately Clozapine > Olanzapine > Risperidone > Haloperidol > Ziprasidone > Aripiprazole (Correll 2008). Consistent with these findings, olanzapine significantly reduced H1 receptor mRNA expression in the hypothalamic arcuate nucleus (Arc) and ventromedial hypothalamic nucleus, and H1 receptor mRNA expression in the Arc was negatively correlated with food intake and fat mass (Han et al. 2008). It is very interesting that olanzapine- and clozapine-induced weight gain/obesity can be successfully controlled by co-administration with aripiprazole in adult schizophrenia patients, without reducing the original olanzapine and clozapine doses (Henderson et al. 2009). Aripiprazole was developed as a potent D2 partial-agonist, 5-HT_{1A} partial-agonist, and also 5-HT_{2A} antagonist (DeLeon et al. 2004). However, aripiprazole has a low histaminergic antagonism and does not affect H1 receptor expression (DeLeon et al. 2004; Han et al. 2008). Instead, aripiprazole is not a simple partial-agonist, but a functionally selective drug that can act as a D2 agonist or D2 antagonist depending on different brain regions (Han et al. 2009). Based on these findings, we recently suggested that aripiprazole's D2 agonistic property may account for the effect of aripiprazole in reducing olanzapine-induced obesity (Deng et al. 2010). It is possible that a co-administration of aripiprazole could be used to control risperidone-induced hyperprolactinaemia through its D2 agonistic effect. In fact, a recent study has found that risperidone treatment adjunctive with aripiprazole significantly decreased ~10 times prolactin levels compared to adjunctive placebo in adults (Kane et al. 2009). It is very important that aripiprazole has been approved by the FDA to be used in youths (aged 13 years and older) for schizophrenia and bipolar disorder, as well as for autism spectrum disorder in children aged 6 to 17 years in 2009. Therefore, it is possible to use aripiprazole in children or adolescents to reduce both olanzapine-induced weight gain and risperidone-induced hyperprolactinemia.

However, further animal studies and clinical trials are necessary before any extended practices are adopted in the paediatric clinics.

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