ELSEVIER

Journal of Affective Disorders 111 (2008) 94–99

Journal of Affective Disorders

www.elsevier.com/locate/jad

Brief report

Changes in outpatient lithium treatment in the Netherlands during 1996–2005

I. Wilting [a,b], P.C. Souverein [a], W.A. Nolen [c], A.C.G. Egberts [a,b], E.R. Heerdink [a,*]

[a] *Division of Pharmacoepidemiology and Pharmacotherapy, Utrecht Institute for Pharmaceutical Sciences, Utrecht University, Faculty of Science, Utrecht, the Netherlands*

[b] *Department of Clinical Pharmacy, University Medical Center Utrecht, Utrecht, the Netherlands*

[c] *Department of Psychiatry, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands*

Received 7 January 2008; received in revised form 20 January 2008; accepted 20 January 2008
Available online 14 March 2008

Abstract

Background: The objectives of the present study were to investigate in outpatients in the Netherlands between 1996 and 2005, changes in 1) the incidence and prevalence of lithium use and 2) lithium use patterns (discontinuation, add-on, and switch).
Methods: Incidence and prevalence of lithium use were determined for each year between 1996 and 2005. In addition, we determined cumulative changes in lithium use (discontinuation, add-on, and switching) at three, six, 12 and 24 months for three separate time-cohorts (1998–1999, 2000–2001 and 2002–2003). Lastly, concomitant use of other drugs used in the treatment of bipolar disorders next to lithium during the 24 months after the first lithium prescription was determined for the three time-cohorts.
Results: Incidence of lithium use was constant at approximately 0.2 per 1000 person-years, prevalence increased with 26% from 0.95 to 1.2 per 1000 persons. The percentage of patients receiving an add-on drug used in the treatment of bipolar disorders was constant over the three time-cohorts, with a significant decrease in use of tricyclic antidepressants. Within the patient group that stopped using lithium, more patients switched from lithium to another agent used in the treatment of bipolar disorders over calendar time, and fewer patients discontinued lithium. There was a significant increase in the use of atypical antipsychotics and valproic acid next to lithium.
Limitations: We did not know the specific diagnosis for which lithium treatment was instituted.
Conclusion: The changes were in line with the increase in alternatives during the last decade and in line with Dutch guidelines.

Keywords: Incidence; Prevalence; Lithium; Atypical antipsychotics; Bipolar disorders

1. Introduction

During the recent 10–20 years the range of pharmacotherapeutic options for the treatment of bipolar disorders has widened significantly. Between the 1960s and 1990s (typical) antipsychotics, antidepressants, carbamazepine and valproic acid were the major treatment options besides lithium. (Bowden et al., 1994; Greil et al., 1997; Prien

* Corresponding author. Utrecht University, Faculty of Science, Utrecht Institute for Pharmaceutical Sciences, Division of Pharmacoepidemiology and Pharmacotherapy, PO Box 80082, 3508 TB Utrecht, the Netherlands. Tel.: +31 30 2537324; fax: +31 30 2539166.
E-mail address: E.R.Heerdink@uu.nl (E.R. Heerdink).

0165-0327/$ - see front matter © 2008 Elsevier B.V. All rights reserved.
doi:10.1016/j.jad.2008.01.019

et al., 1972) During the past two decades several atypical antipsychotics (Sachs and Gardner-Schuster, 2007; Dunner, 2005; Tohen et al., 2005; Sachs et al., 2004) and additional second generation antidepressants became widely available (Nemeroff et al., 2001), as well as antiepileptic mood stabilizers such as lamotrigine (Bowden et al., 2003). There have been reports of a decline in lithium prescription rates over the past years, especially in the U.S., but also in Europe (Fenn et al., 1996; Blanco et al., 2002; Davids et al., 2006). In contrast, a study in Spain reported an increase in lithium use (Castells et al., 2006).

The objectives of the present study were to investigate, changes in 1) the incidence and the prevalence of lithium use and 2) lithium use patterns (discontinuation, add-on, and switch), in outpatients in the Netherlands between 1996 and 2005.

2. Methods

2.1. Setting and study population

Data for this study were obtained from the PHARMO record linkage system (PHARMO RLS) (www.pharmo.nl). (Herings, 1993) The PHARMO RLS currently includes the demographic details and complete medication history of more than two million community-dwelling residents of more than twenty-five population-defined areas in the Netherlands, further linked to hospital admission data (with the exception of psychiatric hospital admissions). Since virtually all patients in the Netherlands are registered with a single community pharmacy, independent of prescriber, pharmacy records are virtually complete with regard to prescription drugs.

For this study, drug dispensing data were used.

Our study population comprised all patients from the PHARMO system having at least one prescription dispensed for lithium (ATC code N05AN01) between 1996 and 2005 at an age of 18 years or older.

The computerized drug dispensing histories contain information concerning the dispensed drug, dispensing date, the prescriber, amount dispensed, prescribed dosage regimen, and the estimated duration of use. For each prescription, the theoretical end date of lithium use was calculated using information on the date of dispensing, the amount of tablets dispensed and the daily dose instruction.

2.2. Prevalence and incidence of lithium use

The prevalence of lithium use was ascertained by dividing the number of users of lithium on the second Wednesday in March, June, September and December of each calendar year between 1996 and 2005 (nominator) by the total number of people living in the catchment area (denominator). Prevalent lithium users were defined as patients for whom the date of the prevalence estimation fell between the dispensing date and the theoretical end date of the lithium prescription.

The incidence of lithium use was calculated by dividing the total number of incident users per calendar year from 1998–2005 (nominator) by the total number of people living in the catchment area (denominator) in the same year. Incident lithium users were defined as patients having received a first prescription of lithium between 1998 and 2005 while not having received a prescription for lithium during at least the preceding 2 years. In addition, patients had to have visited the pharmacy for at least one prescription for another drug than lithium in these 2 years to ensure eligibility.

2.3. Changes in lithium use patterns

Based on the year in which patients received their first lithium prescription, the incident lithium users were divided over three time-cohorts: 1998–1999, 2000–2001 and 2002–2003, rendering at least a 24-month follow-up period possible for all patients. The following changes in lithium use were defined: 1) discontinuation, without switching; 2) add-on to continuing lithium treatment; and 3) switching from lithium to another drug. Discontinuation was defined as not having refilled a lithium prescription within six months after the theoretical end date of the last lithium prescription but having been non-institutionalised (having at least one drug dispensing event for any other drug within the six months after their last lithium dispensing). Add-on was defined as continuing lithium use and starting another drug used in the treatment of bipolar disorders (anticonvulsants, antidepressants or antipsychotics). Switching was defined as the discontinuation of lithium followed by the start of another drug used in the treatment of bipolar disorders within three months after the theoretical end date of the last lithium prescription.

2.4. Data analysis

Baseline patient (age, gender), lithium (prescriber, kinetic profile, salt and daily intake frequency) and co-medication characteristics (baseline use of concomitant drugs used in the treatment of bipolar disorders (anticonvulsants, antidepressants or antipsychotics)) were compared between three separate time-cohorts (1998–1999, 2000–2001, and 2002–2003).