

# 45 - Antipsychotics

## Antipsychotics

Prescribing in children and adolescents CHAPTER 5 these more helpful compared with medication.<sup>7</sup> Robust research about the use of complementary or alternative therapies, their efficacy and potential adverse effects is lacking<sup>8</sup> and certainty of evidence for their use is very low.<sup>9</sup> Adrenergic  $\alpha_2$  agonists Clonidine has been shown in open studies to reduce the severity and frequency of tics but in one study this effect did not seem to be convincingly larger than placebo.<sup>10</sup> Other studies have shown more substantial reductions in tics.<sup>11-14</sup> Therapeutic doses of clonidine are in the order of 3-5mcg/kg, and the dose should be built up gradually. A transdermal patch has also shown effectiveness.<sup>15</sup> The main adverse effects are sedation, postural hypotension and depression. Patients and their families should be informed not to stop clonidine suddenly because of the risk of rebound hypertension. Guanfacine also has some evidence of effectiveness in the treatment of tics.<sup>16,17</sup> The efficacy of clonidine (but not of guanfacine) was demonstrated in a 2023 systematic review and network meta-analysis of double-blind RCTs in TS which included children, adolescents and adults.<sup>9</sup> Adrenergic  $\alpha_2$  agonists may also be used in children with ADHD whose tics deteriorate with stimulant medication.<sup>18</sup> Antipsychotics Adverse effects of antipsychotics may outweigh their beneficial effects in the treatment of tics so it is recommended that clonidine or guanfacine is generally tried first (Figure 5.2). Antipsychotics may, however, be more effective than adrenergic  $\alpha_2$  agonists in alleviating tics.<sup>9</sup> A number of first-generation antipsychotics have been used in TS. In a Cochrane review, pimozide demonstrated robust efficacy in a meta-analysis of six trials.<sup>19</sup> In these trials, pimozide was compared with haloperidol (one trial), placebo (one trial), haloperidol and placebo (two trials) and risperidone (two trials) and was found to be more effective than placebo, as effective as risperidone and slightly less effective than haloperidol in reducing tics. It was associated with less severe adverse effects than haloperidol but did not differ from risperidone in that respect. ECG monitoring is essential for pimozide and haloperidol. Haloperidol is often poorly tolerated. Tiapride may also be effective, but evidence may not be generalisable and it has limited availability.<sup>9</sup> SGAs, in particular aripiprazole, have in recent years been used more commonly for the treatment of TS.<sup>20</sup> Aripiprazole is an effective and well-tolerated treatment of children with TS (and also tics<sup>21</sup>). A 10-week multicentre double-blind randomised placebo-controlled trial (N = 61) demonstrated the efficacy of aripiprazole in tic reduction in TS. Treatment was associated with significantly decreased serum prolactin concentration, increased mean body weight (by 1.6kg), body mass index and waist circumference.<sup>22</sup> Aripiprazole was also found to be effective in another randomised double-blind placebo-controlled trial (N = 133) comparing low-dose aripiprazole (5mg/day if <50kg; 10mg/day if  $\geq$ 50kg), high-dose aripiprazole (10mg/day if <50kg; 20mg/day if  $\geq$ 50kg) or placebo for 8 weeks.<sup>23</sup> At week 8, tics were reduced in both the high-dose group and the low-dose group, with 69% of patients in the low-dose group and 74% in the high-dose group being very much improved or much improved, compared with 38% in the

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