Renal Toxicity of Long-Term Lithium Treatment for Mild Cognitive Impairment

To the Editor: Having read with great interest the recent JCP article by Aprahamian et al1 that examined nephrotoxicity in lithium-treated patients with mild cognitive impairment, I would like to make some remarks on this important topic.

First, regarding how lithium affects renal function, we know that renal toxicity induced by lithium mainly manifests as nephrogenic diabetes insipidus (NDI)2 and that risk for its occurrence is influenced by lithium treatment duration, dose, and plasma level.3 These patients show progressive reduction in urinary concentrating ability that can progress to chronic interstitial nephropathy and permanently impaired renal function.4 Therefore, it would have been informative if Aprahamian et al had also reported data on urinary concentrating ability; such information might have been useful for monitoring NDI duration and would have been complementary to the clinical data presented in their study.

Second, with respect to the study period required to evaluate lithium renal toxicity, when considering the influence of lithium treatment duration on the risk of developing renal toxicity, current data indicate that patients treated with lithium need an average of 13.6 years to develop chronic interstitial nephropathy and more than 15 years to develop end-stage renal failure.5 Furthermore, these effects appear to be progressive, at least for the first decade.6 Accordingly, Aprahamian et al should have used a study period greater than 4 years and close to those of studies previously enumerated.5,6

Third, in relation to neurologic side effects of lithium, we know that lithium neurotoxicity causes neurologic sequelae, such as dementia, among others,7 and that presence of NDI and age >50 years are 2 of the most important risk factors contributing to the appearance of neurotoxicity.8 Because of this, data on neurotoxicity during lithium treatment could have been informative, since this side effect has the potential to hide the effectiveness of lithium on mild cognitive impairment.

Fourth and finally, with regard to coadministered drugs, the study by Aprahamian et al1 was also limited by the fact that the authors did not present data on the use of diuretics (eg, amiloride, thiazides), which can mask renal toxicity (eg, NDI) and/or alter lithium clearance.9

REFERENCES

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Potential conflicts of interest: None reported.

Funding/support: None reported.

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receiving lithium (as compared to placebo) presented with significant improvements in global cognitive function, memory, and attention.\(^2\)

Finally, diuretic use was an exclusion/withdrawal criterion in our study, as were any other medications with known potential drug interaction with lithium.

**References**


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Potential conflicts of interest: None reported.

Funding/support: Funding sources for the study discussed in this letter are listed at the end of the original article (*J Clin Psychiatry* 2014;75(7):e672–e678).

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