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SSRIs and weight gain

Introduction

Paroxetine (Seroxat[®]) and fluoxetine (Prozac[®]) are selective serotonin reuptake inhibitors (SSRIs), which selectively inhibit the presynaptic serotonin reuptake and have minimal anticholinergic effects. Paroxetine was approved for the Dutch market in 1991, fluoxetine in 1989, both for *the treatment of depression* [1,2].

The most frequent adverse drug reactions mentioned in the SPCs of both drugs include nausea, dry mouth, constipation, anorexia, insomnia, headache, dizziness, agitation and disturbed vision. For the other SSRIs citalopram, sertraline, fluvoxamine (but not paroxetine and fluoxetine), weight gain and weight loss are described as well [3-5].

Reports

In June 2003, the Lareb database contained a total of 57 reports on increased weight as a suspected adverse drug reaction associated with the use of one of the aforementioned SSRIs. Of these 57 reports, 40 refer to paroxetine and 5 to fluoxetine.

With regard to the reports referring to paroxetine or fluoxetine, quantitative information about the weight gain was available in 27 cases. The average weight gain in these cases was 11.4 ± 6.3 kg (mean \pm sd) after, on average, 8 (range 1-48) months of SSRI treatment.

Other sources of information

Literature

Initially, SSRIs were considered to have a weight neutral or weight reducing effect (See e.g. [6,7]). Later reports indicate that long-term treatment with SSRIs may be associated with weight gain [8,9].

Fava *et al.* have reviewed the studies in the literature specifically examining weight gain and antidepressant therapy [8]. They conclude that tricyclic antidepressants, and perhaps monoamine oxidase inhibitors, are more likely to cause weight gain than the SSRIs. Paroxetine may be more likely to cause weight gain than the other SSRIs during long-term treatment. Probably, there is a distinction of the weight changing properties of the various SSRIs. Due to the low number of studies it is difficult to estimate the relative risk across antidepressant therapies.

With respect to paroxetine and fluoxetine, weight gain as well as weight loss are described in the literature [10-13].

Databases

With respect to the Lareb database, the Reporting Odds Ratio (ROR) of the combination paroxetine and weight gain is 4.6 (95% CI 3.3-6.5), and for fluoxetine this is 1.5 (95% CI 0.6-3.7). The database of the WHO Monitoring Centre contains 24,242 possible ADRs in relation to paroxetine use. An association between paroxetine and increased weight was suggested in 446 reports resulting in a ROR of 3.0 (95% CI 2.7-3.3) for this combination. The WHO database contains 46,567 possible ADRs associated with the use of fluoxetine, 582 of which refer to weight gain. The ROR of this combination is 2.0 (95% CI 1.9-2.0).

Mechanism

Weight gain during antidepressant treatment can be a sign of improvement in patients whose weight loss was one of the depressive symptoms [14] or a residual symptom in patients who overeat when depressed or an adverse drug reaction. However, significant weight gain during the acute phase of treatment or weight gain that continues despite achieving full remission of the depressive symptoms is likely to be a side effect of antidepressant treatment [8]. The mechanism by which weight gain is induced is not clearly understood. From the close relationship between nutritional intake and serotonin activity, it would be expected that a higher serotonin activity -as induced by SSRI treatment- should induce an anorectic effect, reduced food intake, and subsequently result in a decrease in body weight [9,15]. Although the anorectic action of

fluoxetine and paroxetine is well recognised, long-term studies reveal that the weight-reducing effects are transient, even leading to gain in body weight. The 5-HT_{2c} affinity of fluoxetine and the inhibitory action of paroxetine (and probably fluoxetine) on NO synthase may both have an impact on appetite [9].

Conclusion

Forty cases for paroxetine and five cases for fluoxetine in the database of the Netherlands Pharmacovigilance Centre Lareb show an association with an increase in body weight. These findings are supported by data from the WHO database.

References

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