

CASE REPORT

Quetiapine-Induced Hyperprolactinemic Galactorrhea in an Adolescent Male

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Abstract

Quetiapine is an atypical antipsychotic agent with negligible prolactin-elevating properties. Although little data is available, studies show that it is both effective and safe in a variety of childhood mental illnesses. It has also been suggested to be the treatment of choice in antipsychotic-induced hyperprolactinemia in children. We report a case of a fourteen-year old male with conduct disorder who developed hyperprolactinemia and secondary galactorrhea with standard therapeutic dosages of quetiapine, which remitted shortly after a decrease in dose (German J Psychiatry 2006;9:118-120).

Keywords: atypical antipsychotic, galactorrhea, hyperprolactinemia, quetiapine

Received: 24.3.2006

Published: 13.4.2006

Introduction

Quetiapine is an atypical antipsychotic agent with minimal propensity to induce antipsychotic-associated hyperprolactinemia in standard recommended therapeutic dosages (Small et al., 1997; Stanniland & Taylor, 2000) and if it does so at all, serum prolactin elevation is only transient (de Borja Gonçalves Guerra et al., 2003). The newly accepted explanation for the prolactin-sparing property of quetiapine and other atypical antipsychotic agents is the poor occupancy of dopamine D₂ receptors on lactotrope cells in the anterior pituitary gland compared to striatal dopamine D₂ occupancy (Kapur et al., 2002). This contrasts with the property of all conventional antipsychotics and some atypical agents like risperidone in blocking dopamine D₂ receptors on prolactin-secreting cells in the pituitary gland, removing the main inhibitory effect on prolactin secretion (Wieck & Haddad, 2003).

Although not a first-line drug in children and adolescents, it has been shown to be well tolerated and effective in a wide

range of childhood mental illnesses in a number of small short-term studies (Findling 2002), including bipolar affective disorder (Marchand et al., 2004), disruptive behavior disorders (Findling et al., 2000), pervasive developmental disorders (Hardan et al., 2005), and tic disorders (Párraga et al., 2001). Even in pediatric populations, quetiapine is not characteristically associated with elevation of serum prolactin levels and adverse effects secondary to hyperprolactinemia (McConville et al., 2001; Shaw et al., 2001).

We here describe a case of quetiapine-induced hyperprolactinemia and subsequent galactorrhea in an adolescent. We will discuss the implications of quetiapine with respect to such adverse effect.

Case Report

Patient A is a 14 year-old Caucasian male adopted by a supportive, well-adjusted family of middle socio-economic status at 1 month of age. Developmental history is remark-

able for speech delay and persistent poor achievement at school. He had no significant medical problems. Biological family history is limited.

Patient A was diagnosed with conduct disorder at age 9, which was highly resistant to both behavioral interventions and pharmacological treatment with trials of sulpiride and risperidone successively. Meanwhile, his enduring aggressive, defiant and disruptive behaviour became increasingly uncontained and required hospitalisation. Baseline serum prolactin level off medication at the time was 175 mU/l (normal reference range for males: 53 – 360 mU/l). Quetiapine was started at a dose of 25 mg daily, and titrated to 600 mg daily in accordance with symptomatology over 2 months. He showed marked improvement in all aspects of behavior such that he was discharged from hospital soon after.

After 3 months of maintenance treatment with quetiapine he reported spontaneous discharge from his nipples, which was confirmed to be galactorrhea. Physical examination revealed no other abnormality. He neither complained of visual disturbance nor described symptoms suggestive of raised intracranial pressure. Magnetic resonance imaging of the brain showed normal signal throughout the brain, including a normal pituitary gland. Normal thyroid function tests excluded hypothyroidism from being an underlying cause of galactorrhea. Serum prolactin was found to be 760 mU/l, explaining the likely cause of galactorrhea.

As quetiapine was assumed to be the culprit for such hyperprolactinemia, the maintenance dose was reduced gradually to 400 mg daily over 2 weeks when galactorrhea resolved. Serum prolactin level assayed 2 weeks after symptomatic resolution was 200 mU/l. It has remained within the normal reference range since then. His behavior was subsequently well contained on this dose of quetiapine together with adjunctive psychosocial intervention.

