Lithium in bipolar and other affective disorders: prescribing practice in the UK

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Abstract

The use of lithium for the treatment of mania, prophylaxis of bipolar disorder and augmentation of antidepressants in treatment-refractory unipolar depression is supported by British Association for Psychopharmacology and National Institute for Health and Clinical Excellence guidelines. We describe prescribing patterns with lithium in a large sample of patients with affective disorders. Data were collected during a baseline clinical audit of the quality of lithium monitoring, conducted by the Prescribing Observatory for Mental Health. Thirty-five National Health Service Trusts submitted data for 2776 patients with a diagnosis of affective illness (ICD10 F30–39), 1919 (69%) of whom had bipolar affective disorder. The last recorded lithium level was below the therapeutic range (<0.4 mmol/L) in one in 10 patients. Co-prescribing was common; 57% of bipolar patients were prescribed an antipsychotic and 77% of those with other affective disorders, an antidepressant. We conclude that serum lithium levels within the therapeutic range are maintained in the majority of patients. A high proportion of patients are co-prescribed other psychotropic drugs; such prescribing is consistent with evidence-based treatment guidelines and may reflect difficulty managing the symptoms of affective disorders with lithium monotherapy. A significant minority of patients prescribed lithium had a sub-therapeutic blood level and so may be at high risk of relapse.

Keywords

Lithium, affective disorder, prescribing practice

Introduction

In clinical practice, lithium is widely used for the treatment of mania, prophylaxis of bipolar disorder, and to augment antidepressants in severe or treatment refractory depression. Its use for these indications is supported by the British Association for Psychopharmacology (BAP) and National Institute for Health and Clinical Excellence (NICE) guidelines for bipolar disorder (Goodwin, 2009; National Institute for Clinical Excellence, 2006) and depression (Anderson et al., 2008; NICE 2009).

Lithium has a narrow therapeutic index; serum levels of <0.4 mmol/L are sub-therapeutic and levels >1.0 mmol/L are likely to have an adverse risk–benefit ratio in the majority of patients (British National Formulary, 2009). With respect to the long-term treatment of bipolar disorder, a recent review of the literature (Severus et al., 2008) confirmed that efficacy has not been demonstrated at levels <0.4 mmol/L and concluded that, when initiating long-term lithium treatment, clinicians should initially aim for a serum level of 0.6–0.75 mmol/L. There is some evidence that higher levels may offer additional protection against mania but not depression (Kleindienst et al., 2007; Severus et al., 2008). This evidence base is reflected in both the BAP (Goodwin, 2009) and NICE (2006) guidelines for the management of bipolar disorder, which recommend a lower limit of 0.5 mmol/L and 0.6 mmol/L, respectively, and an upper limit of 1.0 mmol/L for the majority of patients. Within this range, higher levels are suggested for the acute treatment of mania. There are few data relating to optimal serum lithium levels in the treatment of unipolar depression (Crossley and Bauer, 2007); positive studies have employed serum levels of >0.5 mmol/L, with upper limits varying from 0.8–1.1 mmol/L.

Lithium is almost wholly excreted in the urine, so any changes in renal function, fluid balance or electrolyte levels can potentially lead to lithium accumulation and therefore...
toxicity (Anon, 2005). Serum lithium levels >1.0 mmol/L are likely to have an adverse risk–benefit ratio in the majority of patients (British National Formulary, 2009). When the lithium level increases above the upper limit of the therapeutic range, and certainly when it exceeds 1.5 mmol/L, muscle weakness, coarse tremor, slurred speech, seizures and irreversible renal damage can all occur, and ultimately lithium toxicity is life threatening. Even when the level is maintained within the therapeutic range, lithium may be associated with long-term effects on the kidney and thyroid. While adverse effects of lithium on the kidney used to be viewed as only occurring with toxic levels, recent data show a correlation between urinary concentrating ability (Bedford et al., 2008), creatinine levels (Paul et al., 2009) and duration of lithium use. With respect to effects on the thyroid, lithium treatment increases the risk of clinical hypothyroidism up to fivefold (Johnston and Eagles, 1999). As the symptoms of hypothyroidism overlap with those of depression, the underlying cause may remain undiagnosed and untreated unless specific screening tests are undertaken.

Given that lithium has a narrow therapeutic range, is a long-term treatment, that toxicity can be precipitated by changes in renal function, and that adverse effects on the thyroid are clinically significant, regular biochemical testing is indicated in all patients prescribed lithium.

