Drug Safety 2001; 24 (13): 1017-1018
0114-5916/01/0013-1017/$22.00/0

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Lipid Abnormalities Induced by Novel Antipsychotic Drugs

The review by Mantel-Teeuwisse et al.[1] covered many drugs that have unintentional effects on serum lipid levels, but the review excluded many recent findings for novel antipsychotic drugs; possibly because of the publication lag.

In addition to clozapine, as mentioned by Mantel-Teeuwisse et al.,[1] olanzapine has been reported to have significant effects on increasing serum triglyceride levels.[2] The chemical structure of olanzapine resembles that of clozapine, a thienobenzodiazepine derivative,[3] and the agent has almost the same effects as clozapine on bodyweight gain, development of diabetes mellitus and increasing serum lipid levels. Melkersson et al.[4] reported 14 patients receiving olanzapine, of whom 12 gained 1 to 10kg in bodyweight, 8 had hyperleptinaemia, 10 had hyperinsulinaemia, 8 had triglyceridaemia, and 11 had hypercholesterolaemia. Unfortunately, the package inserts for clozapine and olanzapine fail to mention increased triglyceride levels.[2]

Quetiapine also has a similar chemical structure to olanzapine. The package insert for quetiapine describes cholesterol and triglyceride level elevations in the cautions section, and reports increases in cholesterol and triglyceride levels of 11 and 17%, respectively, in pooled 3- to 6-week data.[5]

A review by Wetterling,[6] found that zotepine, which shares a similar chemical structure to clozapine, caused the greatest bodyweight gain of all antipsychotic drugs. However, the literature review found no reports of lipid abnormalities with zotepine. Future trials should include investigation of full lipid profiles as part of their safety protocols.

There may be different effects on lipids in the different chemical types of the novel antipsychotic drugs. Risperidone, with a benzisoxazole structure, has been reported to reverse the hypertriglyceridaemia induced by clozapine.[7] Risperidone is derived from haloperidol, which has been reported to have a safe profile with regard to lipid abnormalities.[8]

Since their introduction, the newer atypical antipsychotic drugs have become more commonly prescribed, often replacing conventional drugs, in patients with schizophrenia. Consequently, interest in their adverse effect profiles has grown. Most attention has been paid to adverse effects such as agranulocytosis, seizure, sedation and bodyweight gain, which have been associated with clozapine use. Little attention has been focused on potential adverse lipid changes. The potential consequences of hyperlipidaemia are significant for obesity, diabetes mellitus, hypertension, venous thromboembolism and exacerbation of coronary artery disease. In light of these data, we recommend that lipid profiles should be routinely monitored in patients receiving novel antipsychotic drugs, especially for patients with cardiovascular risk factors.

Acknowledgements

No financial support from any pharmaceutical company was received for the preparation of this letter. The authors have no financial relationships with any pharmaceutical companies. The authors have received support from various manufacturers of atypical antipsychotic drugs for travel or attending educational rounds. Dr Shen has received honorariums for speeches and consulting fees from various manufacturers of atypical antipsychotic drugs.

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