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Lithium monitoring before and after the distribution of clinical practice guidelines

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Objective: To determine whether distribution of clinical practice guidelines improves lithium monitoring and whether standards of monitoring differed between patients in psychiatric contact and those seen only in primary care.
Method: Standards of monitoring were assessed for patients on lithium in northeast Scotland throughout 1995 and/or throughout 1996. Guidelines were circulated in January 1996 to all local general practitioners and psychiatrists. Monitoring was compared between 1995 and 1996 and for patients with and without psychiatric contact.
Results: Both primary care and psychiatric records were scrutinized for 422 and 403 patients prescribed lithium throughout 1995 and 1996, respectively. While monitoring was poor on several parameters during both years, frequency of measurement of both thyroid and renal function improved in 1996. Standards of monitoring were better for patients in psychiatric care.
Conclusion: Standards of lithium monitoring require further improvement. Locally agreed practice guidelines are helpful but patients on lithium should be in continuing contact with an experienced psychiatrist.

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Introduction

Lithium has been in use for over 30 years in the treatment of patients with serious affective disorders. With only the occasional dissenting view (1) it is widely regarded as the treatment of first choice in the prophylaxis of bipolar affective disorder and is efficacious in recurrent depressive disorders (2–9). For several reasons, efficient monitoring of patients taking lithium is important. There is a relatively narrow therapeutic range with low serum levels proving ineffective and high levels potentially giving rise to significant adverse effects, including death and enduring neurotoxicity (10, 11). Inadequate monitoring of lithium therapy is an unfortunately common cause of medical negligence claims (12–14). Renal and thyroid function can be affected adversely by lithium treatment (15–18) and these parameters require regular assessment. Furthermore, regular monitoring constitutes a focus for continuing patient education about lithium and is likely to improve treatment adherence (2, 4, 6, 19).

Despite its importance, evidence suggests that lithium monitoring is not conducted efficiently. Serum lithium levels, thyroid function and renal function are not monitored with sufficient frequency or regularity, and when serum levels are reported as lying outside the therapeutic range it is not unusual for no action to be taken by the responsible clinician (20–24). Comparisons of the performance of medical attendants has usually but not always found that psychiatric clinics provided less defective monitoring than patients received when they were cared for solely by general practitioners (21, 23, 24). These findings have contributed to a call for all patients on lithium to be seen in specialist 'mood disorder clinics' (2, 25), while others favour locally agreed guidelines between psychiatrists and general practitioners with a 'shared-care' model of management (5, 24, 26). The latter paradigm does seem more logical in view of the general success of shared care for mentally ill patients (27, 28) and the broad

agreement upon the principles of shared care for this patient group (29, 30).

The present study set out to evaluate lithium monitoring among patients, whether they were seen only in primary care or in a general practitioner/psychiatrist shared-care model, before and after the distribution of clinical practice guidelines to general practitioners and to psychiatrists.

Material and methods

Guidelines for lithium monitoring

Clinical practice guidelines for monitoring lithium treatment were formulated from a review of the literature and following discussion between the authors in consultation with relevant professional colleagues. The guidelines were intended to be, as far as possible, evidence-based and to be relevant and acceptable to local general practitioners, psychiatrists and clinical biochemists. Slightly abbreviated guidelines are shown in the Appendix.

Detailed exposition on the process of determining these guidelines is outside the scope of this paper, but a few points merit clarification where they differ from previously suggested guidelines (3, 8, 16, 31, 32) or where previous guidelines are inconsistent. The advocated frequency of serum lithium determinations varies quite widely but the most common view (13, 32, 33), which is in accordance with current British National Formulary advice, is that these should occur with a minimum frequency of every 3 months. While serum levels of 0.8 mmol/l and below are often advised (3, 8, 9, 31, 32) we felt that the evidence for increased efficacy of higher serum levels, at least for some patients (6, 11), justified extending the recommended therapeutic range to 1.0 mmol/l. While annual checks of thyroid function have been advised (3, 8, 31, 32) we felt that since thyroid dysfunction is common, and often emerges early in treatment with lithium (15, 16, 34), biannual checks are merited, although perhaps more importantly in the earlier years of treatment. We agree with Kehoe's suggestion (17) that an otherwise unexplained rise in serum lithium concentration merits further evaluation of renal function.

Subjects

We sought to identify patients maintained on lithium throughout 1995 and/or 1996 who lived within the catchment area of psychiatric services based in Aberdeen. Patients in Orkney and Shetland were omitted due to inaccessibility of case records, leaving a catchment population of around 430 000. With only a very few exceptions all patients would have serum lithium estimations conducted at the local Clinical Biochemistry Laboratories, and we identified patients initially by establishing all those who had serum lithium estimations between September 1994 and the end of 1996. While patients could possibly have been receiving lithium throughout 1995 and/or 1996 and have had no blood tests during that 28-month period, this was deemed most unlikely. Since one of the aims of the study was to investigate the merits of the involvement of psychiatric services, only patients registered at some point with local psychiatric services were included.

