

Reviewer's report

Title: Risk factors of thyroid abnormalities in bipolar patients receiving lithium: a case control study.

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Version: 3 **Date:** 25 Feb 2003

Reviewer: Alberto Bocchetta

Level of interest: A paper whose findings are important to those with closely related research interests

Advice on publication: Accept after discretionary revisions

The main objective of this study was to establish any correlation between erythrocyte : plasma lithium ratio (LR) and thyroid abnormalities in lithium-treated bipolar patients.

The initial analysis using t tests and Fisher's exact tests (Table 1) apparently associated thyroid abnormalities with low LR, but also with other variables such as absence of affective disorder in first degree relatives and female sex. However, only the latter stood logistic regression analysis as the Authors emphasize by their conclusions.

Compulsory revisions:

1) page 5, line 3: Given the relevance of two previous studies (ref 14 and 17) exploring RBC lithium and thyroid function and in view of the negative results from this study, lines 3 to 5 should be replaced as follows: "With regard to thyroid function, Rybakowski et al. reported higher activity of lithium-sodium counter-transport (LSC) in patients with higher TSH from a group of lithium-treated bipolar patients [17]. In the whole group and in female patients LSC was negatively correlated with LR [17]. Johnston et al found a lower LR in patients with side effects including hypothyroidism [14]."

2) Page 5, last two lines: when discussing the effects of gender, the term "thyroid problems" is too generic. The Authors should cite Johnston and Eagles (Br J Psychiatry 1999, 175: 336-339) who reported a higher prevalence of clinical hypothyroidism in women from a group of 718 lithium-patients. Perrild et al (ref 28) reported no gender difference only with regard to goiter and thyroid volume. Valle et al (ref 29) is not cited correctly, because they studied thyroid function in bipolar patients who had not been treated previously with lithium.

3) Since the main objective was to test the predictive role of LR in lithium-related thyroid abnormalities, conclusions should contain a statement summarizing if LR is recommended or not, or if additional studies are warranted.

4) There are some misprints: "anhedonya" (page 2, line 7) should spell "anhedonia"; on page 3, in the Patient selection section of Methods "inclusion bipolar patients" (line 1) is perhaps "inclusion of

bipolar patients". The sentence "Patients with no significant difference in were selected." (lines 3-4) is not clear, please specify.

"Pregnant women were excluded of the study" (line 4) should be "Pregnant women were excluded from the study".

5) In the Sampling section (page 3), an interval of hours after the last dose rather than "at least 11 hours" should be indicated.

Discretionary revisions:

1) The Authors should cite, among potential sources of discrepancies regarding LR and side effects, possible ethnic differences as reported by Strickland et al (Biol Psychiatry 1995, 37: 325-330).

2) The Authors would please cite and comment, if available, any epidemiological study of thyroid abnormalities in the general population from their recruitment area. In fact, conditions which may be endemic in some populations (e.g. iodine supply or peculiar immunogenetic background) may increase the risk associated with lithium exposure. In particular see Bocchetta et al (J Clin Psychopharmacol 2001, 21:594-598) for the role of thyroid autoimmunity.

Competing interests:

None declared.