46 - Other drugs

Other drugs

616 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 5 placebo group. Surprisingly, a higher proportion of children in the low-dose group (18.2%) compared with the high-dose group (9.3%) and placebo group (9.1%) gained clinically significant weight (≥7%) which may have been related to a lower average baseline weight in this group. Several case series also support the use of aripiprazole.24–27 A study evaluating the metabolic side effects of aripiprazole (N = 25) and pimozide (N = 25) in TS over a 24-month period demonstrated that treatment was not associated with significant increase in body mass index. However, pimozide treatment was associated with increases in blood glucose that did not plateau from 12 to 24 months, aripiprazole treatment was associated with increased cholesterol and both medications were associated with increased triglycerides.28 Two meta-analyses support the efficacy of aripiprazole.29,30 One study31 suggests twice-weekly administration may be better tolerated than daily dosing. A small RCT (N = 24) comparing aripiprazole with sodium valproate in children with TS demonstrated a statistically significant difference in tic reduction favouring aripiprazole.32 Risperidone has, in addition to the studies mentioned, also been shown to be more effective than placebo in a small (N = 34) randomised study.33 Fatigue and increased appetite were problematic in the risperidone arm and a mean weight gain of 2.8kg over 8 weeks was reported. One small RCT found risperidone and clonidine to be equally effective.34 A small double-blind crossover study suggested that olanzapine35 may be more effective than pimozide. Sulpiride has been shown to be effective and relatively well tolerated,36 as has ziprasidone.37 Open studies support the efficacy of quetiapine38 and olanzapine.39,40 One very small crossover study (N = 7) found no effect for clozapine.41 Antipsychotic medications may not differ from each other in terms of efficacy for tics, with low to very low certainty of evidence for this comparison.9 Overall, metabolic side effects and weight gain are common with second-generation antipsychotics, even aripiprazole, so benefit/risk ratios need careful discussion.42 Other drugs A small, double-blind placebo-controlled crossover trial of baclofen was suggestive of beneficial effects in overall impairment rather than a specific effect on tics.43 The numerical benefits shown in this study did not reach statistical significance. Similarly, a double-blind placebo-controlled trial of nicotine augmentation of haloperidol found beneficial effects in overall impairment rather than a specific effect on tics.44 These benefits persisted for several weeks after nicotine (in the form of patches) was withdrawn. Nicotine patches were associated with a high prevalence of nausea and vomiting (71% and 40%, respectively). The authors suggest that use as required may be appropriate. Flutamide, an antiandrogen, has been the subject of a small RCT in adults with TS. Modest, short-lived effects were seen in motor but not phonic tics.45 A small RCT showed significant advantages for metoclopramide over placebo46 and for topiramate over placebo. A meta-analysis identified 14 RCTs (all from China) comparing

topiramate with haloperidol or tiapride. It concluded that owing to the overall low quality of the study designs, there is not enough evidence to support the routine use of topiramate in clinical practice.47 Tetrabenazine may be useful as an add-on treatment.48 Ecopipam, a D1 receptor antagonist, was also found to be effective in the treatment of tics in a

Prescribing in children and adolescents CHAPTER 5 randomised placebo-controlled crossover study including children and adolescents with TS.49 A second trial (n = 153)50 confirmed the efficacy of ecopipam. The monoamine depleting agents deutetrabenazine and valbenazine, the selective serotonin 5-HT3 receptor antagonist ondansetron and pergolide, a D1-D2-D3 agonist, are probably not effective.9,51 Case reports or case series describing positive effects have been published for - clomiphene,52 tramadol,53 ketanserin,54 cyproterone,55 levetiracetam,56 pregabalin57 and cannabis.58 A Cochrane review of cannabinoids concluded that there was little if any current evidence for efficacy59 and, despite a strong biological rationale for use, their overall efficacy and safety remain largely unknown.60 Many other drugs have been reported to be effective in single case reports. Patients in these reports all had comorbid psychiatric illness, making it difficult to determine the effect of these drugs on TS alone. Botulinum toxin has been used to treat bothersome or painful focal motor tics, particularly those affecting neck muscles.42 However, a 2018 Cochrane review expressed uncertainty about its place in the treatment of tics owing to the low quality of available evidence.61 There may be a subgroup of children who develop tics and/or OCD in association with streptococcal or other infections or triggers. This group has been given (in the case of Streptococcus) the acronym PANDAS (paediatric autoimmune neuropsychiatric disorder associated with Streptococcus)62 or, more broadly, PANS (paediatric acute- onset neuropsychiatric syndrome).63 This is thought to be an autoimmune-mediated effect, and there have been trials of immune-modulatory therapy in these children as well as treatment with antibiotics for active infections and also as preventative treatment. More research in this area is warranted. *It is extremely rare in practice to get to this point – almost all cases can be effectively treated by recommendations above this point. Not fully effective Poorly tolerated Not effective* Educational and behavioural treatment Clonidine or guanfacine Antipsychotic treatment, e.g. aripiprazole or risperidone Consider older or more experimental treatments (see text) Not fully effective Figure 5.2 Summary of recommendations for the treatment of tics and Tourette’s syndrome.

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