

Bipolar disorder and the elderly

Elderly patients with bipolar disorder can present some of the most difficult management challenges for old age psychiatrists. The National Institute for Health and Clinical Excellence guidelines on bipolar disorder contain few references to the management of this condition in the elderly. In the second of this two part series, **Drs Charlotte O'Callaghan, Biswadeep Majumdar and Anna Richman** discuss acute depression management and long-term prophylaxis.

DR CHARLOTTE O'CALLAGHAN is a specialist registrar in old age psychiatry and **DR ANNA RICHMAN** is a consultant in old age psychiatry, Sir Douglas Crawford Unit, Mossley Hill Hospital, Liverpool. **DR BISWADEEP MAJUMDAR** is a consultant in old age psychiatry at Waterloo Day Hospital, Liverpool

Bipolar disorder in the elderly consists of those who have 'graduated' into old age with the illness, and those who have developed the disorder later on in life. It is reported that up to 10 per cent of those with bipolar disorder will develop the illness over the age of 50 years¹.

The second part of this two part series reviews the management of acute depression and long-term maintenance therapy in older adults with bipolar disorder.

Acute depression

Bipolar depression is poorly studied and there are even fewer studies in the elderly. The National Institute for Health and Clinical Excellence (NICE) guidelines advise the following:

- In general, patients should not be prescribed an antidepressant without mood stabiliser cover
- In mild depression, watch and wait for two weeks, unless there is previous history of severe depressive episodes
- Antidepressant use should be avoided in those with rapid-cycling bipolar disorder
- Specific serotonin re-uptake inhibitors (SSRIs) are first-line therapy
- If no other antipsychotic is prescribed, quetiapine may be used in place of a SSRI
- Lamotrigine is not advocated as a first line treatment

- Where antidepressants are used, they should not be prescribed in the long-term, and should be gradually tapered once the episode has resolved
- Electroconvulsive therapy (ECT) may be considered where there is a severe depressive illness, prolonged or severe manic episode or catatonia.

The elderly are more susceptible to gastrointestinal bleeds in association with administration of SSRIs, and NICE suggests prescription of a gastroprotective drug when co-administering them with NSAIDs. SSRIs have also been associated with the syndrome of inappropriate antidiuretic hormone (SIADH). This becomes more common in those over 80, those who are prescribed other drugs which may cause hyponatraemia, and those with medical co-morbidities, such as reduced renal function, hypothyroidism, stroke, diabetes, chronic obstructive pulmonary disease (COPD) and hypertension. It is therefore suggested that regular blood monitoring should occur to monitor for this in these higher risk groups².

A small open label study of lamotrigine in elderly bipolar patients in an acute depressive episode resulted in an improvement in three out of five patients after six weeks³. A secondary analysis⁴ found lamotrigine to be superior to placebo and lithium in delaying depressive relapse in adults over 55 years of age. ECT is not well studied in the elderly with bipolar disorder¹.

Table 1. Suggested mood stabiliser monitoring^{1,5}

	Valproate	Lithium
Baseline	Full blood count (FBC) Liver function tests (LFTs)	ECG FBC if clinically indicated Renal function & electrolytes Thyroid function
Monitoring	FBC LFTs (six months after initiation of therapy)	Levels one week after dose changes and every three months six monthly: FBC if clinically indicated Renal function & electrolytes Thyroid function

Prophylaxis – mood stabilisers

NICE recommend the use of mood stabilisers as prophylaxis in the following situations:

- After a single manic episode associated with significant risk or adverse consequences
- \geq two acute affective episodes (one of which must be a manic episode)
- Significant impairment, risk of suicide or frequent episodes of depression or hypomania.

Where mood stabilisers are used, NICE recommends that they be continued for at least two years after an acute episode or for up to five years if there is a higher risk of relapse, indicated by previous history of frequent relapse, severe psychosis, ongoing stressful life events, poor social support or substance misuse. Lithium, valproate and olanzapine are all recommended as first line mood stabilisers.

Lithium prophylaxis

The majority of studies solely containing elderly patients are retrospective and naturalistic⁶. One randomised controlled trial (RCT) comparing lithium to lamotrigine or placebo found that lithium significantly delayed the time to manic, but not depressive, recurrence⁷. In studies of people of varying age groups with affective disorder, long-term lithium treatment has been demonstrated to reduce mortality by suicide by 82 per cent⁸. Maintenance lithium therapy has also been demonstrated to reduce the risk of Alzheimer's disease in elderly bipolar patients to that of the

general elderly population; a finding not present in patients maintained on other mood stabilisers⁹.

Lithium is not metabolised and is renally excreted. Older patients have reduced renal clearance, with 35 per cent of renal function being lost by 65 years and 50 per cent by 80 years². Neurotoxicity is experienced at lower concentrations than in younger adults¹⁰ and a higher frequency of lithium toxicity is seen in the elderly, with figures ranging from 11–23 per cent of those prescribed the drug¹¹. Hence, lower serum levels are advised in the elderly¹², with levels of 0.4–0.8mmol/l generally accepted as the optimum range, although anecdotally lower levels have been found to be therapeutic.

Hypothyroidism may occur in up to 20 per cent of patients on lithium, the highest rates occurring in middle aged women². Thiazide diuretics, ACE inhibitors and NSAIDs can all increase lithium levels and renal clearance may be reduced in individuals with congestive cardiac failure or hypertension. Lithium can induce a tremor, which may respond to treatment with propranolol and it can also worsen the tremor of Parkinson's disease¹³. In patients with pre-existing cardiac disease, lithium can increase the risk of arrhythmias, and the risk of sinus node dysfunction may be increased in those prescribed beta-blockers or digitalis¹³. When initiating lithium therapy it is important to consider patient compliance: intermittent treatment with the drug may worsen the prognosis, resulting in a greater than would be expected risk of manic relapse². Where there

Key points

- Elderly patients with bipolar disorder have an increased risk of other medical problems, particularly cerebrovascular disease, which can make bipolar disorder harder to treat.
- Lower medication doses and drug levels are required than for younger bipolar patients.
- Treatment of bipolar disorder in the elderly has a very limited evidence base and more research is needed.
- Suicide risk is high in bipolar disorder in all age groups and lithium reduces this risk.

are co-morbid medical conditions, there may be a poorer response to lithium⁶. It is perhaps because of all these problems that lithium prescription in the elderly is reducing, in favour of valproate^{14,15}.

