48 - Treatment of acute mania or hypomania

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310 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 2 Treatment of acute mania or hypomania Drug treatment is the mainstay of therapy for mania and hypomania. Both antipsychotics and mood stabilisers are effective (although the nomenclature here is unhelpful – most, possibly all, antipsychotics are anti-manic and most mood stabilisers reduce psychotic symptoms in mania). Sedative and anxiolytic drugs (e.g. benzodiazepines) may add to the effects of these treatments. Drug choice is made difficult by the small number of direct comparisons, such that no one individual drug can be recommended over another on efficacy grounds. However, an early network meta-analysis1 suggested that olanzapine, risperidone, haloperidol and quetiapine had the best combination of efficacy and acceptability. Cochrane reviews suggested olanzapine is more effective than both lithium2 and valproate3 when used as monotherapy. Olanzapine may also be more effective than asenapine.4 A 2024 network meta-analysis concluded that tamoxifen was the most effective individual drug.5 The benefit of antipsychotic mood stabiliser combinations (compared with a mood stabiliser alone) is established for those relapsing while on mood stabilisers but less clear for those presenting on no treatment.6–10 The most common study design is for participants to be randomised to continued mood stabiliser alone (a treatment that allows the emergence of mania) or to the failed mood stabiliser with a (newly introduced) No Stop antidepressant treatment Is patient taking anti-manic* medication? Yes *In this context anti-manic = antipsychotic or mood stabiliser. **Lithium may be somewhat less effective in mixed states27 or substance misuse28 and in those with rapid cycling or exhibiting psychotic symptoms.29 Consider: An antipsychotic (if symptoms severe or behaviour disturbed) Or Valproate (avoid in women of child-bearing potential) Or Lithium (if future adherence likely) If response is inadequate after 1–2 weeks Combine antipsychotic and valproate or lithium All patients: consider adding short-term benzodiazepine22–24 (lorazepam or clonazepam) If taking an antipsychotic, check compliance and dose. Increase if necessary. Consider adding lithium or valproate If taking lithium,** check plasma levels, consider increasing the dose to give levels 1.0–1.2mmol/L (to treat the acute episode) and/or adding an antipsychotic If taking valproate, check plasma levels,8,9,25,26 increase dose to give levels up to 125mg/L if tolerated. Consider adding an antipsychotic If taking lithium or valproate

and mania is severe, check level, add an antipsychotic6 If taking carbamazepine, consider adding an antipsychotic (higher doses may be needed as antipsychotic levels reduced) All patients: consider adding short-term benzodiazepine22–24 (lorazepam or clonazepam) Figure 2.1 Treatment of acute mania or hypomania.6–21

Bipolar disorder CHAPTER 2 antipsychotic. Overall, combination treatment with an antipsychotic and a mood stabiliser is more effective and quicker to act than either individual drug used alone.5,30 Most formal guidelines recommend drug combinations as the first choice in mania,31 although single drug treatment may be considered, at least initially, for people presenting on no prior treatment. Figure 2.1 outlines a treatment strategy for mania and hypomania. These recommendations are based on somewhat dated UK NICE guidelines,7 British Association for Psychopharmacology (BAP) guidelines32 and individual references cited in the diagram. Where an antipsychotic is recommended, choose from those licensed for mania/bipolar disorder (i.e. most conventional drugs, aripiprazole, asenapine, olanzapine, risperidone and quetiapine). Valproate use is now heavily restricted, so lithium is likely to be the mood stabiliser most commonly used, at least in younger men and women. An alternative is carbamazepine, but this, like valproate, is teratogenic. Lamotrigine has no activity in mania33 and should not be used. Suggested doses and alternative treatments are outlined in Tables 2.6 and 2.7. Table 2.6 Mania: suggested drug doses. Drug Dose Mood stabilisers Carbamazepine 400mg MR twice daily increasing to 800–-1600mg/day.34,35 Dose may need to be increased after 2 weeks owing to induction of metabolism. Lithium 400mg/day, increasing every 3–4 days according to plasma levels. At least one study has used 800mg as a starting dose.36 Valproate As semi-sodium – 250mg three times daily increasing according to tolerability and plasma levels. Slow-release semi-sodium valproate may also be effective (at 15–30mg/kg)37 but there is one failed study.38 As slow-release sodium valproate – 500mg/day increasing as above. Higher, ‘loading doses’ have been used, both oral39–-41 and intravenous.42–44 The dose is 20–30mg/kg/day. Antipsychotics Aripiprazole 15mg/day increasing up to 30mg/day as required.45 Doses lower than 15mg may not be effective.46 Asenapine 5mg twice daily increasing to 10mg twice daily as required Cariprazine 3mg/day increasing up to 12mg a day as required47 Olanzapine 10mg/day increasing to 15 or 20mg as required Risperidone 2 or 3mg/day increasing to 6mg/day as required. The use of paliperidone in mania is not well supported.48 Quetiapine IR – 100mg/day increasing to 800mg as required. Higher starting doses have been used.49 XL – 300mg/day increasing to 600mg/day on day 2 Haloperidol 5–10mg/day increasing to 15mg if required Benzodiazepines Lorazepam23,24 Up to 4mg/day (some centres use higher doses) Clonzapam22,24 Up to 8mg/day

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