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Effects of antidepressant drugs

428 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 3 and may also be beneficial in paraphilias.27 The short-acting SSRI dapoxetine is an effective treatment for premature ejaculation and is licensed for this indication in many countries.6,28 A systematic review of RCTs with trazodone showed benefit for reducing so-called psychogenic erectile dysfunction.6 Sexual adverse effects can be minimised by careful selection of the antidepressant drug. Data mainly come from observational studies as the assessment of sexual adverse effects in early clinical trials was generally inadequate, often relying on spontaneous reports rather than using validated questionnaires and lacking positive controls.29 Where possible, information contained in this section has been obtained from studies where sexual adverse effects are purposefully and directly investigated. Management strategies for people who do develop sexual dysfunction on antidepressants are summarised in Table 3.18. No single approach can be considered ideal,6 so individual assessment is recommended. Post-SSRI sexual dysfunction Sexual dysfunction with antidepressants is largely dose dependent13 and is generally considered to be fully reversible.13 However, there have been reports of long-lasting sexual dysfunction where the symptoms have continued despite discontinuation of SSRIs/SNRIs.30 The term post-SSRI sexual dysfunction (PSSD) has been used to describe these symptoms. Reported PSSD symptoms include decreased libido, erectile dysfunction, delayed ejaculation, anorgasmia and vaginal dryness.31,32 In men, decreased genital sensation and numbness, pleasureless orgasm and premature ejaculation are also commonly reported symptoms of PSSD.31 The prevalence and pathophysiology of Table 3.18 Management of sexual adverse effects. Strategy Details

1. Rule out other possible causes33 ■ ■Depressive symptoms are associated with impaired sexual functioning. Compare sexual functioning on antidepressants with sexual functioning before antidepressants, not before the onset of depressive illness. ■ ■Consider other possible contributing causes (e.g. alcohol/substance misuse, diabetes, atherosclerosis, cardiac disease, and central and peripheral nervous system conditions). Other medications could be implicated, including both non-psychotropics (e.g. diuretics, beta-blockers) and other psychotropics.

2. Switch to a lower-risk antidepressant23 ■ ■Lower-risk antidepressants include agomelatine, bupropion, mirtazapine, vilazodone, vortioxetine and moclobemide.13 Of these, agomelatine, bupropion and vortioxetine34 have the best evidence supporting a more favourable sexual adverse effect profile.13 Non-pharmacological treatment strategies ■ ■Waiting for spontaneous remission: widely used, although least effective method.24 Remission may occur in a small number of people (5–10%) but can take up to 4–6 months.13 Impractical for many patients, although it might be considered in milder cases.30 ■ ■Dose reduction: can be considered in patients who have achieved full remission on an antidepressant6 ■ ■Drug holidays: intermittently missing one or two doses prior to planned sexual activity may possibly help but risks discontinuation symptoms.13,35,36 Not an effective strategy with fluoxetine, owing to its long half-life.13 Lowering doses by a half for two consecutive days prior to sexual activity is another possible strategy.24 (Continued)

Depression and anxiety disorders CHAPTER 3 PSSD remain uncertain.32,45,46 One estimate put the risk at 1 in 216 patients treated.47 Diagnosis relies on taking an accurate history of medications, symptom onset, symptom profile and eliminating other possible causes.31 Healy and co-workers have proposed diagnostic criteria for PSSD.48 Treatment strategies for PSSD remain anecdotal and no definitive treatments exist, although serotonin antagonists, dopaminergic agents and vortioxetine have been used.31 Multidisciplinary management is essential, possibly including urology and endocrinology.31 Table 3.18 (Continued) Strategy Details Pharmacological treatments ■ ■Phosphodiesterase inhibitors: both sildenafil and tadalafil have been shown to improve sexual functioning in men with antidepressant-related erectile dysfunction.23,37 Sildenafil is supported by the most evidence.38 Limited evidence in women, although one RCT found benefits.23 ■ ■Bupropion: may be useful in women at higher doses (300mg/day).37 Lower doses may be ineffective.23 A positive RCT in men39 was later retracted. ■ ■Mirtazapine: evidence is mixed. Open studies suggest some benefit for antidepressant- induced sexual dysfunction, but negative results were reported in one RCT.33 ■ ■Transdermal testosterone: RCTs provide evidence of efficacy in women with SSRI/ SNRI-emergent loss of libido40 and in men who continue to take serotonergic antidepressants with low or low-normal testosterone levels41 ■ ■Others:13 many other agents have been studied; many have little effectiveness. Buspirone was effective in one study for citalopram- or paroxetine-induced sexual dysfunction, but ineffective in another study with fluoxetine. Cyproheptadine has been used successfully in case reports of SSRI-induced sexual dysfunction in men and for anorgasmia in women. Loratadine was effective in a small open study for men with SSRI-induced erectile dysfunction. Amantadine was effective in earlier studies for SSRI-induced sexual dysfunction, but recent results have been negative. Yohimbine may be effective for medication-induced sexual dysfunction and improvements were reported by patients in two small studies (although results were nonsignificant). Bethanechol appears to help with TCA--induced sexual dysfunction when taken before sexual activity. Granisetron has been superficially evaluated. Flibanserin and bremelanotide are approved by the FDA for treatment of hypoactive sexual desire disorder in premenopausal women42 but there are no data to support use for antidepressant-induced sexual dysfunction. Pine bark extract was found to be superior to placebo in one meta-analysis.38 ■ ■Augmenting agents in treatment-resistant depression: some drugs used as an adjunct for treatment-resistant depression have been associated with improvement in sexual functioning in secondary analyses. Aripiprazole improved sexual functioning and desire, though only in women.24 Adjunctive brexpiprazole is associated with modest improvements.43 Pimavanserin, used as an add-on treatment to SSRIs/SNRIs, improved sexual functioning.44 FDA,

Food and Drug Administration; TCA, tricyclic antidepressant.

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