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An investigation into lithium monitoring

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The quality of lithium monitoring in a health district serving a population of 450 000 was studied over a period of a year. The following instances of poor monitoring were found: too frequent monitoring in stabilised patients, and failure to take action when lithium values fell below 0.3 mmol/l or rose above 1.0 mmol/l. Ways of improving the standard of monitoring are considered.

Precautionary measures can be overdone. The *British National Formulary* (BNF; British Medical Association & Royal Pharmaceutical Society of Great Britain, 1995) used to advocate routine monthly monitoring of serum lithium. Schou (1988) suggested that routine monitoring is not worth the cost or effort, a refreshing statement on a topic that needed simplification. The issue turns on whether patients, once stabilised, will remain so. Kehoe & Mander (1992) found that in 18 of 458 patients there was a gradual increase in serum lithium concentration during the course of a year, sufficient to require dose reduction. Such patients were found to have an unexplained 18% lower creatinine clearance rate than controls (Kehoe, 1994). This is important because 95% of ingested lithium is excreted renally (Dyson *et al*, 1987). Until more is known, it is reasonable to follow the current BNF (1995) recommendation of monitoring at 3-monthly intervals or even 6-monthly in young and middle-aged patients who are reliable (Ferrier *et al*, 1995).

However, there is no disagreement that it is essential to estimate serum lithium at the start of treatment, during intercurrent illness, and if there is the slightest suspicion of intoxication.

The study

The Biochemistry Laboratory of the Shropshire District Health Authority, one of the 23 district laboratories in the West Midlands Region, keeps a record of all lithium estimates, together with information culled from the request forms. The quality of monitoring was assessed from these data which covered the interval from 1st January 1991 to 31st October 1992. All estimates were included in the study.

The time elapsing between two consecutive estimates is referred to as the 'interval' of the second estimate.

The estimates were considered as four classes, the boundaries being derived from the BNF (1995):

- 0–0.3 mmol/l: probably too low to be effective;
- 0.4–1.0 mmol/l: the recommended therapeutic range;
- 1.1–1.4 mmol/l: effective but high, and usually incurring unnecessarily severe side-effects; and
- 1.5 and above, 'toxic'.

If any lithium value lay outside the BNF range (0.4–1.0 mmol/l), or if any interval was six months or more, or less than one month, further information was sought from case notes and from family doctor records.

Findings

General

The mean value of the 2697 lithium estimates was 0.63 mmol/l; 213 (7.9%) fell below the BNF range, 64 (2.4%) fell in the range 1.1–1.4 mmol/l, and 14 (0.5%) were in the toxic range.

Frequency of estimation

For this analysis, only intervals of 28 days or more were considered, shorter intervals not being regarded as routine. The median of these intervals was 62 days, and the mean within-patient interval was 70.2 days (s.d.=29.3 days).

Poor monitoring

In 47 patients, no action was taken when serum lithium values fell to 0.3 mmol/l or below. Several patients were treated for many months with what were probably sub-therapeutic doses, one being maintained at 0.1 mmol/l for 172 days and another between 0.1 and 0.3/l for 366 days.

In 24 patients, no action was taken when lithium values rose above the *BNF* range. The worst instances were: values all above 1.0 mmol/l for 368 days with a final value of 1.4 mmol/l, itself not prompting action for a further 58 days; 72 days between one estimate of 1.2 mmol/l and the next; 90 days between an estimate of 1.4 mmol/l and the next (at 1.5 mmol/l); 28 days between an estimate of 1.3 mmol/l and the next (at 1.8 mmol/l).

Finally, one 84-year-old patient had a serum value of 2.1 mmol/l as a result of a diuretic. Warnings in values of 1.4 and 1.2 mmol/l 18 and 15 days earlier had gone unheeded.

Too frequent monitoring is illustrated by a patient who had 21 estimates in 616 days despite all being in the therapeutic range and including a run of eight successive estimates at 0.5 mmol/l at 28 day intervals.

Incidental findings

One patient developed neurotoxicity at therapeutic lithium levels because of the co-prescription of verapamil.

Comment

The mean within-patient interval length of 70.3 days, less than the *BNF* recommendation, indicates that some patients stabilised on lithium are being monitored more often than is necessary.

Another statistic suggesting a lack of rationale in choosing the monitoring interval for stabilised patients is the large *within*-patient standard deviation of interval at 29.3 days. A large *between*-patient variation in interval could be justified on the grounds that some patients might require more frequent monitoring than others: those maintained at the upper end of the *BNF* range, or predisposed to renal disease because of diabetes mellitus, hypertension or the insidious development of prostatic hypertrophy. There is, however, only one rationale for such a large

within-patient variation. This is an early recommendation that, once stabilised, the monitoring interval should be progressively lengthened (Schou, 1986). This effect was found to account for only 3.6% of the within-patient variance and adjusting for it reduced the standard deviation by only half a day to 28.8 days. There remained, therefore, an appreciable within-patient variation in interval length even after this initiation effect is allowed for.

In contrast to this over-scrupulous monitoring of stabilised patients, there were lapses: failing to take precautions when prescribing diuretics, and failing to take action when lithium levels rose above 1.0 mmol/l, risking unnecessary side-effects, or fell below 0.4 mmol/l, risking relapse. The notes of those patients maintained outside the *BNF* range stated no reasons for doing so.

How might lithium monitoring be improved? Education is vitally important (see previous paper). Since consistent procedure minimises error, there is a strong case for adopting a common regimen and preparation within a District or Trust. If a psychiatrist wishes to treat any individual patient otherwise, then it seems reasonable that he or she should undertake the monitoring.

Finally, lithium monitoring should itself be monitored. In particular, only high standard long-term monitoring will identify those patients whose lithium values gradually increase, and thus lead to a greater understanding of the extent and nature of this phenomenon.

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