

Ranking of therapeutic and toxic side-effects of lithium carbonate

ROBERT COLGATE, Senior House Officer in Psychiatry, Glan Rhyd and Pen-y-Fai Hospitals, Bridgend CF31 4LN

The purpose of this study was to establish whether any agreement existed about the side-effects of lithium carbonate between the consultant psychiatrists in a single health district responsible for care of patients maintained on lithium therapy.

Since the first modern report on the actions of lithium carbonate and lithium citrate by Cade in 1949, a number of authors have commented on the adverse effects of lithium salts, both at therapeutic levels and in toxicity. The original paper stated that "symptoms of over-dosage are referable mainly to the alimentary and nervous systems", and since then significant effects upon the kidneys and the thyroid gland have been described.

Cade also commented on the importance of compliance with lithium medication, describing poor compliance as a factor associated with relapses of manic excitement. Compliance with and perceived effects of any medication are closely related, and in general, unwanted or unacceptable adverse effects reduce compliance. Subsequent relapse may then follow.

With respect to lithium, the relationship between compliance and adverse effects has received more attention recently (Peet & Harvey, 1991 and Delaney, 1991), mainly in an attempt to identify factors associated with full compliance with lithium therapy, and conversely, factors related to poor compliance, particularly those amenable to improvement. One aim of this research is to achieve a sustained reduction in the rate of relapse symptoms as a result of improved compliance.

The study

A questionnaire was developed from the *British National Formulary* (1991), by listing in order the side effects of lithium carbonate. Symptoms of severe overdosage were omitted. The symptoms were divided into two lists on the basis of whether they occurred at therapeutic level (13 items), or were associated with early toxicity (12 items). Also included were two brief questions concerning management of lithium therapy (see Appendix).

A copy of the questionnaire was sent to the 11 consultant psychiatrists and one senior registrar in Mid Glamorgan Health District, with a letter

explaining the purpose of the enquiry and a pre-paid envelope. Respondents were requested to rank the two lists of symptoms in order of clinical importance. Replies were made anonymously.

Findings

Nine questionnaires were returned, yielding nine usable replies for list one and eight for list two, response rates of 75% and 66.7% respectively. Assigning a score of one to the highest ranked symptom, two to the next and so on through to 13 for the lowest ranked symptom, the cumulative totals shown in Table I were obtained. (NB The lower the total score, the higher the ranking.)

Hypothyroidism and kidney changes were ranked as the most clinically important symptoms at therapeutic level, with fine tremor and minor gastrointestinal upset the least critically important. Similarly, ataxia, lack of coordination and dysarthria were ranked highest, and blurred vision, anorexia and mild drowsiness lowest as symptoms of early or mild toxicity.

Analysis of the significance of the spread of these cumulative totals using Friedman's statistic yielded probability values of $P < 0.001$ for list one and $P < 0.01$ for list two.

The two questions concerned with management of patients maintained on lithium were completed on nine questionnaires and produced a wide range of responses. The suggested maximum time between lithium estimations varied between six weeks and 12 months, with a median value of three months. (One reply quoted 16 hours, but this was considered to be erroneous.) The suggested maximum time between thyroid estimations varied between ten weeks and 12 months with a median of six months.

Comment

This study investigated the extent of agreement between senior clinicians with regard to the side effects of lithium. Despite the small sample size, it was striking that both at therapeutic levels, and in early toxicity, certain symptoms were consistently rated as more clinically important and others less so.

TABLE I

<i>List 1</i>	<i>Cumulative Total</i>
Kidney changes	30
Hypothyroidism	32
Hypokalaemia	46
ECG changes	53
Oedema	57
Goitre	58
Exacerbation of psoriasis	65
Polyuria	66
Polydipsia	67
Raised antidiuretic hormone	70
Weight gain	73
Fine tremor	98
Minor gastrointestinal upset	140

<i>List 2</i>	<i>Cumulative Total</i>
Ataxia	29
Dysarthria	29
Lack of coordination	35
Coarse tremor	41
Vomiting	44
Sluggishness	55
Giddiness	55
Muscle weakness	59
Diarrhoea	60
Blurred vision	70
Mild drowsiness	71
Anorexia	76

The degree of deviation from an average value was statistically highly significant.

This information could be employed in at least two ways. Firstly, in clinical management, attention could be focussed on some rather than all of the numerous possible symptoms and side effects of lithium so that detection and awareness of those symptoms deemed to be of clinical importance would be improved. The results of this study indicate that detection of hypothyroidism, and recognition of ataxia and dysarthria are suitable for such attention.