With respect to clinical efficacy it has been calculated that, in the acute management of mania, for every six patients treated with lithium one will respond (number needed to treat (NNT) = 6; Storosum et al., 2007). The NNTs to prevent relapse into mania or depression in bipolar disorder are 10 and 14, respectively (Geddes et al., 2004). With respect to the treatment of unipolar depression, lithium is recommended in BAP and NICE guidelines as an antidepressant augmentation strategy, rather than for use as monotherapy, and in such situations the NNT = 5 (Crossley and Bauer, 2007). Although these effect sizes are very worthwhile clinically, a significant proportion of patients do not gain adequate benefit from lithium alone and it therefore follows that many are likely to require treatment with an additional mood stabilizer, antipsychotic and/or antidepressant; this is recognized in both the BAP and NICE guidelines. For many patients, lithium is a long-term treatment.

We report here on the clinical use of lithium, specifically the doses used, serum levels achieved, and the prevalence of prescriptions for other psychotropic drugs in a large sample of patients divided into two broad diagnostic subgroups, those with bipolar disorder and those with other affective disorders.

Method

The Prescribing Observatory for Mental Health (POMH-UK) conducts quality improvement programmes that start with a baseline audit of practice against evidence-based standards followed by the delivery of change interventions and finally a re-audit 12–18 months later. Further information about POMH can be found at www.rcpsych.ac.uk/pomh.

In October 2008, 35 National Health Service Trusts in the UK that provide specialist mental health services participated in a baseline audit of the quality of lithium monitoring. Clinical teams in these Trusts selected their own audit samples from their caseloads using a variety of methodologies, and could enter data for as many patients as they wished. The following data were collected for each patient prescribed lithium: age, gender, ethnicity, diagnosis (bipolar or other affective disorder), and the names of other prescribed psychoactive drugs. For those patients who were receiving maintenance treatment, in that lithium was initiated at least one year ago, the dose and most recent serum level in the year prior to the audit date were also recorded. In addition, data related to the frequency of biochemical monitoring were collected for this latter group; these are not reported here. Data were entered onto a web-based form and submitted to POMH UK via a secure web system.

For the subset of patients with bipolar illness, the demographic and other clinical variables collected were compared with those from the subset of patients with other affective disorders, using simple descriptive statistics. Categorical variables were compared using $\chi^2$ and continuous variables using independent samples $t$-tests.

The association between age and daily lithium dosage was examined in the subsample of patients ($n = 2027$) with a serum level within the recommended therapeutic range, that is between 0.4 and 1.0 mmol/L. Dosage was compared between two subgroups, those aged less than 65 years and those 65 years or older, using an independent samples $t$-test. Data were analysed using SPSS.

Assessment of bias in the sample

All mental health Trusts in the UK were defined according to the population they served at the local authority level. Where a Trust’s boundary was not contiguous with local authority boundaries (four Trusts), the population served was defined according to electoral wards. This information was established from each Trusts’ website (20 October 2009) and corroborated by telephone with each Trust’s Communications Department.

Annual Health Check (AHC) 2007/8 ratings for ‘Quality of Services’ and ‘Use of Resources’ were obtained for each Trust in England from the Care Quality Commission (http://www.cqc.org.uk/guidanceforprofessionals/healthcare/nhsstaff/annualhealthcheck200708.cfm; accessed 30 October 2009). Ratings were on a four-point Likert scale; weak, fair, good and excellent. Comparable data for Trusts outside of England were not available and so contributing Trusts from Wales ($n = 2$), Scotland ($n = 1$) and Northern Ireland ($n = 2$) were not included. Nevertheless, we considered that these quality indicators should be included to assess whether the volunteer sample of Trusts was over-representative of any sector of Trust performance.

Sociodemographic and economic indicators were estimated from the 2001 Census of Great Britain for each Trust. These included: proportion of men, proportion of children (aged less than 16 years), proportion of retired age persons (aged 6 years and older), proportion of single people (never married), proportion UK born, proportion from white ethnic groups, proportion with a limiting long-term illness, proportion with self-reported health rated as ‘not good’ and
the proportion of people from low social classes (defined as either semi-routine and routine occupations, long-term unemployed or unclassifiable occupations). For each Trust in the UK we also constructed the Townsend index for deprivation from selected census variables (http://cdu.mimas.ac.uk/related/deprivation.htm; accessed 30 October 2009). Scores are standardized with a mean of zero and standard deviation of one, with higher scores indicating greater deprivation.

