

Brief report

# Trends in lithium prescription in Spain from 1985 to 2003

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## Abstract

Lithium use for bipolar disorder has decreased in the United States. We aimed at studying lithium prescription in Spain from 1985 to 2003. Prescription data, expressed in daily defined dose per 1000 inhabitants per day, were obtained. Lithium prescription increased uninterruptedly from 0.21 to 0.79 DID. The psychiatric reform in Spain and a broader definition of BD during the last decades are possible explanations for this rise.

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## 1. Introduction

Lithium is the drug with the best evidence of efficacy for the treatment of bipolar disorder (BD) and it has been considered the first-line long-term treatment for BD since its introduction 40 years ago (Fieve, 1999; Goodwin, 2002). Nevertheless, in recent years, new drugs with demonstrated efficacy for BD have been introduced. Anticonvulsants, such as valproate derivatives (Macritchie et al., 2003), carbamazepine (Emilien et al., 1996), lamotrigine (Goodwin et al., 2004) and topiramate (McIntyre et al., 2002), and atypical antipsychotics (for a review: Vieta and Goikolea, 2005; Yatham, 2005), have proved their efficacy for the management of

several clinical expressions of BD. These therapeutic novelties have, in practice, meant a change of general recommendations for all phases of BD management published in consensus guidelines (American Psychiatric Association, 2002; Bauer et al., 1999; Sachs et al., 2000; Suppes et al., 2002). In this context, several reports show a decrease of lithium use in the treatment of BD during the previous decade in the United States (Blanco et al., 2002; Goodwin et al., 2003). This change in bipolar treatment patterns, however, may differ between countries. We aimed at studying the evolution of lithium prescription in Spain during the two past decades.

## 2. Subjects and methods

Lithium purchase data from 1985 to 2003 were used as an approach to assess lithium prescription. Since 1970, lithium has been marketed in Spain by means of a

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single presentation containing 100 capsules of 400 mg each. Annual lithium purchase data were obtained from the ECOM database of the Spanish Ministry of Health, which contains the retail community pharmacy sales data of medicinal products reimbursed by the Spanish National Health System (SNHS) that covers the whole Spanish population. In addition, sales data from 1991 to 2001 were gathered from IMS Health in order to complete lithium consumption with data from private practice or other sources of drug distribution in Spain. Lithium consumption results were standardized by using the defined daily dose (DDD) per 1000 inhabitants per day (DID), according to the definition of WHO Collaborating Center for Drug Statistics Methodology (WHO Collaborating Centre for Drug Statistics Methodology, 1998). WHO DDD definition is “the assumed average maintenance dose per day for a drug used for its main indication in adults” whose value for lithium is 880 mg/d. In addition, the indication for lithium prescription was obtained from 2000 to 2002 from IMS Health data. Population data from 1985 to 2003 were obtained from estimates of the Spanish National Statistics Institute (Instituto Nacional de Estadística).

### 3. Results

SNHS lithium purchase increased from 63,990 units in 1985 to 271,828 in 2003 and the number of inhabitants in Spain increased from 38,473,418 to 42,717,064 respectively. This means that lithium prescription increased from 0.21 DID in 1985 to 0.79 DID in 2003 (Fig. 1). The mean (range) annual lithium increase was 7.73% (1.3–14.3). We can distinguish two periods according to figure slope; from 1985 to 1997 which saw an annual lithium increase mean (range) of 10.3% (4.8–14.3%) while it rose 2.5% (1.3–2.9%) from 1998 to 2003. According to

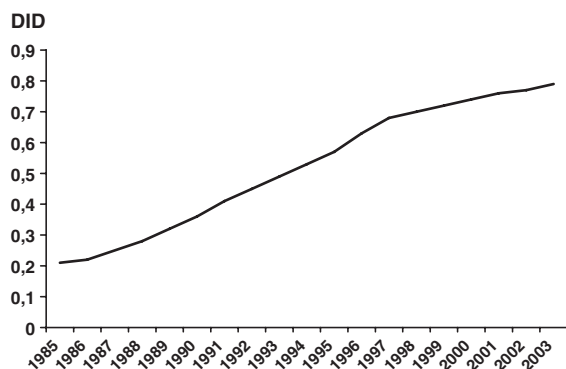


Fig. 1. Trends in lithium consumption from 1985 to 2003 in Spain. DID: defined daily dose per 1000 inhabitants per day.

IMS Health data, lithium consumption increased from 0.55 DID in 1991 to 0.95 DID in 2001. The percentage of lithium prescription covered by the SNHS showed a small increase, from 74.5% of total prescriptions in 1991 to 80% in 2001. According to IMS Health Survey, from 2000 to 2002, about a half of the lithium prescriptions were for bipolar affective disorder (50.1% to 57.2%). Other mood disorders accounted for a quarter of lithium prescriptions (23.9% to 27.7%), while the rest was used to treat psychotic disorders and other psychiatric disorders.

### 4. Discussion

Lithium prescription has increased almost fourfold during the last 19 years in Spain. Surprisingly, this rise has occurred even though lithium is an old medicine without marketing promotion and with a narrow therapeutic range that requires special monitoring. Other drugs marketed in Spain for BD are valpromide since 1985, carbamazepine since 1986, risperidone since 2003 and lamotrigine, olanzapine and quetiapine since 2004 (Consejo General de Colegios Oficiales de Farmacéuticos, 1986, 1987, 2004 and 2005). The authorization of carbamazepine and valpromide for BD, apparently, had little impact on the increasing trend of lithium prescription. However, the slower increase in the consumption trend from 1998 onwards could be explained by the full coverage of the population susceptible to be treated. Nevertheless, lithium prescription in Spain, 0.79 DID in 2003, is still lower than that of Scandinavian countries: 1.4 DID for Sweden and 1.4 DID for Norway in 2000 and 1.1 in Denmark DID in 1999, but higher than Slovenia, 0.2 DID in 2000 (Furst and Kocmur, 2003). These data suggest that there is still some space for increase. An additional explanation for this deceleration could be an initial off label use of atypical antipsychotics for the treatment of BD prior to their approval for this condition.

There are several possible explanations for the overall increase. First, a reform of public psychiatry was implemented in Spain from 1985 to 1996, widening the access of psychiatric patients to the SNHS (Vazquez-Barquero and Garcia, 1999) and moving psychiatric approach from a psychoanalytical to a biological and psychopharmacological approach (Guimon et al., 1987). This reform may have resulted in increased clinical experience with lithium and as such may have changed the stigma of being an unsafe drug with difficult management. This change in lithium's safety perception among clinicians provides an additional explanation of the increase in lithium prescription in Spain. Moreover, lithium is very economical and this may be an additional

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