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Lower estimated glomerular filtration rates in patients on long term lithium: a comparative study and a meta-analysis of literature

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Abstract

Background: Several studies have shown that long-term lithium use is associated with a subtle decline in estimated glomerular filtration rate. This study compared mean estimated glomerular filtration rates (eGFR) in patients on long term lithium, against matched controls.

Methods: Patients with bipolar affective disorder, who are on lithium (for at least a year), were compared against controls that were matched (1:1) for age, gender and presence or absence of diabetes or hypertension. The eGFR was calculated from creatinine values according to the 'modification of diet in renal disease study' (MDRD) formula and was compared between cases and controls. A meta-analysis was performed to compare our findings with similar studies in literature.

Results: Forty seven patients met the inclusion criteria. They were matched with 47 controls. The eGFR values of lithium users were significantly lower ($p = 0.04$) compared to controls. This difference persisted between the subgroup of lithium users without comorbidities (diabetes and hypertension) and their controls but disappeared for lithium users with comorbidities and their controls. Nonetheless, lithium users had lower eGFR values in both subgroups. A meta-analysis of 9 studies showed a significant lowering in the glomerular filtration rate in lithium users compared to controls [mean difference -10.3 ml/min (95% confidence interval: -15.13 to -5.55 , $p < 0.0001$)].

Conclusions: Lithium causes a subtle decline in glomerular filtration rate; renal function needs to be monitored in patients on lithium treatment.

Background

Lithium is an effective and inexpensive drug that has been used for years to treat bipolar affective disorder. It is a monovalent cation that is well absorbed by the gastrointestinal system and completely excreted by the kidneys. Lithium is freely filtered in the glomeruli and 90% of the filtered load is reabsorbed in the proximal tubule [1]. Renal dysfunction caused by lithium is termed lithium nephropathy, and can manifest in many ways [2]. Firstly, lithium may induce a transient natriuresis by antagonizing aldosterone. Secondly, it can cause nephrogenic diabetes insipidus which is the most common renal ill-effect of lithium. Thirdly, lithium toxicity may

predispose to acute kidney injury (due to pre-renal failure secondary to polyuria or lithium induced neuroleptic malignant syndrome) [3]. Lithium is also known to cause a distal renal tubular acidification defect [2,4].

However, whether lithium plays a contributory role to the development of chronic kidney disease (CKD) is unclear. Traditionally, lithium has not been considered as a cause of CKD. Recent findings have challenged that view. One study showed that while a majority (85%) of patients on long term lithium had normal estimated glomerular filtration rates (eGFR), 15% had reduced eGFRs [5]. Another study assessed the eGFR values of two cohorts of patients; a group on long term lithium (up to 33 years) and a group of lithium naïve patients treated with other mood stabilizers. Patients on long term lithium had significantly lower eGFR values (corrected for age and gender) [6]. These observations raise the possibility of

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