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Extrapyramidal symptoms

126 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 1 ANTIPSYCHOTIC ADVERSE EFFECTS Extrapyramidal symptoms The EPS associated with antipsychotic medication can be stigmatising, distressing, potentially disabling and act as a disincentive to taking medication.1,2 EPS are commonly overlooked and underdiagnosed or misdiagnosed in clinical practice.3,4 These movement disorders tend to be dose-related and are less likely to occur with SGAs, particularly clozapine, olanzapine, quetiapine and aripiprazole,2,5 compared with FGAs such as haloperidol. Generally it is agreed that the greater use of SGAs has led to a reduction in the frequency of EPS,6 although the prevalence of EPS of any description in community samples may exceed 30%.7 The incidence of EPS is often steeply dose- related for most drugs (clozapine and quetiapine are possible exceptions) and this relationship extends beyond the licensed dose range for some drugs.8 Patients who experience one type of EPS may be more vulnerable to developing others.9 Substance misuse increases the risk of dystonia, akathisia and TD,10,11 and there is some evidence for an association between alcohol use and akathisia.12,13 Vulnerability to EPS may be partly genetically determined.14–16 Establishing the prevalence of antipsychotic-induced EPS is problematic, given that similar movement disorders may be seen in never-medicated patients with schizophrenia.17–19 In one study of such patients at first episode, 1% had dystonia, 8% parkinsonian symptoms and 11% akathisia.19 Parkinsonian symptoms and other motor abnormalities in this context may be associated with cognitive impairment19,20 and poor long--term psychosocial functioning.21 In another study of never-treated patients with established psychotic illness, 9% exhibited spontaneous dyskinesias and 17% parkinsonian symptoms.22 Table 1.28 details the most common EPSEs.

Table 1.28 Most common extrapyramidal side effects. Dystonia (uncontrolled muscular spasm) Pseudoparkinsonism (bradykinesia, tremor, muscle rigidity, etc.) Akathisia (restlessness)23 Tardive dyskinesia (TD) (abnormal involuntary movements) Signs and symptoms24 ■ ■Muscle spasm in any part of the body, e.g. ■ ■eyes rolling upwards (oculogyric spasm) ■ ■head and neck twisted to the side (torticollis) ■ ■The patient may be unable to swallow or speak clearly. In extreme cases, the back may arch or the jaw dislocate. ■ ■Acute dystonia can be both painful and very frightening ■ ■Tremor and/or rigidity ■ ■Bradykinesia (decreased facial expression, flat monotone voice, slow body movements, inability to initiate movement) ■ ■Bradyphrenia (slowed thinking) ■ ■Salivation ■ ■Pseudoparkinsonism can be mistaken for depression or negative

symptoms of schizophrenia ■ ■A subjectively unpleasant state of inner restlessness with a desire or compulsion to move23,25 ■ ■Foot stamping when seated ■ ■Constantly crossing/uncrossing legs ■ ■Rocking from foot to foot when standing ■ ■Constantly pacing up and down ■ ■Akathisia can be mistaken for psychotic agitation and has been linked with suicidal ideation26 and aggression towards others27 ■ ■A wide variety of movements can occur,28 such as: ■ ■lip smacking or chewing ■ ■tongue protrusion (‘fly catching’) ■ ■choreiform hand movements (‘piano playing’) ■ ■dystonic and choreoathetoid movements of the limbs ■ ■Severe orofacial movements can lead to difficulty speaking, eating or breathing. Movements are worse when under stress. Rating scales (see Martino et al. 2023)29 ■ ■No specific scale ■ ■Small component of general EPS scales ■ ■Simpson–Angus EPS Rating Scale30 ■ ■Barnes Akathisia Rating Scale3,31 ■ ■Abnormal Involuntary Movement Scale32,33 Prevalence ■ ■Approximately 10%34 but more common:35 ■ ■in young males ■ ■in those who are antipsychotic-naïve ■ ■with high-potency medications (e.g. haloperidol) ■ ■Dystonic reactions are rare in the elderly ■ ■Approximately 20%36 but more common in: ■ ■elderly females ■ ■those with pre-existing neurological damage (head injury, stroke, etc.) ■ ■Wide variation but approximately 25%37 for acute akathisia with FGAs, lower with SGAs ■ ■The relative liability of individual antipsychotic medications for akathisia is uncertain,2 but there is consensus that the incidence is lowest for olanzapine, quetiapine and clozapine38,39 ■ ■5% of patients per year of antipsychotic exposure.40 More common in respect to:41 ■ ■age ■ ■affective illness ■ ■schizophrenia ■ ■higher doses ■ ■acute EPS early in treatment ■ ■Lower incidence in those on SGAs.42,43 TD may be associated with neurocognitive deficits.44 (Continued)

