Should lithium and ECT be used concurrently in geriatric patients?

Ana Hategan, MD, and James A. Bourgeois, OD, MD

Delirium has been described as a potential complication of concurrent lithium and electroconvulsive therapy (ECT) for depression, in association with a range of serum lithium levels. Although debate persists about the safety of continuing previously established lithium therapy during a course of ECT for mood symptoms, withholding lithium for 24 hours before administering ECT and measuring the serum lithium level before ECT were found to decrease the risk of post-ECT neurocognitive effects.[1]

We have found that the conventional practice of holding lithium for 24 hours before ECT might need to be re-evaluated in geriatric patients, as the following case demonstrates. Only 24 hours of holding lithium therapy might result in a lithium level sufficient to contribute to delirium after ECT.

CASE REPORT

An older woman with recurrent unipolar psychotic depression

Mrs. A, age 81, was admitted to the hospital with a 1-week history of depressed mood, anhedonia, insomnia, anergia, anorexia, and nihilistic somatic delusions that her organs were "rotting and shutting down." Treatment included nortriptyline, 40 mg/d; lithium, 150 mg/d; and haloperidol, 0.5 mg/d. Her serum lithium level was 0.3 mEq/L (reference range, 0.6 to 1.2 mEq/L); the serum nortriptyline level was 68 ng/mL (reference range, 50 to 150 ng/mL). CT of the head and an electrocardiogram were unremarkable.

A twice-weekly course of ECT was initiated.

The day before Treatment 1 of ECT, the serum lithium level (drawn 12 hours after the last dose) was 0.4 mEq/L. Lithium was withheld 24 hours before ECT; nortriptyline and haloperidol were continued at prescribed dosages.

Right unilateral stimulation was used at 50%/mC energy (Thymatron DG, with methohexital anesthesia, and succinylcholine for muscle relaxation). Seizure duration, measured by EEG, was 57 seconds.

Mrs. A developed postictal delirium after the first 2 ECT sessions. The serum lithium level was unchanged. Subsequently, lithium treatment was discontinued and ECT was continued; once lithium was stopped, delirium resolved. ECT sessions 3 and 4 were uneventful, with no post-treatment delirium. Seizure duration for Treatment 4 was 58 seconds. She started breathing easily after all ECT sessions.

After Treatment 4, Mrs. A experienced full remission of depressive and psychotic symptoms. Repeat CT of head, after Treatment 4, was unchanged from baseline.

What is the role of lithium?

Mrs. A did not exhibit typical signs of lithium intoxication (diarrhea, vomiting, tremor). Notably, lithium has an intrinsic anticholinergic activity[2]; concurrent nortriptyline, a secondary amine tricyclic antidepressant with fewer anticholinergic side effects than other tricyclics,[2] could precipitate delirium in a vulnerable patient secondary to excessive cumulative anticholinergic exposure.

No prolonged time-to-respiration or time-to-awakening occurred during treatments in which concurrent lithium and ECT were used; seizure duration with and without concurrent lithium was relatively similar.

There are potential complications of concurrent use of lithium and ECT:

Dr. Hategan is Associate Clinical Professor, Department of Psychiatry and Behavioural Neurosciences, Division of Geriatric Psychiatry, Michael G. DeGroote School of Medicine, Faculty of Health Sciences, McMaster University, Hamilton, Ontario, Canada. Dr. Bourgeois is Clinical Professor, Vice Chair of Clinical Affairs, Department of Psychiatry/Langley Porter Psychiatric Institute, Consultation-Liaison Service, University of California San Francisco Medical Center, San Francisco, California.

Disclosures
The authors report no financial relationships with any company whose products are mentioned in this article or with manufacturers of competing products.