Method

General practice and psychiatric records of patients identified as above were scrutinized. Guidelines were circulated to all local psychiatrists and general practitioners in January 1996 and consultants in general adult psychiatry (whose catchments are based on general practice populations) were asked to discuss the guidelines and issues relating to lithium monitoring with the general practitioners whose patients they served. The possible effects of distributing the guidelines were investigated by comparing adherence to the standards set out therein between patients taking lithium throughout 1995 (prior to guideline distribution) and those on lithium throughout 1996. Patients were included in the analyses only if both general practice and psychiatric records had been reviewed. Comparisons were also made between patients who were looked after solely by the primary care team and those whose care was shared between the primary care and psychiatric teams. These groups were generally distinct but, when doubt existed, 'shared-care' patients were defined as those whose case remained open to psychiatric services, while 'general practice patients' were those whose psychiatric case had been closed.

Results

In 1995, 422 patients satisfied the inclusion criteria above, as did 403 patients in 1996. Without seeing both psychiatric and primary care notes we could not be certain as to how complete a sample these numbers represented of all patients taking lithium throughout the 2 years. Between 1995 and 1996 patient groups, there was a fall in the total number of general practice records scrutinized (635 against 576) while the numbers of psychiatric records available rose slightly from 740 to 751. General practice records of patients found to have stopped lithium from scrutiny of the psychiatric records were not pursued, explaining the lower figures of

general practice records reviewed, and the decline in numbers between 1995 and 1996 resulted principally from some practices becoming unwilling to have their records scrutinized on a second occasion.

1995 (pre-guidelines) vs. 1996 (post-guidelines)

In both years 63% of the patients were females and their mean age was close to 54 years. Two of the parameters within the guidelines showed statistically significant improvement between 1995 and 1996. An increased proportion of patients had two or more thyroid function tests (186/422 [44%] vs. 222/403 [55%], odds ratio 0.64 [95% CIs 0.45–0.85], $\chi^2 = 10.00$, $P = 0.002$) and more patients had creatinine checked once or more (301/422 [71%] vs. 315/402 [78%], odds ratio 0.69 [95% CIs 0.50–0.79], $\chi^2 = 5.09$, $P = 0.024$). Between 1995 and 1996, there were no statistically significant changes in the percentages having four or more serum lithium estimations (54% in both years), or being seen at least four times by a doctor (74% vs. 76%, respectively). In both years, less than 9% of general practice and psychiatric case records indicated clearly that patients were on lithium. When lithium levels outside the therapeutic range were recorded, appropriate action (as in the guidelines — see Appendix) was taken for low levels on 144/156 (92%) of occasions in 1995 and on 153/158 (97%) of occasions in 1996. For high levels, the corresponding figures were 72/90 (80%) and 77/94 (82%).

Shared-care vs. primary-care monitoring

Adherence to guideline parameters were compared for patients seen in shared-care arrangements and those seen in primary care only. Comparisons for 1996 are shown in Table 1. While comparisons were also conducted for 1995, the post-guidelines 1996 figures are perhaps more instructive. The only difference of note between 1995 and 1996 was that shared-care patients with low serum lithium levels more often received an appropriate response than their primary care counterparts in 1995, but this difference did not exist in 1996. As Table 1 shows, apart from marking case records and responding to lithium levels outside the therapeutic range, in 1996 monitoring was conducted more efficiently among patients seen in shared-care arrangements.

Discussion

Guscott and Taylor (2) wrote that 'there are serious deficiencies in current modes of lithium surveillance' and our findings support that conclusion. Monitoring of patients on lithium continued to exhibit several inadequacies, even after the distribution of clinical practice guidelines to psychiatrists and general practitioners. In 1996, only just over half of patients on lithium throughout the year had serum lithiums checked four times or more often, and a very similar proportion had thyroid function tested twice or more. Over 20% of patients did not have renal function tested at all during that year. While appropriate action was usually taken for low levels (perhaps partly because 'do nothing' was an acceptable option, and researchers may have erred on the side of generosity in interpreting clinicians' inactivity), appropriate action was not taken on nearly 20% of the occasions on which a high level was recorded. While this figure is lower than that reported in other areas of the United Kingdom (23, 24), the dangers inherent in a high serum lithium level are such that inactivity can never be justified. The finding that so few casenotes of patients on lithium (10%) were clearly marked was disappointing, since it is possible that this very simple expedient may have acted as a prompt to more regular monitoring.