To assess possible biases, in each section the mean for each sociodemographic and economic indicator for the contributing Trusts was compared with the UK mean using a one sample $t$-test. Statistically significant differences (at the 95% confidence level) were reported. Any statistically significant variable was correlated against the key outcomes to assess whether the bias may have affected the results. Similarly, Annual Health Check ratings were correlated with key outcomes. Where there was evidence that the bias may have affected the outcomes, the direction and effect of this bias were described in order to quantify the likely effect. While we acknowledge that lack of statistical significance is not synonymous with lack of bias for the relevant variables, this approach was a pragmatic method of guiding this analysis.

**Results**

Data were received for 2776 patients with a diagnosis of affective illness (ICD10 F30–39), 1919 (69%) of whom had bipolar affective disorder. Lithium treatment was initiated at least 1 year ago in 1734/1919 (90%) of the bipolar sub-sample and 717/857 (84%) of those with other affective disorders.

The demographic characteristics of the two sub-samples are shown in Table 1. Overall, patients with a diagnosis of bipolar illness differed from those with other affective disorders with respect to age and gender; they were more likely to be male (41.5% vs 34.4%; $\chi^2 = 12.549, df = 1, p < 0.01$), and were younger (mean age 53.5 vs 61.9 years, $t = -13.061, df = 1552.456, p < 0.01$). Of those patients younger than 65 years, 76% had a diagnosis of bipolar disorder while the respective figure in those over 65 years was 54% ($\chi^2 = 142, p < 0.001$). Seventy-three percent of men had a diagnosis of bipolar disorder, compared with 67% of women ($\chi^2 = 12.55, p < 0.001$). There was no difference in the proportion of those with a diagnosis of bipolar disorder (79.8%) or other affective disorder (80.6%) who were White, the most common ethnic group.

<table>
<thead>
<tr>
<th>Key demographic characteristics</th>
<th>Patients with a diagnosis of bipolar disorder</th>
<th>Patients with other affective disorders within ICD10 F30–39</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>$N = 1919$</td>
<td>$N = 857$</td>
</tr>
<tr>
<td>Male: n (%)</td>
<td>797 (41.5)</td>
<td>295 (34.4)</td>
</tr>
<tr>
<td>White/White British</td>
<td>1532 (79.8)</td>
<td>691 (80.6)</td>
</tr>
<tr>
<td>Black/Black British</td>
<td>44 (2.3)</td>
<td>3 (0.4)</td>
</tr>
<tr>
<td>Asian</td>
<td>96 (5.0)</td>
<td>21 (2.5)</td>
</tr>
<tr>
<td>Mixed or other</td>
<td>40 (2.1)</td>
<td>8 (0.9)</td>
</tr>
<tr>
<td>Data missing</td>
<td>207 (10.8)</td>
<td>134 (15.6)</td>
</tr>
<tr>
<td>Age</td>
<td>Mean age in years (SD)</td>
<td></td>
</tr>
<tr>
<td>Age range in years</td>
<td>53.5 (14.9)</td>
<td>61.9 (15.9)</td>
</tr>
<tr>
<td>Age bands n (%)</td>
<td>35 (1.8)</td>
<td>6 (0.7)</td>
</tr>
<tr>
<td>16–24 years</td>
<td>165 (8.6)</td>
<td>35 (4.1)</td>
</tr>
<tr>
<td>25–34 years</td>
<td>368 (19.2)</td>
<td>95 (11.1)</td>
</tr>
<tr>
<td>45–54 years</td>
<td>469 (24.4)</td>
<td>146 (17.0)</td>
</tr>
<tr>
<td>55–64 years</td>
<td>396 (20.6)</td>
<td>161 (18.8)</td>
</tr>
<tr>
<td>65 years and over</td>
<td>486 (25.3)</td>
<td>414 (48.3)</td>
</tr>
<tr>
<td>Lithium dose (mg/day)</td>
<td>Mean (SD)</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>0.63 (0.2)</td>
<td>0.60 (0.2)</td>
</tr>
<tr>
<td>&lt;0.1 n (%)</td>
<td>30 (1.7)</td>
<td>14 (2.0)</td>
</tr>
<tr>
<td>0.1–0.39</td>
<td>130 (7.5)</td>
<td>75 (10.5)</td>
</tr>
<tr>
<td>0.4–0.59</td>
<td>463 (26.7)</td>
<td>224 (31.2)</td>
</tr>
<tr>
<td>0.6–0.79</td>
<td>651 (37.5)</td>
<td>253 (35.3)</td>
</tr>
<tr>
<td>0.8–0.99</td>
<td>307 (17.7)</td>
<td>101 (14.1)</td>
</tr>
<tr>
<td>≥1.0</td>
<td>69 (4)</td>
<td>9 (1.3)</td>
</tr>
<tr>
<td>None documented</td>
<td>84 (4.8)</td>
<td>41 (5.7)</td>
</tr>
</tbody>
</table>

