27 - Depression in older adults

Depression in older adults

688 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 6 Depression in older adults The prevalence of most physical illnesses increases with age and physical problems such as cardiovascular disease, chronic pain, diabetes and Parkinson's disease are associated with a high risk of depressive illness.1,2 The morbidity and mortality associated with depression are increased in older adults3 as older people are more likely to be physically frail and therefore vulnerable to serious consequences from self-neglect (e.g. life- threatening dehydration or hypothermia) and immobility (e.g. venous stasis). Suicide is relatively more common in older people.4 Mortality is reduced by effective treatment of depression.5 A meta-analysis of placebo-controlled and antidepressant-controlled studies found a response rate of 51% in older patients,6 similar to that for the adult population.7 There is a common perception that older patients do not respond as well or as quickly to antidepressants as their younger counterparts,8 perhaps because of structural brain changes or higher rates of physical comorbidity.9 It may be that biological age is more relevant than chronological age.10 The presence of physical illness, as well as baseline anxiety and reduced executive functioning, is also associated with poorer treatment outcomes.11 Nonetheless, even in older people, it may still be possible to identify non- responders as early as 4 weeks into treatment.12,13 A Cochrane review examined the efficacy and associated withdrawal rates of different classes of antidepressants in older people and found that SSRIs and tricyclics have similar efficacy, but TCAs are associated with higher withdrawal rates.14 A 2022 population study found non-TCA antidepressants to have broadly similar effectiveness.15 In the UK, NICE guidance for depression in adults recommends starting with an SSRI in the first instance (sertraline is commonly used first line in older people). When switching to another antidepressant, NICE recommends switching initially to a different SSRI or a better tolerated newer-generation antidepressant (this effectively indicates mirtazapine). Subsequently, an antidepressant of a different pharmacological class that may be less well tolerated is recommended, for example venlafaxine or lofepramine.16 The OTIMUM trial17 found that augmenting with aripiprazole or bupropion was better than switching to bupropion in 'treatment- resistant geriatric depression'. Network meta-analysis suggests that quetiapine, duloxetine, agomelatine, imipramine and vortioxetine have the highest efficacy in major depressive disorder in older people, although individual data are somewhat inconsistent.18 Two studies have found that, in older people who had recovered from an episode of depression and had received antidepressants for 2 years, over 60% relapsed within 2 years if antidepressant treatment was withdrawn.19,20 Some of this relapse may have been a result of the

speed and method of antidepressant discontinuation.21 Deprescribing antidepressants in older people presents a particular conundrum. Effective treatment should usually be continued, especially if depression was severe or recurrent. Ineffective treatment (i.e. was never effective or has become ineffective) should usually be withdrawn owing to the risk of adverse effects and interaction with polypharmacy regimens.22

Prescribing in older people CHAPTER 6 There is no ideal antidepressant in older people; all are associated with problems. TCAs are broadly considered to be agents of last resort owing to the increased risk of cardiac conduction abnormalities and because of anticholinergic effects. Although SSRIs are generally better tolerated than TCAs14 they do, however, increase the risk of gastrointestinal bleeds, particularly in the very old and those with established risk factors such as a history of bleeds or who are on treatment with an NSAID, steroid or warfarin. The risk of other types of bleed such as haemorrhagic stroke may also be increased23,24 (see Chapter 3). In older people, this increase in risk of stroke may persist after cessation of antidepressants.25 Older people are also particularly prone to develop hyponatraemia26 when starting SSRIs and most other antidepressants (see Chapter 3), as well as postural hypotension and falls27 (the clinical consequences of which may be increased by SSRI-induced osteopenia28). TCAs may also increase fracture risk.29 Table 6.8 summarises the use of antidepressants in older adults. Trazodone was once widely used in elderly populations30 but sedation and postural hypotension may be dose limiting. It retains some utility in depression occurring in dementia.31 Agomelatine is effective in older patients, is well tolerated and has not been linked to hyponatraemia.32,33 Its use is limited by the need for frequent blood sampling to check LFTs. Vortioxetine and duloxetine have also been shown to be effective and reasonably well tolerated in the older person34 but the caveats related to SSRIs are relevant here. A general practice database study found that, compared with SSRIs, ‘other antidepressants’ (venlafaxine, mirtazapine, etc.) were associated with a greater risk of a number of potentially serious adverse effects in the old (stroke/transient ischaemic attack [TIA], fracture, seizures, attempted suicide/self-harm) as well as increased all- cause mortality.26 However, SSRIs showed the highest risk for falls and hyponatraemia. All classes of antidepressant were associated with an increased risk of a range of adverse outcomes compared with no use. The study was observational and so could not separate the effect of antidepressants from any increased risk inherent in the group of patients treated with these antidepressants. Polysaturated fatty acids (fish oils) may be helpful in mild to moderate depression (compared with placebo),35 as may memantine.36 Methylphenidate seems effective in older people37 and may be useful where a rapid onset of action is required. There is some evidence that esketamine and ketamine are rapidly effective in people over 65 (without worsening cognition).38,39 The effect of antidepressants on cognition in later life is still debated – some studies find antidepressants to worsen cognitive outcomes,40–42 others find no effect.43 The choice of antidepressant may affect the risk – highly anticholinergic medicines undoubtedly worsen cognition and are known to increase the likelihood of developing dementia.44 Depression in dementia is probably best treated by cognitive or physical therapies rather than antidepressants.45 Antidepressants are of doubtful benefit.45–48 The same might be said for their use in the treatment of MCI in older people.49 Ultimately, choice is determined by the individual clinical circumstances of each patient, particularly physical comorbidity and concomitant medication (both prescribed and ‘over the counter’).

