

Lithium Benefit in ALS Refuted

The year's meeting included a number of presentations on amyotrophic lateral sclerosis (ALS), including several that focused on lithium carbonate as a potential treatment.

Robert Miller, California Pacific Medical Center, San Francisco, California, presented results from a 12-month study that found lithium carbonate had no benefit on disease progression or survival in ALS, and was potentially harmful. The study included 107 patients with ALS who were treated with the oral medication and compared with 249 historical controls who had been assigned to placebo in a recent trial of minocycline.

The mean dose of lithium was 395 mg (to provide a blood level of 0.37 mEq/L),

and two thirds of patients in each treatment group were taking riluzole by choice. The slope of decline in Amyotrophic Lateral Sclerosis Functional Rating Scale–Revised (ALSFRS-R) scores was significantly greater with lithium (1.20 points/month) than with placebo (1.01 points/month; *P* value not given). In the lithium group, a more rapid decline was evident among the 37 patients who were taking the drug alone rather than in combination with riluzole and, in fact, accounted for most of the decrease. Forced vital capacity (FVC) declined by 2.85 mL/month with lithium vs 2.97 mL/month with placebo, respectively, a difference that was not significant. Rates of death were similar in the 2 groups (16 and 19 patients, respectively). Survival was worse, albeit not

significantly so, with lithium alone compared with lithium plus riluzole. Adverse events with lithium included 146 falls (compared with 81 in the placebo group) and 123 occurrences of neurologic problems (compared with 88 in the placebo group), which primarily took the form of dizziness, tremor, incoordination, and confusion. Serious adverse events were significantly greater among patients who received lithium, with or without riluzole, than among historical placebo controls (62 vs 40), and mostly related to disease progression.

The findings of this study are consistent with those of the Northeast and Canadian Amyotrophic Lateral Sclerosis Consortia's study reported online by *The Lancet Neurology* (April 6, 2010) and presented at the AAN meeting by Swati P. Aggarwal, Massachusetts General Hospital, Boston, Massachusetts. Dr. Aggarwal reported that the double-blind, placebo-controlled study of 84 patients with ALS was stopped at the first interim analysis (6 months), at which time 22 of 40 patients (55%) on lithium experienced a decrease of at least 6 points on the ALSFRS-R or died compared with 20 of 44 patients (45%) on placebo.

Lithium carbonate also failed to demonstrate beneficial effects in a larger, Italian study of ALS patients, which was detailed by Adriano Chio, University of Torino, Torino, Italy, who presented additional results to those announced in fall 2009 when the study was halted.

A total of 171 patients were randomized to receive lithium at therapeutic doses designed to achieve target blood levels of 0.4 to 0.8 mEq/L or in subther-

Costs and Outcomes in Alzheimer's Disease

Among Medicare beneficiaries in the United States, the annual cost of care is markedly higher in patients with Alzheimer's disease (AD) than in those without AD, reported Kara Suter, Moran Company, Arlington, Virginia. These observations emerged from a review of records representing more than 2 million Medicare enrollees, 4% of whom had AD. The total health care expenditure for 2008 was 30% higher in patients with AD than in case-matched controls (\$16,102 vs \$10,712, respectively) and more than twice that in the general Medicare population. At least part of the cost differential was likely due to age, as patients ≥ 85 years old accounted for 44% of the AD population compared with 11% of overall Medicare beneficiaries. Furthermore, data gathered between 2003 and 2008 showed that comorbidities (including conditions of particular interest, such as epilepsy, injuries, and depression) were far more common among patients with AD as compared with those who did not have AD. On the other hand, the magnitude of the differences in expenditures may have been underestimated, as data on Medicaid recipients were not included, Dr. Suter explained. The study also found that the 4-year survival rate was considerably lower among patients with AD than in matched non-AD patients and the overall Medicare population (18% vs 30% vs 58%, respectively). ■

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apeutic doses to produce blood levels of 0.2 to 0.4 mEq/L. The patients also received riluzole 50 mg twice daily during the study. Although the study was designed to last 15 months, an interim analysis prompted the safety committee to stop the trial because 68.4% of participants (117/171) had died or withdrawn. The reasons for study discontinuation were death or tracheostomy, serious adverse events, or patient-perceived lack of efficacy of lithium. A total of 37% of the patients who withdrew did so due to adverse events or lack of efficacy—a rate 2 times higher than in previously reported studies. Adverse events were particularly common in patients who had FVCs $\leq 80\%$ at the time of enrollment. At the time the study was stopped, the groups receiving therapeutic and subtherapeutic lithium doses had similar rates of overall adverse events and serious adverse events. The 2 groups also exhibited no significant differences in the monthly decrease in scores on the ALSFRS-R or the composite primary endpoint of survival, tracheostomy, or ≥ 2 previously defined adverse events. ■