LITHIUM NEPHROPATHY: A LONG-TERM COMPLICATION OF CHRONIC LITHIUM THERAPY

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A. Hercegovac, R. Hoekstra, T. Bosch, A.M. Van Alphen
## Faculty Disclosure

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x  No, nothing to disclose

Yes, please specify:
Introduction

• Bean-shaped organs serving several regulatory roles:
  ➢ Natural filter of the blood (gfr)
  ➢ Acid-base balance
  ➢ Regulation osmolarity
  ➢ Regulation blood pressure
  ➢ Secretion of hormones
Lithium-induced nephropathy

- Chronic kidney disease prevalence 10 – 35 %
  HR ± 2
- End stage renal disease prevalence 0.5 – 1.5 %

(Shine et al., 2015; Aiff et al., 2015; Bocchetta et al., 2015; Rej et al., 2014; Close et al., 2014; McKnight et al., 2012; Bendz et al., 2010; Tredget et al., 2010; Presne, 2003)
Risk factors

- Hypertension, diabetes, ischemic heart disease
- Women, age
- >2 yrs lithium use, lithium levels, lithium intoxication
Lithium-induced nephropathy

- Pathological findings consist of tubulo-interstitial nephritis, focal segmental glomerulosclerosis and renal (micro)cysts
- Asymptomatic
Aim

• Prevalence

• Role of duration of therapy, serum lithium concentration, lithium intoxication, comorbidity
Study Design

• Retrospective cohort study
• Study population: 1751 patients on lithium therapy
• Follow-up period 2000-2015
Definition renal failure:

- Renal insufficiency: $\geq 2 \times \text{MDRD}<60$, interval $>6$ weeks in between, last measured MDRD-GFR during follow up $<60$ ml/min
Statistics

- Prevalence
- Two subgroups: with and without renal failure
- Logistic regression analysis
## Results

<table>
<thead>
<tr>
<th>Total study population</th>
<th>All patients</th>
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<tbody>
<tr>
<td>Number of patients (N)</td>
<td>1751</td>
</tr>
<tr>
<td>Female/male ratio</td>
<td>1.36 (1010/741)</td>
</tr>
<tr>
<td>Age at onset lithium therapy (y)</td>
<td>44.4 ± 13.4</td>
</tr>
<tr>
<td>Duration lithium therapy (y)</td>
<td>10.9 ± 9.6</td>
</tr>
<tr>
<td>Mean serum lithium concentration (mmol/L)</td>
<td>0.68 ± 0.14</td>
</tr>
<tr>
<td>Smoking: number/total group (%)</td>
<td>821/1297 (63.3)</td>
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<tr>
<td>Cardiovascular disease: number/total group (%)</td>
<td>220/1492 (14.7)</td>
</tr>
<tr>
<td>Hypertension: number/total group (%)</td>
<td>297/1493 (19.9)</td>
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<tr>
<td>Diabetes Mellitus: number/total group (%)</td>
<td>217/1491 (14.6)</td>
</tr>
</tbody>
</table>
Results

• Prevalence renal failure in study population 17.4%

• Prevalence ESRD 1.1%
## Results

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Odds ratio</th>
<th>P-value</th>
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<tbody>
<tr>
<td>Mean serum lithium concentration</td>
<td>7.62</td>
<td>0.004</td>
</tr>
<tr>
<td>Duration lithium therapy</td>
<td>1.10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gender</td>
<td>2.16</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lithium intoxication</td>
<td>0.93</td>
<td>0.87</td>
</tr>
<tr>
<td>Age at onset lithium therapy (y)</td>
<td>1.06</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cardiovascular events</td>
<td>1.58</td>
<td>0.02</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.84</td>
<td>0.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.86</td>
<td>0.002</td>
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</table>
Lithium intoxication

- Patients without renal failure (n=192): 10 intoxications
- Patients with renal failure (n=52): 1 intoxication
Results

No renal insufficiency

Renal insufficiency
Discussion

Limitations current study design:

- Retrospective design
- Absence of control group
- Calculation MDRD-GFR
- Incomplete documentation psychiatric medical records with regard to comorbidities
Conclusions

- Prevalence renal failure comparable to previous reports
- End-stage renal disease very rare
- No association with episodes of lithium intoxication
- Association with female gender, age at onset lithium therapy, duration of lithium therapy and comorbidity
Conclusions

• Majority of lithium users preserves stable renal function

• Lithium nephropathy = multifactorial disease important role classical risk factors renal failure!
Future plans

• Discontinuation of lithium prevents further deterioration of renal function?

• Can amiloride therapy ameliorate decline in renal function?

• Increasing awareness of classical cardiovascular risk factors in patients receiving lithium treatment