Plasma prolactin and bone mineral density in patients on long-term risperidone

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Having read with interest the article ‘Prolactin, hyperprolactinaemia and antipsychotic treatment: a review and lessons for treatment of early psychosis’ by Cookson J (*J Psychopharmacol* 2012; 26(5 Suppl.): 42–51) about bone demineralization in patients on long-term risperidone resulting from higher levels of prolactin, I would like to join the discussion, focused on the evolution of bone mineral density (BMD), by providing our own data from a study conducted on a small cohort of patients on long-term parenteral risperidone combined treatment, where we analysed prolactin, sex hormones, cortisol and thyroid-stimulating hormone (TSH) in blood samples, and calculated the BMD as a function of prolactin and estradiol. We observed that the risk of pathological BMD for osteoporosis in women increased year after year reaching the maximum value in the 7th year. The data analysis suggests that hypoestrogenism, produced by the administration of antipsychotics, raises prolactin, thereby increasing the risk of pathological BMD, when risperidone is administered alone or in combination with other antipsychotics, as described in the following brief summary of the research.

Patients and method

A total of 59 outpatients, 63% female, age 44 ± 16 years, body mass index (BMI) 29.5 ± 6 kg/m², were on combined antipsychotic treatment including parenteral risperidone 52 ± 24 mg, over 6 ± 3 year. A blood sample was drawn from each patient at 09:00, to measure prolactin, estradiol, testosterone, cortisol and TSH.

Hypogonadism was defined as testosterone <3.0 ng/ml and hypoestrogenism was defined as Estradiol <40 pg/ml.

The BMD was calculated using the following relation:

$$\Delta \text{BMD}/29.5 = 2 \exp [\Delta E/22] \quad (E = \text{estradiol})$$

adding an annual reduction of 2% (age contribution).

Results and discussion

Prolactin 1828 ± 793 $\mu\text{UI/ml}$, estradiol 19 ± 13 pg/ml, testosterone 0.6 ± 0.3 ng/ml, cortisol 21 ± 7 $\mu\text{g/dl}$ and TSH 3.4 ± 2.0 $\mu\text{UI/ml}$ for females (f) and prolactin 667 ± 282 $\mu\text{UI/ml}$, estradiol 22 ± 3 pg/ml, testosterone 3.9 ± 1.6 ng/ml, cortisol 17 ± 6 $\mu\text{g/dl}$ and TSH 2.6 ± 1.6 $\mu\text{UI/ml}$ for males (m).

On the one hand, from the data, the maximum annual increase in the probability risk value for osteoporosis and osteopenia were as follows: odds ratio (OR) values for osteopenia [5.3 (f) and 2.4 (m)] were reached in the 4th year of treatment for women and men, respectively; OR values for osteoporosis [3.18 (f) and 4.5 (m)] were reached in 7th year of treatment for women and 17th year for men.

On the other hand, the OR value for patients on risperidone (cases) *versus* healthy people (controls) was higher than 4 for both osteopenia and osteoporosis.

Finally, the OR value for women on risperidone *versus* men on risperidone was higher than 4 and 2 in osteopenia and osteoporosis, respectively.

Conclusion

Hypoestrogenism was present in 25 (75%) females and hypogonadism in 11 (42%) males.

Based on a dose–response curve of estradiol levels *versus* BMD decrease, we identified the critical periods for the appearance of pathological BMD: the highest increase in osteopenia OR occurs in the 4th year of treatment, for males and females, while increase in osteoporosis OR occurs in the 7th year only for females.

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The patients who are taking risperidone have a higher risk of pathological BMD, related to some extent to hypoestrogenism and/or hypogonadism, compared with healthy people (OR >4).

Conflict of interest statement

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