Table 1.28 (Continued) Dystonia (uncontrolled muscular spasm) Pseudoparkinsonism (bradykinesia, tremor, muscle rigidity, etc.) Akathisia (restlessness)23 Tardive dyskinesia (TD) (abnormal involuntary movements) Time taken to develop ■ ■Acute dystonia can occur within hours of starting antipsychotic medication (minutes if the IM or IV route is used) ■ ■TD occurs after months to years of antipsychotic treatment ■ ■Days to weeks after the start of antipsychotic medication or an increase in dose ■ ■Acute akathisia occurs within hours to weeks of starting antipsychotic medication or increasing the dose ■ ■Akathisia that has persisted for several months or so is called ‘chronic akathisia’. Tardive akathisia tends to occur later in treatment and may be exacerbated or provoked by antipsychotic dose reduction or withdrawal.23 ■ ■Months to years ■ ■The proportion of cases showing reversibility on cessation of antipsychotic medication is unclear and may partly depend on age28 Treatment ■ ■Anticholinergic drugs given orally, IM or IV depending on the severity of symptoms35 ■ ■Remember the patient may be unable to swallow ■ ■Response to IV administration will be seen within 5 minutes ■ ■Response to IM administration takes around 20 minutes ■ ■TD may respond to ECT45,46 ■ ■Where severe symptoms do not respond to simpler measures including switching to an antipsychotic with a low propensity for EPS, botulinum toxin may be effective47,48 ■ ■Several options are available depending on the clinical circumstances: ■ ■Reduce the antipsychotic dose ■ ■Change to an antipsychotic medication with a lower propensity for pseudoparkinsonism (see section on relative liability of antipsychotic medications for adverse effects) ■ ■Prescribe an anticholinergic. The majority of patients do not require long-term anticholinergic agents. Use should be reviewed at least every 3 months. Do not prescribe at night (symptoms usually absent during sleep). ■ ■Reduce the antipsychotic dose ■ ■Change to an antipsychotic drug with lower propensity for akathisia (see sections on akathisia and relative liability of antipsychotic medications for adverse effects) ■ ■A reduction in symptoms may be seen with25,49,50 low-dose propranolol, 30–80mg/day; clonazepam (low dose); 5HT2 antagonists such as cyproheptadine,46 mirtazapine,49 trazodone,51,52 mianserin53 and

cyproheptadine46 may help, as may possibly diphenhydramine54 ■ ■Note that all of the above medications are unlicensed for this indication ■ ■Anticholinergics are generally unhelpful unless possibly if akathisia is part of a general EPS spectrum55,56 ■ ■Stop anticholinergic if prescribed ■ ■Reduce dose of antipsychotic medication ■ ■Change to an antipsychotic with lower propensity for TD;57–60 note that data are conflicting61,62 ■ ■Clozapine is the antipsychotic most likely to be associated with resolution of symptoms.63,64 Quetiapine may also be useful in this regard.65 ■ ■Both valbenazine66 and deutetrabenazine67–69 have a positive risk–benefit balance as add-on treatments.67,70 There is also some evidence for tetrabenazine and Ginkgo biloba71 as add-on treatments. For other treatment options,72,73 see the review by the American Academy of Neurology74 and the section on treatment of TD in this chapter.

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