Table 1. Demographic characteristics, lithium dose and most recently recorded serum level for patients with bipolar and other affective disorders.
The relationship between lithium dose and serum level in those patients prescribed lithium for more than one year can be found in Figures 1a and 1b, with further details of the proportion of patients whose last documented lithium level was below, within, and above the therapeutic range being shown in Table 1. In the subgroup of patients whose last recorded serum level was within the therapeutic range, lithium dosage was compared between those patients aged less than 65 years (mean daily dosage 804 mg; SD 257) and those 65 years or older (mean daily dosage 485 mg; SD 210). The results of a two-sample t-test indicated a significant difference in mean daily dose between the two age groups (t = 32.6, df 1915, p < 0.001).

For those with a diagnosis of bipolar disorder, the mean dose of lithium prescribed (736 mg) was higher than that for those with other affective disorders (598 mg; t = 11.308, df = 1425, p < 0.01), although the mean serum lithium levels achieved were numerically similar at 0.63 and 0.60 mmol/L, respectively. The proportion of patients whose last recorded lithium level was <0.4 mmol/L was 9.2% for those with bipolar disorder and 12.4% for those with other affective disorders; in 30 (1.7%) and 14 (2.0%) patients, respectively, the concentration of lithium in their blood was below the laboratory cut-off for detection. For 84 (4.8%) patients with bipolar disorder and 41 (5.7%) with other affective disorders, there was no recorded lithium level in the last year. There was no difference between those patients with bipolar disorder whose last recorded lithium level was below the 0.4 mmol/L therapeutic threshold and those whose last level was above this threshold, with respect to age (mean 55 years in both groups) or gender (41.6% vs 40.9% male), or ethnicity (89.1% vs 96.6% White; χ² = 5144, df = 3, p = 0.162). In 44 (2.5%) patients with bipolar disorder and six (0.8%) with other affective disorders, the last measured serum lithium level was >1.0 mmol/L.

Other psychotropic drugs in addition to lithium were prescribed for 1544/1919 (80.5%) patients with bipolar disorder and 763/875 (87.2%) with other affective disorders. These other drugs were classified as antipsychotics, antidepressants or other mood stabilizers. In patients with bipolar (or other affective disorders), co-prescription consisted of one or more drug(s) from all three of these classes in 3.6% (2.4%), and two classes in 29.1% (29.9%), while 27.3% (7.3%) were prescribed only an antipsychotic, 15.5% (46.4%) only an antidepressant, and 5.0% (1.1%) only a mood stabilizer in addition to lithium. Overall, 56.7% of bipolar patients were prescribed an antipsychotic and 77.0% of those with other affective disorders, an antidepressant, see Figure 2.

In the sub-sample of patients with bipolar disorder, an antidepressant was prescribed for 25% of those younger than 35 years, 34.5% of those aged 35–44, 34.5% of those aged 45–54, 39.4% of those aged 55–64 and 42% of those aged 65 years and above (χ² = 20.547, df = 4, p < 0.001).

### Assessment of bias in the sample

Trusts that contributed data were slightly under-represented in terms of the proportion of people of white ethnicity (88.9% vs 93.2%; p = 0.05) compared with the UK population as a whole. However, at Trust level this variable was not significantly correlated to either the number of cases submitted, the number of cases with bipolar disorder or those treated with high doses of lithium, suggesting this bias did not have a significant effect on the results. There was no difference in the proportions of men, children (aged 16 years and younger), retired persons (aged 64 years and older), single people (never married), people from low social classes (defined as either semi-routine and routine occupations, long-term unemployed or unclassifiable occupations) or those with a limiting long-term illness or self-reported health rated as ‘not good’. Further, neither were AHC ratings correlated with any of these outcomes. Thus, the differences in the populations served by contributing Trusts compared with the population as a whole were not associated with lithium prescription; the results from the audit sample are very likely to represent the entirety of UK mental health Trusts.

