MOTOR NEURON DISEASE

Lithium ALS trial interrupted following safety doubts

Serious doubts about the safety of lithium carbonate as a treatment for patients with amyotrophic lateral sclerosis (ALS) have been raised after halting of a trial that saw adverse and serious adverse effects in its participants, even at low doses.

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The lithium carbonate trial was instigated by a research group in Italy following reports that this drug had an improved neuroprotective effect over riluzole, the only currently approved pharmacological treatment for ALS. However, the high rate of discontinuation of the drug by the participants caused the trial to be interrupted. The adverse effects experienced by patients were not specific to the dose administered (therapeutic versus subtherapeutic).

In the trial, 171 patients with ALS were randomly assigned to receive different doses of lithium carbonate (target blood levels were 0.4–0.8 mEq/l for the 'therapeutic' group, and 0.2–0.4 mEq/l for the 'subtherapeutic' group). No placebo group was included.

Despite high levels of adherence to the treatment, nearly 69% of patients had discontinued the trial by the time of the interim analysis, owing to death, tracheotomy, severe disability, adverse events (including dermatological, gastrointestinal and musculoskeletal disturbances) or serious adverse events (such as recurrent cystitis, deep vein thrombosis, and cardiac disturbance including fatal arrhythmia), or because of lack of efficacy.

In discussing the outcomes of their trial, the investigators recognize that the absence of a placebo was a limitation, although they had anticipated that the subtherapeutic dosage would act as a pseudoplacebo.

The investigators had been prompted to determine an appropriate dose of lithium carbonate for the treatment of ALS by the ready availability of this drug, which could tempt patients to administer self-medication. In addition, the promising indications from previous studies, including improved patient survival and delay of onset of ALS—which had been widely publicized—meant that patients with ALS were anxious for further news on how lithium carbonate could improve their disabilities.

The findings from the halted trial indicate that patients with ALS tolerate lithium poorly compared with psychiatric patients, as indicated by the increased rate of worsening of the disease, the authors conclude. Despite the promising outcomes of previous smaller trials, lithium carbonate cannot, on the basis of the new data, be recommended as a safe therapy for patients with ALS.

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