

07 - Choice of antidepressant and relative adverse

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338 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 3 Onset of action It is widely believed that antidepressants do not exert their effects for 2–4 weeks, or even longer. This is a myth. All antidepressants show a pattern of response where the rate of improvement is highest during weeks 1 and 2 and lowest during weeks 4 to 6. Early response strongly predicts later remission.¹¹ Statistical separation from placebo is seen at 2–4 weeks in individual trials (hence the idea of a lag period of no effect) but after only 1 or 2 weeks in (statistically more powerful) meta-analyses.^{12,13} Thus, where large numbers of patients are treated and detailed rating scales are used, an antidepressant effect is usually statistically evident at 1 week. In clinical practice using simple observations, an antidepressant effect in an individual is usually seen by 2 weeks.¹⁴ In individuals where no antidepressant effect is evident after 2–3 weeks of treatment, a change in dose or drug should be considered. It is important, however, to be clear about what constitutes ‘no effect’. Different patterns of response have been identified,¹⁵ and in some individuals response is slow to emerge. However, in those ultimately responsive to treatment, all will very probably have begun to show at least minor improvement at 3–4 weeks. Thus, those showing no discernible improvement at this time will likely never respond to the prescribed drug at that dose. In contrast, those showing small improvements at 3–4 weeks (i.e. improvement not necessarily meeting criteria for ‘response’ but observable nonetheless) may go on to respond fully.¹⁶ A meta-analysis¹⁷ has shown that if antidepressant (citalopram, paroxetine or sertraline specifically) trials are examined for effects on depressed mood alone (rather than the total HAM-D score) then both a rapid effect and a dose-response relationship (as already noted) are clearly evident. Choice of antidepressant and relative adverse effects Selective serotonin reuptake inhibitors are well tolerated compared with older tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs), and are universally recommended as first-line pharmacological treatment for depression.¹⁸ There is a suggestion from network meta-analyses^{1,19} that some individual antidepressants may be more effective overall than others but this has not been consistently

demonstrated in head-to-head studies. Adverse effect profiles of antidepressants do differ. For example, paroxetine has been associated with more weight gain and a higher incidence of sexual dysfunction, and sertraline with a higher incidence of diarrhoea than other SSRIs.²⁰ Dual reuptake inhibitors such as venlafaxine and duloxetine tend to be tolerated less well than SSRIs but better than TCAs. With all drugs there is marked inter-individual variation in tolerability, which is not easily predicted by knowledge of a drug's likely adverse effects. A flexible approach is usually required in finding the right drug for a particular patient. The Psymatik Treatment Optimizer may be helpful.²¹ As well as headache and GI symptoms, SSRIs as a class are associated with a range of other adverse effects including sexual dysfunction (see relevant section in this chapter), hyponatraemia (see section on antidepressant-induced hyponatraemia in this chapter) and GI bleeds (see section on SSRIs and bleeding in this chapter). TCAs have a number of adverse cardiovascular effects (hypotension, tachycardia and QTc prolongation) and are particularly toxic in overdose²² (see section on overdose in Chapter 13). The now rarely used MAOIs have the potential to interact with tyramine-containing

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