Clinical experience would suggest that undetected hypothyroidism still occurs, and a recent case report (Goddard, 1991) graphically outlined the dangers of lithium toxicity. Indeed, in this case ataxia had developed the day before presentation.

Outcome indicators related to these clinical features might allow a clinically relevant audit. For example, Schou (in Jefferson, 1990) has suggested that the incidence of hypothyroidism in a cohort of patients maintained on lithium should be two per hundred treatment years. An audit comparing the observed v. the expected incidence would reveal any discrepancy. A higher figure might indicate an

underlying population incidence above average, but a lower figure might suggest that some cases were being missed, and appropriate action taken.

Secondly, in the area of patient education, emphasis on certain symptoms might achieve greater levels of awareness of both early toxicity and side effects amenable to treatment, with a potential to improve compliance. Also, a firm indication of the maximum recommended times between lithium checks and estimations of thyroid function would assist understanding and compliance. It is clear from the range of answers supplied in this study that such a firm indication is lacking.

There were no questions in this study related to drug interactions with lithium, or to intercurrent illness. Clearly, these factors are major contributors to actual cases of lithium toxicity and a clinical audit would ideally incorporate such events. Furthermore, the number of questionnaires returned was small, and replication of the findings is important. However, I feel that given the complexity of lithium therapy, any steps towards simplifying management at a clinical level are worthy of close attention. (A recent personal communication from the Joint Formulary Committee of the British Medical Association and the Royal Pharmaceutical Society of Great Britain has indicated that as a result of the study findings, an analysis of the current presentation of side-effects would be undertaken for the next edition of the *British National Formulary*.)

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Appendix*List 1*

- Minor gastrointestinal upset
- Fine tremor
- Polyuria
- Polydipsia
- Weight gain
- Oedema
- Goitre
- Raised antidiuretic hormone secretion
- Hypothyroidism
- Hypokalaemia
- ECG changes
- Exacerbation of psoriasis
- Kidney changes

List 2

- Blurred vision
- Anorexia
- Vomiting
- Diarrhoea
- Muscle weakness
- Mild drowsiness
- Sluggishness
- Giddiness
- Ataxia
- Coarse tremor
- Lack of coordination
- Dysarthria

Question 1: Maximum time between lithium estimations . . .

Question 2: Maximum time between thyroid estimations . . .

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'Emergency' referrals to a South London community mental handicap team (CMHT)

S. GRAVESTOCK, Lecturer, Section of Psychiatry of Mental Handicap, Guy's Hospital, London SE1 9RT; and J. BICKNELL, Emeritus Professor of the Psychiatry of Mental Handicap, St George's Hospital Medical School, London SW17 0RE

As more people with mental handicaps* (MH) live in the community, in line with government community care policies (Department of Health, 1989), referrals to CMHTs* and other community based services will increase. Such referrals may be routine, urgent or emergency, come from various sources, and concern health and social care needs.

Wandsworth is a large south London borough with a multi-cultural, mobile general population and many deprived inner city areas. The Wandsworth CMHT is a well-established multidisciplinary community based team serving the specialist health care needs and selected specialist social work needs of adults with MH in the district health authority catchment area. The team has input from community mental handicap nurses, psychiatrists, psychologists, specialist social workers, and other therapists.

The team operates an open referral system and holds weekly team meetings, aiming to work primarily with known clients offering planned assessment,

**Use of the terms people with 'mental handicaps' (MH) and 'CMHT' should be considered broadly interchangeable with the recently adopted terms learning difficulties or disabilities and similar other-named community teams serving such people.*

inputs and regular reassessment of needs using a developmental/crisis prevention model as described by Sines & Bicknell (1985) and Wallace (1989). Some CMHTs have considered the implications of also providing crisis responses to meet the more urgent needs of clients and carers, but there has been little research of such work.

The study

The sample was all 'emergency' referrals received over the six months agreed by the team to fit their previously decided empirical definition of an 'emergency'.

"An unforeseen or rapid occurrence demanding rapid action if the wellbeing of the client or caregroup is to be restored to or maintained at the previous level of functioning."

The aims were:

(a) to monitor emergency referrals, team interventions and client descriptive outcomes within two weeks of referral, using a simple self-devised semi-structured questionnaire completed by the managing team member(s)