Discussion

To the best of our knowledge, this is the first case reporting galactorrhea associated with quetiapine-induced hyperprolactinemia in medical literature. On the Naranjo nomogram, a total score of 7 was obtained, indicating quetiapine as being probably causative for such elevation of serum prolactin and its subsequent acute adverse effect.

Hyperprolactinemia induced by an atypical antipsychotic in children, as in the case of adults, is classically associated with risperidone. This correlation has been generally uncontested and well documented by several authors, including Cesena et al. (2002), Hardan et al. (1996), Stevens et al. (2005), Frazier et al. (1999), Masi et al. (2001), Saito et al. (2004) and Buhagiar et al. (unpublished data). Hyperprolactinemic galactorrhea has also been reported in pediatric subjects treated both with risperidone (Hardan et al., 1996; Cesena et al., 2002) and with olanzapine (Alfaro et al., 2002).

On the other hand, quetiapine does not typically cause significant elevation in serum prolactin in both adults (Dickson et al., 2000; Garver 2000) and children (McConville et al.,

2000; Shaw et al., 2001). In an open-label, rising-dose trial assessing quetiapine (up to 800 mg per day) in 10 adolescents with psychotic disorders, McConville et al. reported no unexpected side-effects effects. Likewise, Shaw et al. (2001) assessed the effectiveness and safety of quetiapine (mean dose 467 mg per day) over 8 weeks in 15 adolescents with psychosis. No statistically significant increase in prolactin levels from baseline levels took place at the end of this open-label study.

Generally little data is available regarding the implication of prolonged antipsychotic-associated hyperprolactinemia in children due to lack of long-term studies (Masi et al., 2001). Indeed, given such paucity of data, it has even been suggested that children with risperidone-induced hyperprolactinemia be switched to quetiapine on the basis of its prolactin-sparing property (Toren et al., 2004).

Notwithstanding, Saito et al. (2004) in a prospective study of hyperprolactinemia associated with atypical antipsychotic agents in children and adolescents, indeed did encounter 1 of 6 children who developed hyperprolactinemia after 11 weeks of treatment with quetiapine. Similarly, Stevens et al. (2005) in a cross-sectional medical chart review, reported 4 out of 20 boys who developed a dose-dependent elevation of serum prolactin with quetiapine treatment. Nonetheless, no clinically observable acute adverse effects were reported in any of the subjects, unlike our subject who developed hyperprolactinaemic galactorrhea with quetiapine. In a way, our subject also seems to have developed dose-dependent fluctuation of serum prolactin, in keeping with the latter findings.

Conclusion

Despite that quetiapine is considered to be a prolactin-sparing atypical antipsychotic, quetiapine-induced hyperprolactinemia may very rarely be encountered as a side-effect in susceptible individuals, and therefore clinicians should be aware that switching to quetiapine in cases of hyperprolactinemia induced by another atypical antipsychotic may not necessarily be warranted. Even more unusual, hyperprolactinaemic-galactorrhea associated with quetiapine may appear. Quetiapine-induced hyperprolactinemia and secondary galactorrhea both seem to subside by reducing the dose or stopping the drug.

References

- Alfaro CL, Wudarsky M, Nicolson R, Gochman P, Sporn A, Lenane M, Rapoport JL. Correlation of antipsychotic and prolactin concentrations in children and adolescents acutely treated with haloperidol, clozapine, or olanzapine. *J Child Adolesc Psychopharmacol* 2002; 12: 83-91.
- Cesena M, Gonzalez-Heydrich J, Szigethy E, Kohlenberg TM, DeMaso DR. A case series of eight aggressive