With geriatric patients, withholding lithium before ECT might need to be reconsidered

- prolongation of the duration of muscle paralysis and apnea induced by commonly used neuromuscular-blocking agents (eg, succinylcholine)
- post-ECT cognitive disturbance.[1,3,4]

There is debate about the safety of continuing lithium during, or in close proximity to, ECT. In a case series of 12 patients who underwent combined lithium therapy and ECT, the authors concluded that this combination can be safe, regardless of age, as long as appropriate clinical monitoring is provided.[4] In Mrs. A's case, once post-ECT delirium was noted, lithium was discontinued for subsequent ECT sessions.

Because further ECT was uneventful without lithium, and no other clear acute cause of delirium could be identified, we concluded that lithium likely played a role in Mrs. A's delirium. Notably, nortriptyline had been continued, suggesting that the degree of anticholinergic blockade provided by nortriptyline was insufficient to provoke delirium post-ECT in the absence of potentiation of this effect, as it had been when lithium also was used initially.

Guidelines for dosing and serum lithium concentrations in geriatric patients are not well-established; the current traditional range of 0.6 to 1.2 mEq/L, is too high for geriatric patients and can result in episodes of lithium toxicity, including delirium.[5] Although our patient's lithium level was below the reference range for all patients, a level of 0.3 mEq/L can be considered at the low end of the reference range for geriatric patients.[5] Inasmuch as the lithium-assisted post-ECT delirium could represent a clinical sign of lithium toxicity, perhaps even a subtherapeutic level in a certain patient could be paradoxically "toxic."

Although the serum lithium level in our patient remained below the toxic level for the general population (>1.5 mEq/L), delirium in a geriatric patient could result from:

- age-related changes in the pharmacokinetics of lithium, a water-soluble drug; these changes reduce renal clearance of the drug and extend plasma elimination half-life of a single dose to 36 hours, with the result that lithium remains in the body longer and necessitating a lower dosage (ie, a dosage that yields a serum level of approximately 0.5 mEq/L)
- the CNS tissue concentration of lithium, which can be high even though the serum level is not toxic
- an age-related increase in blood-brain barrier permeability, making the barrier more porous for drugs
- changes in blood-brain barrier permeability by post-ECT biochemical induction, with subsequent increased drug availability in the CNS.[5,6]

What we recommend

Possible interactions between lithium and ECT that lead to ECT-associated delirium need further elucidation, but discontinuing lithium during the course of ECT in a geriatric patient warrants your consideration. Following a safe interval after the last ECT session, lithium likely can be safely re-introduced 1) if there is clinical need and 2) as long as clinical surveillance for cognitive side effects is provided—especially if ECT will need to be reconsidered in the future.

Two additional considerations:

- Actively reassess lithium dosing in all geriatric psychiatric patients, especially those with renal insufficiency and other systemic metabolic considerations.
- Actively examine the use of all other anticholinergic agents in the course of evaluating a patient's candidacy for ECT.

References

1. American Psychiatric Association. The practice of electroconvulsive therapy: recommendations for treatment, training, and privileging. A task force report of the American Psychiatric Association. 2nd ed. Washington, DC: American Psychiatric Publishing; 2001.
2. Chew ML, Mulsant BH, Pollock BG, et al. Anticholinergic activity of 107 medications commonly used by older adults. J Am Geriatr Soc. 2008;56(7):1333-1341.
3. Hill GE, Wong KC, Hodges MR. Potentiation of succinylcholine neuromuscular blockade by lithium carbonate. Anesthesiology. 1976;44(5):439-442.
4. Dolenc TJ, Rasmussen KG. The safety of electroconvulsive therapy and lithium in combination: a case series and review of the literature. J ECT. 2005;21(3):165-170.
5. Shulman KI. Lithium for older adults with bipolar disorder: should it still be considered a first line agent? Drugs Aging. 2010;27(8):607-615.
6. Grandjean EM, Aubry JM. Lithium: updated human knowledge using an evidence-based approach. Part II: clinical pharmacology and therapeutic monitoring. CNS Drugs. 2009;23(4):331-349.