Table 1. Lithium monitoring for patients seen in primary care alone or in shared care arrangements, 1996 cohort

	Primary care ($n=129$)	Shared care ($n=274$)	Odds ratios (95% CIs)
Number having 4 or more serum lithiums (%)	50 (38.8)	168 (61.3)	2.50 (1.59–3.94), $\chi^2 = 17.97$, $P<0.001$
Appropriate action for low levels (%)	36/38 (94.7)	117/120 (97.5)	2.17 (0.17–19.58), $\chi^2 = 0.72$, *P*, NS
Appropriate action for high levels (%)	27/35 (77.1)	50/59 (84.7)	1.65 (0.50–5.37) $\chi^2 = 0.86$, *P*, NS
TSH level twice or more (%)	57 (44.2)	165 (60.2)	1.91 (1.23–2.99) $\chi^2 = 9.11$, $P=0.003$
Creatinine level once or more (%)	90 (69.8)	225 (82.1)	1.99 (1.19–3.33), $\chi^2 = 7.84$, $P=0.005$
Seen at least 4 times by doctor (%)	56 (43.4)	251 (91.4)	14.23 (7.93–25.69), $\chi^2 = 112.26$, $P<0.001$
Case records clearly marked *	26 (10.1)	46 (8.4)	1.22 (0.72–2.08), $\chi^2 = 0.61$, *P*, NS

* Figures for both psychiatric and primary care records.

The frequency with which thyroid and renal function was monitored increased from 1995 to 1996, and it is likely that this was attributable to the distribution of clinical practice guidelines in January 1996. The multidisciplinary production of these guidelines and the encouragement of face-to-face meetings to discuss them between psychiatrists and general practitioners were designed to promote 'ownership' of the guidelines and their implementation (35, 36) while remaining mindful of the risk of 'guideline overload' among doctors (37). The improvement associated with receipt of clinical practice guidelines, while statistically significant, may be regarded as clinically small, for example with regard to the 7% increase in patients' receiving annual renal function checks, and changes in practice associated with the distribution of guidelines have previously proved to be transitory (38).

Patients who were in shared-care arrangements experienced better monitoring across the majority of parameters examined compared with patients seen in primary care only during both 1995 and 1996. As has been noted previously (23), such comparisons may be unfair to general practitioners, since patients are not allocated randomly to the type of supervision they receive; patients who are well stabilized on lithium and are well educated about their illness and their therapy may be looked after by the primary care team for those very reasons, and it could be argued that less stringent monitoring is required for this type of patient. However, such was the extent of the differences between the two groups, and given the widespread view that psychiatric services should focus principally upon patients with more severe forms of mental disorder (and patients on lithium would surely fall into this category), it seems appropriate to agree with the conclusion of Cookson (5) that: 'it is desirable that all patients receiving it (lithium) should have access to advice from a doctor with up-to-date knowledge of the treatment, and this would usually be an experienced psychiatrist'.

Recommendations

It would seem appropriate for lithium monitoring guidelines to be agreed locally between psychiatrists, general practitioners and clinical biochemists perhaps with room for modification within particular general practice/psychiatry partnerships. One standard criterion might be that all patients, after stabilization on lithium, should be seen with at least annual frequency by an experienced psychiatrist. Individualized 'lithium monitoring plans', distributed to primary care teams, psychiatric teams and to the patients themselves may constitute a simple and useful step in improving standards of lithium monitoring.

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Appendix

Lithium monitoring guidelines

Once a patient is stabilized on lithium carbonate as a prophylactic treatment for affective disorder, we suggest that the following guidelines be adopted:

(i) Serum lithium level should be checked at least four times in each calendar year.
(ii) Serum lithium levels should be maintained between 0.5 and 1.0 mmol/l, when taken 10–16 h after the most recent dose.
(iii) TSH should be monitored at 6 monthly intervals.
(iv) Urea and electrolytes and creatinine should be measured annually.
(v) The patient should be reviewed by a doctor at least four times in each calendar year.
(vi) The case records of each patient should be clearly marked to show that he or she is on lithium.

Action for low serum lithium levels

If the level is *low* (below 0.5 mmol/l), do one of the following:

(i) if the patient has remained well at low levels, and maintaining the patient at low levels is part of an overt management plan, *do nothing*;
(ii) if the level is part of a pattern of levels which have bordered on being too low, *increase the dose and recheck the serum level*;
(iii) if non-compliance is suspected as the cause *then contact the patient to let him/her know about the low level and then recheck serum level.*

Action for high serum lithium levels

If the level is *high* (over 1.0 mmol/l), do one of the following:

(i) if there is a suspected explanation for the high level, *recheck serum level*;
(ii) if the level is part of a pattern of levels which have bordered on being too high, *decrease the dose and recheck serum level*;
(iii) if there is no clear explanation for the high level then *the level should be rechecked in tandem with investigation of renal function*, a deterioration of which may account for the high serum level;
(iv) when serum levels exceed 1.5 mmol/l, lithium should be stopped, at least temporarily.