Using lithium

Lithium was first used as a mood stabiliser in 1949[1] and has since been a very popular psychiatric drug. Being a simple chemical it is not a profitable drug. Moreover, its use is not without adverse/side-effects. Both anticonvulsants and atypical antipsychotics (including lithium) are being used to treat a significant percentage of patients suffering from bipolar mood disorders. A recent survey in the United States found that the use of lithium remained relatively stable while that of anticonvulsants nearly doubled from 1994 to 2003.[2] Occasionally lithium is also used to augment other antidepressant drugs. The mechanism of action for this simple ion's mood stabilising or antidepressant action is unknown, despite many years of research.

Lithium has been used in thousands of psychiatric patients over the years. Available in different preparations and formats such as extended release forms, it is a monovalent cation, which is minimally protein bound and excreted by the kidneys. High concentrations are toxic, while its mood stabilising effect only occurs within a certain range of concentrations. Thus, it is a drug with a narrow therapeutic range (NTR) and lithium level monitoring is considered important to ensure an adequate response and avoid toxicity. Serum lithium levels are generally adjusted to between 0.5 mmol/L and 1.2 mmol/L for maximum benefits. Levels above 1.5 mmol/L are generally associated with some toxic effects. Adverse effects at levels above 2.0 mmol/L could be very serous and life-threatening. It is advisable to stop lithium immediately when signs of toxicity are noticed, without waiting for serum lithium level confirmation. Most psychiatrists would aim for a level between 0.6 to 0.8 mmol/L.[3] Serum lithium levels are commonly checked before the morning lithium dose and around 12 hours after the last or late evening lithium dose. A recent survey in the United States indicated that the proportion of patients on lithium not being monitored was low,[4] in contrast to digoxin, theophylline, and other drugs with similar NTRs.

Serum lithium levels cannot be reliably predicted from the dosage. While tissue level monitoring helps the prescribing physician adjust the dosage to avoid acute toxicity, clinicians prescribing lithium should be aware that toxicity may occur even when the level is within the therapeutic range. Lithium is toxic to many organs, particularly after long-term use. Metabolic adverse effects are particularly dangerous and include hypothyroidism, hyperparathyroidism and calcium level changes, weight gain and nephrogenic diabetes insipidus. Hypothyroidism is a well-known side-effect of lithium, particularly in older females with a history of hypothyroidism. Goitre occurs in some patients on lithium and if treatment was to continue during pregnancy, the neonate should be checked for goitre and hypothyroidism as well. In addition, patients may report other adverse effects related to the cardiovascular system (syncope, electrocardiographic abnormalities, circulatory failure), nervous system (blurred vision, tremors, vertigo, ataxia, nystagmus), kidneys (renal impairment), and gastro-intestinal disturbance (nausea, vomiting, diarrhoea). Lithium drug-drug interactions, particularly in polypharmacy situations, are common in the elderly. Concomitant non-steroidal anti-inflammatory drugs, diuretics, renin-angiotensin inhibitors, theophylline, and antibiotics have all been reported to cause elevations in lithium level and all of them are commonly prescribed together in geriatric patients.

Ng et al[5] in this issue report on their experience in using lithium to treat thyrotoxicosis. In this sense, an adverse effect is exploited for good use. Similarly, lithium-induced leukocytosis has been medically exploited in the management of certain leukopenic conditions. Clinicians using lithium should be aware of all these effects and be prepared to manage them. They should also appreciate that they are more likely to occur in the paediatric and geriatric populations. With all these possible adverse effects and interactions in mind, a full medical history and laboratory investigations should be undertaken before the initiation of lithium therapy. Investigations should include renal and liver function, thyroid function, electrocardiogram, blood counts, and biochemistry. Renal function tests should be repeated every 2 to 3 months and thyroid function tests once or twice during the first 6 months and then semi-annually or annually in stable patients, or whenever indicated.[3] With careful clinical monitoring for all these potentially dangerous adverse affects, plus periodic laboratory examination for serum lithium level as well as renal, liver, and thyroid function, many patients will stand to benefit from lithium therapy.

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