Table 6.8 Antidepressants and older people. Anticholinergic side effects (urinary retention, dry mouth, blurred vision, constipation) Postural hypotension Sedation Weight gain Safety in overdose

Other side effects Drug interactions Older tricyclics50 Moderate to severe with all TCAs All can also cause central anticholinergic effects (confusion, impaired cognition) All can cause postural hypotension Dosage titration is required Variable: from moderate with imipramine to profound with amitriptyline All tricyclics can cause weight gain All are toxic in overdose (seizures, cardiac arrhythmia) Seizures, anticholinergic-induced cognitive impairment Increased risk of bleeds with serotonergic drugs Mainly pharmacodynamic: increased sedation with benzodiazepines, increased hypotension with diuretics, increased constipation with other anticholinergic drugs, etc. Lofepramine Moderate, although constipation/sweating can be severe Can be a problem but generally better tolerated than older tricyclics Minimal Few data, but lack of spontaneous reports may indicate less potential than older tricyclics Relatively safe Raised LFTs Less likely to cause hyponatraemia than other TCAs and SSRIs SSRIs50,51 Dry mouth with paroxetine – probably best avoided in older people Unlikely, but an increased risk of falls is documented with SSRIs Sometimes seen with paroxetine and fluvoxamine Unlikely with the other SSRIs Paroxetine and possibly citalopram may cause weight gain Others are weight neutral Safe with the possible exceptions of citalopram and escitalopram which have the greatest effect on QT. Still much less toxic than TCAs GI effects and headaches, hyponatraemia, increased risk of bleeds in the older person (add gastroprotection if also on an NSAID or aspirin), orofacial dyskinesia with paroxetine, cognitive impairment,41 interstitial lung disease52,53 Fluvoxamine, fluoxetine and paroxetine are potent inhibitors of several hepatic cytochrome enzymes (see Chapter 3). Sertraline is safer and citalopram, escitalopram and vortioxetine are safest.

Mirtazapine, mianserin and trazodone are sedative with significant hangover in older people Venlafaxine, duloxetine have neutral effects Agomelatine aids sleep Venlafaxine and duloxetine can cause hypotension at lower doses, but usually increase BP at higher doses Occasional postural hypotension with trazodone Dizziness common with agomelatine Others54,55 Minimal with mirtazapine, trazodone and venlafaxine* Can be observed with reboxetine* Duloxetine* – few effects Agomelatine has no anticholinergic potential *Noradrenergic drugs may produce ‘anticholinergic’ effects via norepinephrine reuptake inhibition. GI, gastrointestinal; TCA, tricyclic antidepressant. Insomnia and hypokalaemia with reboxetine Nausea with venlafaxine and duloxetine Weight loss and nausea with duloxetine Possibly hepatotoxicity with agomelatine – monitor LFTs Cognitive impairment reported with trazodone41 but may be no worse than other antidepressants56 Venlafaxine is more toxic in overdose than SSRIs, but safer than TCAs Others are relatively safe Highest risk with mirtazapine, although older people are not particularly prone to weight gain Low incidence with agomelatine Duloxetine inhibits CYP2D6 Moclobemide and venlafaxine inhibit CYP450 enzymes. Check for potential interactions. Reboxetine has a low interaction potential. Agomelatine should be avoided in patients who take potent CYP1A2 inhibitors. Interstitial lung disease with SNRIs53

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