58 - Combination treatment

Combination treatment

Bipolar disorder CHAPTER 2 risperidone LAI is well supported by RCTs39 and naturalistic studies.40 The prescribing of LAI SGAs is generally encouraged despite some labelling restrictions41–44 (see ‘Antipsychotic long-acting injections in bipolar disorder’ earlier in this chapter). Box 2.1 summarises recommendations from NICE for prescribing in bipolar disorder. Optimising lithium treatment45 For adults with bipolar disorder the standard lithium plasma level should be 0.6–0.8mmol/L with the option to reduce it to 0.4–0.6mmol/L in cases of good response but poor tolerance, or to increase it to 0.8–1.0mmol/L in cases of insufficient response and good tolerance. For children and adolescents no consensus exists, but the majority of the International Society for Bipolar Disorders (ISBD)/International Study Group on Lithium (IGSLI) task force endorsed this same recommendation. For the elderly, a more conservative approach may be adopted, usually aiming for 0.4–0.6mmol/L, with the option to go to, at most, 0.7 or 0.8mmol/L at age 65–79 years, and only to 0.7mmol/L over age 80 years. Combination treatment A significant proportion of patients with bipolar illness fail to be treated adequately with a single mood stabiliser,11 so combinations of mood stabilisers46,47 or a mood stabiliser and an antipsychotic47,48 are commonly used.49 Also, there is evidence that where combination treatments are effective in mania or depression, then continuation with the same combination provides optimal prophylaxis.28,48 Overall, combination treatments offer better protection against relapse than monotherapy.7 The use of polypharmacy needs to be balanced against the likely increased adverse effect burden. Combinations of olanzapine, risperidone, quetiapine or haloperidol with lithium or valproate are recommended by NICE27 and by BAP guidelines.6 Alternative antipsychotics (e.g. aripiprazole) are also options in combinations with lithium or valproate, particularly if these have been found to be effective during the treatment of an acute episode of mania or depression.28,50 Carbamazepine is considered to be third line. Lamotrigine may be useful in bipolar II disorder27 but seems only to prevent recurrence of depression.51 Lurasidone may have broadly similar long-term efficacy, both as monotherapy and when combined with a mood stabiliser.33,52 Extrapolation of currently available data suggests that lithium plus an SGA is probably the polypharmacy regimen of choice. There are naturalistic data to support combinations of three treatments; in one study53 the two best treatments were lithium + valproate + quetiapine followed by lithium + valproate + olanzapine. Box 2.1 NICE recommendations27 ■ ■When planning long-term pharmacological interventions to prevent relapse, take into account drugs that have been effective during episodes of mania or bipolar depression. Discuss with the person whether they prefer to continue this treatment or switch to lithium, and explain that lithium is the most effective long-term treatment for bipolar disorder. ■ ■Offer lithium as a first-line, long-term pharmacological treatment for bipolar disorder and if lithium is insufficiently effective, consider adding valproate. If lithium is poorly tolerated,

consider valproate or olanzapine instead, or if it has been effective during an episode of mania or bipolar depression, quetiapine. ■ ■Do not offer valproate to women of child-bearing potential. Ensure adequate contraception in men taking valproate. ■ ■Discuss with the person the possible benefits and risks of each drug for them.

328 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 2 Monotherapy with antipsychotics can be considered where mood stabilisers are poorly tolerated or where adherence cannot be assured.54 A meta-analysis of long-term antidepressant treatment found that continued treatment was more likely to induce a switch to mania than prevent a depressive episode.55 The STEP-BD study found no significant benefit for continuing (compared with discontinuing) an antidepressant and worse outcomes in those with rapid-cycling illness.56 A more recent study found that neither escitalopram nor bupropion had any effect on relapse of depression.57 There is thus essentially no strong support for long-term use of antidepressants in bipolar illness although some bipolar patients may relapse into depression when antidepressants are discontinued.20 Box 2.2 and Table 2.12 summarise prophylaxis and maintenance treatment, respectively, in bipolar disorder. Box 2.2 Summary of prophylaxis in bipolar disorder First line: lithium monotherapy Second line: olanzapine, aripiprazole, risperidone or quetiapine in combination with valproate* or lithium Third line: alternative antipsychotic (lurasidone, asenapine or ziprasidone) or alternative mood stabiliser (carbamazepine or lamotrigine) in combination Fourth line: antipsychotic with two mood stabilisers ■ ■Always maintain successful acute treatment regimens (e.g. mood stabiliser + antipsychotic) as prophylaxis ■ ■Avoid long-term antidepressants if possible *Not in women of child-bearing potential. Table 2.12 Summary of maintenance in bipolar disorder.7,57 Prevents mania Prevents depression Monotherapy Antipsychotics Aripiprazole Yes No Asenapine Yes No Olanzapine Yes Yes Paliperidone Yes No Risperidone Yes No Quetiapine Yes Yes Mood stabilisers (MS) Lamotrigine No Yes Lithium Yes Yes Valproate Yes (?) Yes Antidepressants No No Combination treatment Antipsychotic + MS Yes Yes Valproate + lamotrigine Yes (?) Yes

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