### Discussion

Our findings suggest that, within psychiatric services, lithium is more commonly prescribed in younger adults for the treatment or prophylaxis of bipolar disorder, and in older adults for other affective disorders, most likely treatment-resistant depression. This may reflect the earlier age of onset of bipolar versus unipolar disorder (Johnson et al., 2000) and/or earlier use of lithium in the treatment of bipolar disorder. Notably, although the mean dose of lithium prescribed was higher in the bipolar group than the group with other affective disorders, the mean serum lithium levels achieved were similar. This may reflect both the age distribution of the two diagnostic groups where it is consistent with an age-related decline in renal function, and the lack of a distinct therapeutic range for the use of lithium in the management of treatment-resistant depression.

In the total sample, nearly three-quarters (73%) had a serum level within the therapeutic range, and this was achieved with lower doses in the elderly. Regarding lithium levels above the therapeutic range, the most recently documented serum lithium level was >1.0 mmol/L in a small proportion of patients in both diagnostic groups; in those with bipolar disorder, some levels were very high in that they were above 1.2 mmol/L. It is possible that the target range was 1.0–1.2 mmol/L in some patients with difficult-to-treat illness, but levels >1.2 mmol/L were unlikely to be intentional. These very high levels were not obviously dose related (see Figures 1a and 1b), and the most likely explanations include problems with renal clearance of lithium either in the short-term due to dehydration, or in the longer-term due to deteriorating renal function, taking a higher dose than prescribed, having blood taken less than 12 hours after the last dose, or taking other drugs that can reduce renal clearance of lithium such as NSAIDs, ACE inhibitors or diuretics (Juurlink et al., 2004).

Patients with levels >1.2 mmol/L may have symptoms of acute lithium toxicity, and are at increased risk of developing renal impairment.

The last recorded serum lithium level was below the 0.4 mmol/L therapeutic threshold in 1 patient in 11 with bipolar disorder and 1 patient in 8 with other affective disorders. If a higher threshold of 0.6 mmol/L is used, the respective figures would be 1 in 3, and approaching 1 in 2, respectively.
Figure 1. (a) Most recently recorded lithium dose and lithium serum level for patients treated with lithium for more than 1 year with a diagnosis of bipolar disorder ($N = 1734$). (b) Most recently recorded lithium dose and lithium serum level for patients treated with lithium for more than 1 year with a diagnosis of affective disorder other than bipolar disorder ($N = 717$).
Certainly those patients with a serum lithium level below 0.4 mmol/L are unlikely to be deriving clinically worthwhile benefit from lithium treatment and may be at high risk of relapse (Crossley and Bauer, 2007; Mitchell, 2007; Severus et al., 2008). Lithium protects against suicidality in both bipolar (Goodwin et al., 2003) and unipolar disorder (Guzzetta et al., 2007); given the high suicide rate associated with affective disorders (Baldessarino and Tondo, 2003; Sartorius, 2001), the clinical consequences of suboptimal treatment may be considerable.

As all patients in our sample for whom serum level data were collected had been receiving treatment with lithium for longer than 1 year, it is unlikely that the sub-therapeutic levels identified were due to the optimal treatment dose not yet being reached; the most likely explanation is partial or non-adherence to the prescribed dose. Poor adherence to prescribed psychotropic medication is a common clinical problem, with a high estimated attrition rate from treatment with mood stabilizers, in that only a third of patients with bipolar disorder are still taking their medication a year after it was prescribed (Mitchell, 2007). Further, a recent US study based on prescription records reported that a quarter of patients were partially adherent to mood stabilizing drugs including lithium, a fifth were non-adherent and that sub-optimal adherence was more likely in patients who were young and Black (Saljotovic et al., 2007). These data were based on the quantities of mood stabilizers issued over time and so allowed detection of at least some covert, as well as overt non-adherence. The non-adherence rate reported by Saljotovic et al. is considerably higher than is suggested by our data, and we did not replicate their findings with respect to the demographic factors associated with non-adherence. There are several potential explanations for the apparent lower non-adherence rate in our study. First, we collected the last recorded serum level only and so cannot know if suboptimal adherence was shown by different patients at different times. The literature relating to adherence would suggest that this is likely to be the case (Mitchell, 2007). Second, a high proportion of those patients who had no recorded serum level over the last year may also have been non-adherent, which would result in us significantly underestimating the magnitude of this problem. Third, some individuals in our sample were hospitalized patients, where the administration of medicines was likely to be supervised. Lastly, some of those patients with a serum level between 0.4 and 0.6 mmol/L may have had a higher target lithium level but been only partially adherent to treatment. Guidelines in the UK relating to the management of bipolar disorder recommend that patients should be informed that erratic compliance with lithium can increase the risk of relapse (NICE, 2006), and that maintenance treatment may not be indicated if adherence is poor (Goodwin, 2009). It is possible that these guidelines have influenced clinicians with respect to selecting patients for lithium treatment.