- young children treated with risperidone. *J Child Adolesc Psychopharmacol* 2001; 12: 337-345.
- De Borja Gonçalves Guerra A, Castel S, Benedito-Silva AA, Calil HM. Neuroendocrine effects of quetiapine in healthy volunteers. *Int J Neuropsychopharmacol* 2005; 8: 49-57.
- Dickson RA, Seeman MV, Corenblum B. Hormonal side effects in women: typical versus atypical antipsychotic treatment. *J Clin Psychiatry* 2000; 61 Suppl 3: 10-5.
- Findling RL, McNamara NK, Gracious BL. Pediatric uses of atypical antipsychotics. *Expert Opin Pharmacother* 2000; 1935-45.
- Findling RL. Use of quetiapine in children and adolescents. *J Child Adolesc Psychopharmacol* 2004; 14:287-94.
- Frazier JA, Meyer MC, Biederman J, Wozniak J, Wilens TE, Spencer TJ, Kim GS, Shapiro S. Risperidone treatment for juvenile bipolar disorder: a retrospective chart review. *J Am Acad Child Adolesc Psychiatry* 1999; 38: 960-5.
- Garver DL. Review of quetiapine side effects. *J Clin Psychiatry* 2000; 61 Suppl 8: 31-3.
- Hardan A, Johnson K, Johnson C. Case Study: Risperidone treatment of children and adolescents with developmental disorders. *J Am Acad Child Adolesc Psychiatry* 1996; 35: 1551-1556.
- Hardan AY, Jou RJ, Handen BL. Retrospective study of quetiapine in children and adolescents with pervasive developmental disorders. *J Autism Dev Disord* 2005; 35: 387-91.
- Kapur X, Langlois P, Vinken A, Megens AHP, De Coster R, Andrews JS. The differential effects of atypical antipsychotics on prolactin elevation are explained by their differential blood-brain disposition: a pharmacological analysis in rats. *J Pharmacol Exp Ther* 2002; 302: 1129-1134.
- Marchand WR, Wirth L, Simon C. Quetiapine adjunctive and monotherapy for pediatric bipolar disorder: a retrospective chart review. *J Child Adolesc Psychopharmacol* 2004; 14: 405-11.
- Masi G, Cosenza A, Mucci M. Prolactin levels in young children with pervasive developmental disorders during risperidone treatment. *J Child Adolesc Psychopharmacol* 2001; 11: 389-394.
- McConville BJ, Arvanitis LA, Thyrum PT, Yeh C, Wilkinson LA, Chaney RO, Foster KD, Sorter MT, Friedman LM, Brown KL, Heubi JE. Pharmacokinetics, tolerability, and clinical effectiveness of quetiapine fumarate: an open-label trial in adolescents with psychotic disorders. *J Clin Psychiatry* 2000; 61: 252-60.
- Párraga HC, Párraga MI, Woodward RL, Fenning PA. Quetiapine treatment of children with Tourette's syndrome: report of two cases. *J Child Adolesc Psychopharmacol* 2001; 11: 187-91.
- Saito E, Correll CU, Gallelli K, McMenemy M, Parikh UH, Malhotra AK, Kafantaris AK. A prospective study of hyperprolactinemia in children and adolescents treated with atypical antipsychotic agents. *J Child Adolesc Psychopharmacol* 2004; 14: 350-358.
- Small JG, Hirsch RS, Arvanitis LA, Miller BG, Link CG. Quetiapine in patients with schizophrenia. A high- and low-dose double-blind comparison with placebo. *Arch Gen Psychiatry* 1997; 54:549-557.
- Shaw JA, Lewis JE, Pascal S, Sharma RK, Rodriguez RA, Guillen R, Pupo-Guillen M. A study of quetiapine: efficacy and tolerability in psychotic adolescents. *J Child Adolesc Psychopharmacol* 2001; 11: 415-424.
- Stanniland C, Taylor D. Tolerability of Atypical Antipsychotics. *Drug Saf* 2000; 22: 195-214.
- Stevens JR, Kymissis PI, Baker AJL. Elevated prolactin in male youth treated with risperidone and quetiapine. *Child Adolesc Psychopharm* 2005; 15: 893-900.
- Toren P, Ratner S, Laor N, Weizman A. Benefit-risk assessment of atypical antipsychotics in the treatment of schizophrenia and comorbid disorders in children and adolescents. *Drug Saf* 2004; 27: 1135-1156.
- Wieck A, Haddad PM. Antipsychotic-induced hyperprolactinemia in women: pathophysiology, severity and consequences. *Br J Psychiatry* 2003; 182: 199-204.