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Sex differences in side effects of second-generation antipsychotics

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Background

Sex was the strongest determinant of subjective tolerability of antipsychotic drugs in a recent study (Barbui et al., 2005) and the authors suggested that studies should no longer consider men and women as a homogenous group. The aim of this review is to investigate whether sex differences exist for susceptibility to adverse effects of second-generation antipsychotics (SGAs).

Materials and methods

Results are based on a Medline search for controlled trials of all atypical antipsychotics.

Results

It is known that pharmacokinetics differ between females and males, with a higher activity in females for CYP3A4 and CYP2D6. Yet, significantly higher plasma levels in women have only been demonstrated for olanzapine and clozapine. Regarding side effects, although not well studied, some of them such as hyperprolactinaemia, weight gain and cardiac effects are reported to affect more often women. There is -although controversial- evidence for more pronounced prolactin levels in females. There are also some published studies that indicate that metabolic syndrome (visceral adiposity, hyperglycaemia, hypertension and dyslipidaemia) induced by SGAs is more frequent in females. Lastly, the risk of QT prolongation is again higher in females. There is no evidence for sex differences in SGAs causing extrapyramidal symptoms, acute dystonia or any other movement disturbance.

Conclusions

In conclusion, there is some evidence of sex differences in side effects of the SGAs. However, data are obtained by posthoc analysis, not to mention that clinical trials of new therapeutic drugs have been conducted, for the most part, with male participants. Future studies with a primary focus on sex differences are required and will help to determine how these differences should influence clinical management.