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References

50 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 1 alternative to SGAs where SGAs are poorly tolerated (usually because of metabolic changes) or where FGAs are preferred by patients themselves. Some FGAs may be less effective than some non-clozapine SGAs (amisulpride, olanzapine and risperidone may be slightly more efficacious)4,5 but any differences in therapeutic efficacy seem to be modest. Two large, independent and pragmatic studies, CATIE6 and CUtLASS,7 found few important differences between SGAs and FGAs (mainly perphenazine and sulpiride, respectively). The main drawbacks of FGAs are acute EPS, hyperprolactinaemia and TD. Hyperprolactinaemia is probably unavoidable in practice because the dose that achieves efficacy is too close to the dose that causes hyperprolactinaemia. Even when not symptomatic, hyperprolactinaemia may grossly affect hypothalamic function.8 Raised prolactin is also associated with sexual dysfunction,9 as are the autonomic effects of some SGAs.10 Notably, some SGAs (risperidone, paliperidone, amisulpride) increase prolactin to a greater extent than FGAs.11 All FGAs are potent dopamine antagonists, which are liable to induce dysphoria.12 Perhaps as a consequence, some FGAs may produce smaller benefits in quality of life than some SGAs.6 Tardive dyskinesia very probably occurs more frequently with FGAs than SGAs13–16 (notwithstanding difficulties in defining what is ‘atypical’), although there remains some uncertainty16–18 and the dose of FGA used is a crucial factor.19 A complicating aspect is the occurrence of TD in untreated schizophrenia,20 which may mean that antipsychotics do not necessarily cause TD but simply fail to suppress it to varying degrees. Among SGAs, partial agonists may have the lowest risk of TD.21 Careful observation of patients and the prescribing of the lowest effective dose are essential to help reduce the risk of this serious adverse event.22,23 Even with these precautions, the risk of TD with some FGAs may be unacceptably high.24 A good example of the relative merits of SGAs and a carefully dosed FGA comes from a trial comparing paliperidone palmitate with low-dose haloperidol decanoate.25 Paliperidone produced more weight gain and prolactin change but haloperidol was associated with significantly more frequent akathisia and parkinsonism, and, numerically, a higher incidence of TD. Efficacy was identical. References

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