

Introduction

Lithium is one of the most effective long-term therapies for mood disorders, protecting against both depression and mania and reducing suicidal risk^[1]. However, lithium presents some clinical disadvantages, namely its narrow therapeutic index which requires routine biochemical monitoring, the slow onset of action in acute mania; and acute adverse effects like thirst, unpleasant taste, and tremor^[2].

Since lithium is an unpatented drug, it has not been commercially promoted and the potential for adverse effects has been used as a deterrent against its use^[3]. According to a recent systematic review the risk of hypothyroidism is increased about six-fold in patients undergoing lithium therapy^[4]. However, whether the widespread practice of treating hypothyroidism in patients given lithium should be mandatory is unclear since most such patients are asymptomatic and the diagnosis is purely biochemical. To our knowledge no review/work has established the relative safety of low lithium doses or dosing on alternative days.

Aims

To access whether lithium is associated with thyroid dysfunction and if dosage and/or duration of treatment influences that association in patients with Unipolar Depression (UD), Bipolar Disorder (BD) and Schizoaffective Disorder (SD).

Methods

Retrospective analysis of laboratory and medication data from patients admitted to Centro Hospitalar Psiquiátrico de Lisboa, between September 2014 and February 2015, from specialized inpatient Units (Mood and OCD Disorders and Schizophrenic and Schizoaffective Disorders units) with the diagnosis of BD, UD and SD (ICD-10 - F31; F32 and F33; F25) who had a thyroid assessment performed during their admission.

Results

During the selected period, 301 patients were admitted. After eliminating patients with other diagnoses (n=101) and patients without a thyroid assessment (n=64) 136 patients were included (42 males and 94 females). Of these 94 had BD, 41 UD, and 11 SD and only 39 were first admissions.

The majority of patients were discharged without lithium therapy particularly if it was their first admission (p<0.01).

As expected lithium prescription is more common in BD (p<0.01).

Type of thyroid dysfunction	Lithium treatment		Fisher's Exact Test	
	Present	Absent		
Hypo-thyroidism	Subclinical	4	8	p=0.321
	Clinical	4	2	

Table 1. Association between Lithium and Hypothyroidism

Admissions	Lithium treatment	Thyroid Dysfunction		X ² Test
		Present	Absent	
First admission	Present	5	6	p=0.181
	Absent	32	15	
Readmission	Present	29	33	P=0.03
	Absent	56	22	

Table 2. Association between lithium exposure and thyroid dysfunction

Lithium is associated with thyroid dysfunction in general (p<0.05) but not with either clinical or subclinical hypothyroidism or hyperthyroidism in particular.

This association was not dependent on dosage (p>0.05). Although hypothyroidism is associated with replacement therapy the majority of patients with hypothyroidism are not medicated. Lithium therapy is associated with thyroid dysfunction in patients with previous inpatient stays (p<0.05) but not if it was their first admission (p>0.05).

Conclusions

As expected, lithium therapy is associated with thyroid dysfunction. However, we found no evidence that higher doses pose a greater risk. On the other hand, the fact that lithium is associated with thyroid dysfunction on readmissions but not on the first admission suggests that prolonged usage may be necessary for this side effect to develop.

Future studies should include not only dosage but also lithium serum levels and prospective studies regarding this subject are lacking. It would also be important to assess whether lithium dosage reduction or termination would lead to a recovery of thyroid function.

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Conflict of Interest

The Authors have no conflict of interest to declare.

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