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Kidney International (2014) **86**, 856–857; doi:10.1038/ki.2014.176

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Lithium and renal tumors: a critical comment to the report by Zaidan *et al.*

To the Editor: Zaidan *et al.*¹ reported a high prevalence of renal tumors in tertiary referred patients previously treated with lithium and suffering from impaired renal function, as compared to the prevalence in patients who had similar renal impairment but who had not been treated with lithium. The authors concluded that their study provided clear evidence for a potential association between long-term lithium treatment and an increased risk of renal solid tumors. Owing to methodological shortcomings this interpretation is questioned by the members of the International Group for the Study of Lithium (IGSLi), an association of experts on long-term treatment with lithium (<http://www.igsl.org>).

The study design is a case-series design and not a 'retrospective cohort study' as claimed by the authors. All patients initiated on lithium (and controls) were not identified and followed over time, implying that time at risk and cumulative events over time were not determined. Therefore, risks or incidence rate ratios as reported cannot be estimated.² The observed difference in prevalence of tumors between the two patient samples may be explained by other factors than the effects of lithium, such as differential use of medications and differential referral patterns. Lithium-treated patients are generally under careful observation for renal symptoms, even if not causally related to lithium, and non-lithium-treated patients may suffer from even serious renal problems that never lead to tertiary referral or renal imaging.

In conclusion, we find that no causal relation between lithium and solid renal tumors can be inferred from the study. Even we acknowledge that renal impairment *per se* occasionally may occur after long-term lithium treatment.³ We still consider lithium as a safe treatment, provided close

monitoring is done, and as the cornerstone in the long-term management of bipolar disorder.⁴

1. Zaidan M, Stucker F, Stengel B *et al.* Increased risk of solid renal tumors in lithium-treated patients. *Kidney Int* 2014; **86**: 184–190.
2. Dekkers OM, Egger M, Altman DG *et al.* Distinguishing case series from cohort studies. *Ann Intern Med* 2012; **156**: 37–40.
3. Bendz H, Schon S, Attman PO *et al.* Renal failure occurs in chronic lithium treatment but is uncommon. *Kidney Int* 2010; **77**: 219–224.
4. Licht RW. Lithium: still a major option in the management of bipolar disorder. *CNS Neurosci Ther* 2012; **18**: 219–226.

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Kidney International (2014) **86**, 857; doi:10.1038/ki.2014.178



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The Authors Reply: We thank Licht *et al.*¹ for their interest in our study on the increased prevalence of renal tumors in lithium-treated patients with chronic kidney disease (CKD).²

Licht *et al.* raised some concerns about the study design.¹ In the first part of our study, we identified all patients treated with lithium for bipolar disorder and regularly followed up for their CKD at the outpatient clinic. Thus, lithium exposure was ascertained. Then, we compared the proportion of renal tumors between lithium-treated and gender-, age-, and estimated glomerular filtration rate-matched lithium-free patients, sampled from the unexposed patients followed in our departments, and showed that it was greater in lithium-treated patients.² Contrary to what Licht *et al.* mentioned, we did not estimate relative risks and incidence rate ratios between the two groups. Instead, we calculated the number of expected cases of renal cancer in lithium-treated patients by gender and for each 5-year stratum using the French national estimates of renal cancer,³ and showed increased standardized incidence ratios of renal cancers in lithium-treated patients compared to the general population. Collectively, we reported an association and not a causal effect.⁴ Moreover, our results cannot be generalized to all lithium-treated patients because we did not explore a large population of lithium-treated patients without CKD. Finally, our work does not question the benefit of lithium in the management of bipolar disorders, but alerts nephrologists and psychiatrists