Valproate prophylaxis

The role of valproate in long-term prophylaxis does not appear to have been studied in the elderly. Valproate causes less cognitive impairment than lithium¹³ and may have a lower rate of side effects in the elderly. In the elderly, the free fraction of the drug increases, and the clearance is reduced. If administered with high doses of aspirin, unbound valproate levels may be increased four fold. Valproate may increase the unbound fraction of warfarin and reduce clearance of some tricyclic antidepressants¹¹. Hepatotoxicity occurs rarely, and is usually seen within the first six months of therapy¹³. Pancreatitis can rarely occur (<one per cent of patients) and valproate has also been associated with Parkinsonism in elderly patients¹⁶. It is suggested in elderly hypomanic or euthymic patients to commence on a dose of 500mg nocte, increasing by 250–500mg/day every few days, according to response and side effects¹⁷. *Table 1* outlines suggestions for monitoring when using valproate or lithium.

Olanzapine prophylaxis

In a mixed age-group RCT, patients prescribed olanzapine were found to have similar relapse rates to those taking lithium. Those on olanzapine had a lower risk of manic or mixed episode recurrence¹⁸.

Lamotrigine prophylaxis

One RCT in elderly bipolar patients found that lamotrigine significantly delayed the time to depressive recurrence, but not manic⁷.

References

1. Sajatovic M. Treatment of bipolar disorder in older adults. *Int J Geriatr Psychiatr*, 2002; **17**: 865–73
2. Taylor D, Paton C, Kerwin R. The Maudsley Prescribing Guidelines. [9th edition] (London: Informa Healthcare, 2007): 210–11
3. Robillard M, Conn D. Lamotrigine use in geriatric patients with bipolar depression. *Can J Psychiatry* 2002; **47**: 767–70
4. Sajatovic M, Gyulai L, Calabrese J, et al. Response to mood stabilisers in older patients with bipolar I disorder. American Psychiatric Association Annual Meeting; 2004 May 1–6; New York. Quoted in Sajatovic M, Madhusoodanan S, Coconcea N. Managing bipolar disorder in the elderly: defining the role of the newer agents. *Drugs Aging* 2005; **22**(1): 39–54
5. National Institute for Clinical Excellence (2006) Clinical Guideline 38. Bipolar disorder: the management of bipolar disorder in adults, children and adolescents, in primary and secondary care. London: NICE
6. Young R, Gyulai L, Mulsant BH, et al. Pharmacotherapy of bipolar disorder in old age. *American Journal of Geriatric Psychiatry*, 2004; **12**(4): 342–57
7. Sajatovic M, Gyulai L, Calabrese JR, et al. Maintenance treatment outcomes in older persons with bipolar I disorder. *The American Journal of Geriatric Psychiatry* 2005; **13**(4): 305–11
8. Tondo L, Hennen J, Baldessarini. Lower suicide risk with long-term lithium treatment in major affective illness: a meta-analysis. *Acta Psychiatrica Scandinavica* 2001; **104**: 163–72
9. Nunes P, Forlenza O, Gattaz W. Lithium and risk for Alzheimer's disease in elderly patients with bipolar disorder. *British Journal of Psychiatry* 2007; **190**: 359–60
10. Sproule B, Hardy B, Shulman K. Differential pharmacokinetics of lithium in elderly patients. *Drugs & Aging*, 2000; **16**(3): 165–77
11. Sajatovic M, Madhusoodanan S, Coconcea N. Managing bipolar disorder in the elderly: defining the role of the newer agents. *Drugs Aging* 2005; **22**(1): 39–54
12. Umapathy C, Mulsant B, Pollock B. Bipolar disorder in the elderly. *Psychiatric Annals* 2000; **30**(7): 473–80
13. Van Gerpen M, Johnson J, Winstead D. Mania in the geriatric patient population: a review of the literature. *The American Journal of Geriatric Psychiatry* 1999; **7**(3): 188–202
14. Shulman K, Rochan P, Sykora R, et al. Changing prescription patterns for lithium and valproic acid in old age: shifting practice without evidence. *BMJ* 2003; **326**: 960–61
15. Sanderson D. Use of mood stabilisers by hospitalised geriatric patients with bipolar disorder. *Psychiatric Services*, 1998; **49**: 1145–48
16. Aziz R, Lorberg B, Tampi R. Treatments for late-life bipolar disorder. *The American Journal of Geriatric Pharmacotherapy*, 2006; **4**(4): 347–64
17. Goodwin G. Evidence-based guidelines for treating bipolar disorder: recommendations from the British Association for Psychopharmacology. *Journal of Psychopharmacology* 2003; **17**(2): 149–73
18. Tohen M, Shulman K, Satlin A. First-episode mania in later life. *Am J Psychiatry* 1994; **151**(1): 130–32

Conclusion

Bipolar disorder in the elderly is associated with both medical and psychiatric co-morbidities, and can prove more difficult to assess and treat than in the younger adult. This is further complicated by a limited evidence base informing treatment decisions. Robust placebo controlled studies of psychological and pharmacological treatments are required for all phases of bipolar disorder in the elderly.

Conflict of interest: none declared.