The BAP guideline for bipolar disorder (Goodwin, 2009) supports the use of lithium; (1) alone or in addition to an antipsychotic in the treatment of an episode of mania; (2) as a first-line option for prophylaxis where mania predominates with, if required, the addition of valproate or an antipsychotic; (3) as a second-line option where depression predominates with, if required, the addition of quetiapine or lamotrigine, and; (4) in addition to a selective serotonin reuptake inhibitor (SSRI) for the treatment of an episode of bipolar depression. Recommendations in the NICE guideline are broadly similar (NICE, 2006). We found that over 80% of patients with bipolar disorder who were prescribed lithium were considered to require combination treatment with an antipsychotic, other mood stabilizer, or antidepressant. Previous reports of prescribing practice in bipolar disorder have described frequent co-prescribing (Kupfer et al., 2002; Lloyd et al., 2003). Our study replicates these findings, and the high prevalence of prescribing of multiple psychotropic drugs illustrates how difficult it can be to manage the symptoms of bipolar disorder. The high proportion of patients who are prescribed an antipsychotic is consistent with the evidence base supporting the use of these drugs as mood stabilizers (Altamura et al., 2008; Tohen et al., 2004), and is consistent with the recommendations in evidence-based guidelines (Goodwin, 2009; NICE, 2006). In bipolar disorder, episodes of depression are approximately three times as
common as episodes of mania, and the time spent depressed far exceeds that spent in the manic phase (Judd et al., 2002, 2003; Perlis et al., 2006). Further, there is evidence that periods of euthymia decrease in both frequency and duration over time (Kessing et al., 2004). Consistent with these observations, over a third of patients in our sample were prescribed an antidepressant, and the prevalence of such prescribing increased with age. This is despite the most recent evidence finding no support for the efficacy of antidepressants (at least SSRIs and bupropion) in bipolar depression (Sachs, 2007).

The BAP (Anderson et al., 2008) and NICE (2009) guidelines for depression support the use of lithium to augment an antidepressant in treatment-resistant depression. Both guidelines also support the use of antipsychotic augmentation of antidepressants in psychotic and treatment-resistant depression. We found that almost 90% of patients with other affective disorders received at least one other psychotropic drug in addition to lithium, most commonly an antidepressant and/or an antipsychotic. This is generally consistent with these recommendations.

Limitations of the study

Our data were collected as part of a quality improvement programme that focused on biochemical monitoring in patients who were prescribed lithium and whose care was provided by specialist mental health services. The sample was selected by participating Trusts, drawn from a variety of care settings, and may have been biased towards hospitalized patients and those who were in frequent contact with services because their illness was difficult to treat. Further interpretation of our findings is limited by the broad diagnostic categories used; for example, the proportions of patients with bipolar disorder who were acutely unwell with either a manic or depressive episode, or who were receiving maintenance treatment on which they were stable at the time data were collected are unknown. It is also possible that some blood samples were taken at the wrong time in relation to the last dose of lithium, rendering the results of analysis uninterpretable. Nevertheless, the strengths of our study are that the sample was large relative to other published studies of lithium use, and was drawn from over half the specialist mental health services across the UK and would seem, from our analysis, to be representative of clinical practice. In addition, data were collected directly from clinical records and so were more likely to be complete than data from administrative databases that are set up primarily for billing purposes and subsequently utilized in data mining studies.

Conclusions

In conclusion, lithium is widely used for the treatment of bipolar and other affective disorders, and serum levels within the recommended therapeutic range are maintained in the majority of patients. Lower doses are prescribed for patients over 65 years of age compared with younger patients. Co-prescription of other psychotropic medication with lithium is the rule rather than the exception. In those patients receiving lithium as maintenance treatment, partial or non-adherence may be relatively common and this places patients at increased risk of relapse. A small proportion of patients had very high serum lithium levels and therefore an increased risk of both acute toxicity and longer-term renal damage.

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