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Schizophrenia and related psychoses CHAPTER 1 Effects of antipsychotic medications on plasma lipids Morbidity and mortality from cardiovascular disease are higher in people with schizophrenia than in the general population.1–3 Dyslipidaemia is an established risk factor for cardiovascular disease, together with obesity, hypertension, smoking, diabetes and sedentary lifestyle. Specifically, reduced high-density lipoprotein (HDL) cholesterol and raised triglyceride levels are included in the definition of the metabolic syndrome.4 The majority of patients with schizophrenia have several of these cardiometabolic risk factors and can be considered at ‘high risk’ of developing cardiovascular disease. Dyslipidaemia is treatable and intervention is known to reduce morbidity and mortality.5 Aggressive treatment is particularly important in people with diabetes, the prevalence of which is increased two- to three-fold over population norms in people with schizophrenia (see section on diabetes and impaired glucose tolerance). Effect of antipsychotic medications on lipids Antipsychotic medications show a marked variation in their effects on total cholesterol, low-density lipoprotein (LDL) cholesterol, HDL cholesterol and triglycerides.6,7 Regarding FGAs, phenothiazines are known to be associated with increases in trigly cerides and LDL cholesterol and decreases in HDL8 cholesterol, but the magnitude of these effects is poorly quantified.9 Haloperidol seems to have minimal effect on lipid profiles.8 Although there are relatively more data pertaining to some SGAs, they are derived from a variety of sources and are reported in different ways, making it difficult to compare such medications directly. While cholesterol levels can rise, the most profound effect of antipsychotic medications seems to be on triglycerides. Raised triglycerides are, in general, associated with obesity and diabetes. From the available data, clozapine and olanzapine6,10 would seem to have the greatest propensity to increase lipids, while quetiapine and risperidone have a moderate propensity.11,12 Aripiprazole, lurasidone and ziprasidone appear to have minimal adverse effect on blood lipids6,10,13–18 and may even modestly reverse dyslipidaemias associated with previous antipsychotics.17,19,20 For cariprazine and brexpiprazole, the effects on plasma lipids would also appear to be relatively limited.6,21–24 Iloperidone causes some weight gain but may not have an equivalent impact on cholesterol or triglycerides.6,25,26 Early RCT data suggest that lumateperone is not associated with any significant effects on plasma cholesterol or triglycerides in the short term, compared with placebo.27 Olanzapine In people with schizophrenia, olanzapine has a relatively high propensity to induce dyslipidaemia,6,7 which is characterised by elevated levels of plasma triglyceride, total cholesterol and LDL cholesterol and can occur in the first 4 weeks of treatment.28 Triglyceride levels have been shown to increase by 40% over the short (12 weeks) and medium (16 months) term.29,30 Levels may continue to rise for up to a year.31 Up to two- thirds of patients treated with olanzapine have raised triglycerides32 and just under 10% may develop severe hypertriglyceridaemia.33 While weight gain with olanzapine is generally associated with increases

in both cholesterol30,34 and triglycerides,33 severe hypertriglyceridaemia can occur independently of weight gain.33 In one study, patients

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