

Seasonal Patterns of Medications for Treating Attention-Deficit/Hyperactivity Disorder: Comparison of Methylphenidate and Atomoxetine

Yu-Chiau Shyu, PhD^{1,2}; Sheng-Yu Lee, MD, MS^{3,4}; Shin-Sheng Yuan, PhD⁵; Chun-Ju Yang, MS^{1,6}; Kang-Chung Yang, MS^{7,5}; Tung-Liang Lee, PhD⁸; and Liang-Jen Wang, MD, MPH⁹

¹Community Medicine Research Center, Chang Gung Memorial Hospital, Keelung, Keelung, Taiwan; ²Institute of Molecular Biology, Academia Sinica, Nankang, Taipei, Taiwan; ³Department of Psychiatry, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan; ⁴Department of Psychiatry, College of Medicine and Hospital, National Cheng Kung University, Tainan, Taiwan; ⁵Institute of Statistical Science, Academia Sinica, Taipei, Taiwan; ⁶Institute of Biopharmaceutical Sciences, National Yang-Ming University, Taipei, Taiwan; ⁷Genome and Systems Biology Degree Program, National Taiwan University and Academia Sinica, Taipei, Taiwan; ⁸Department of Experimental Radiation Oncology, University of Texas MD Anderson Cancer Center, Houston, Texas, United States; and ⁹Department of Child and Adolescent Psychiatry, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan

ABSTRACT

Purpose: Medication is a first-line effective treatment for attention-deficit/hyperactivity disorder (ADHD). Currently, immediate-release methylphenidate (IR-MPH), the osmotic, controlled-release formulation of methylphenidate (OROS-MPH), and atomoxetine (ATX) are the only 3 medications approved in Taiwan for the treatment of ADHD. Short-term discontinuation of ADHD treatment is often seen among patients undergoing drug therapy. The goal of this study was to evaluate potential seasonal patterns in ADHD prescriptions and compare the seasonal changes of IR-MPH, OROS-MPH, and ATX use.

Methods: Taiwan's National Health Insurance database was used to gather information on patients diagnosed with ADHD (N = 145,269) from January 2000 to December 2011. The monthly data regarding person-days and receipt of treatment with IR-MPH, OROS-MPH, and ATX were analyzed. Time series analyses and autoregressive integrated moving average models were used to examine the seasonal patterns in person-days receiving ADHD pharmacotherapy. A general linear model with a post hoc test was used to determine the differences in monthly consumption of ADHD medications.

Findings: This study comprised 145,269 patients (mean age: 7.7 years; 78.6% were boys) diagnosed with ADHD. The prescriptions of IR-MPH (seasonal autoregressive: estimate [SE], 0.92 [0.04], $t = 22.87$,

$P < 0.001$) and OROS-MPH (estimate [SE], 0.84 [0.09], $t = 9.41$, $P < 0.001$) both showed significant seasonal patterns, but ATX prescriptions did not (estimate [SE], 0.50 [0.55]; $t = 0.90$; $P = 0.373$). IR-MPH and OROS-MPH prescriptions shared similar seasonal trends. The mean person-days of consumption in July were lower than in other months, with the exception of February and August. Meanwhile, for ATX, the person-days of consumption in February were the lowest. The mean person-days in February were significantly lower than in March and May but did not differ from those in other months.

Implications: The seasonal patterns of IR-MPH and OROS-MPH use coincide with school holidays. These findings suggest that discontinuing a drug during the holiday period may be popular for people undergoing ADHD pharmacotherapy, especially with regard to methylphenidate prescriptions. However, additional research is necessary to determine whether temporary discontinuation of drug therapy is related to patient outcomes. (*Clin Ther.* 2016;38:595–602) © 2016 Elsevier HS Journals, Inc. All rights reserved.

Accepted for publication January 20, 2016.

<http://dx.doi.org/10.1016/j.clinthera.2016.01.015>
0149-2918/\$ - see front matter

© 2016 Elsevier HS Journals, Inc. All rights reserved.

Key words: ADHD, drug adherence, epidemiology, pharmacotherapy, stimulant.

INTRODUCTION

Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder that begins in childhood and consists of symptoms such as inattention, hyperactivity, and impulsivity.¹ ADHD affects ~5% to 7% of school-aged children worldwide.^{2,3} Pharmacotherapy is an effective therapeutic option and has regularly been the first choice for managing ADHD.⁴ Stimulants and nonstimulants are the 2 main categories of medication that have been approved for the treatment of ADHD, although countries differ with regard to the medications and preparations that they have available.⁵ In patients for whom drug treatment is deemed appropriate, immediate-release methylphenidate (IR-MPH), an osmotic, controlled-release formulation of methylphenidate (OROS-MPH), and atomoxetine (ATX) were the only 3 drugs approved for the treatment of ADHD in Taiwan before 2011.⁶

IR-MPH is a short-acting stimulant (duration of effect, 2–3 hours), whereas OROS-MPH is an extended-release stimulant (duration of effect, 8–12 hours).⁷ Stimulants work by increasing dopamine levels in the synaptic cleft⁸ and may have such common adverse effects as decreased appetite, insomnia, headache, and abdominal pain.⁹ As a result, many children who receive medication for ADHD in primary care do not continuously follow the medical advice given.^{10,11} Some widespread reasons for discontinuing treatment and poor drug adherence include intolerable adverse effects, ineffectiveness, and social stigma.^{12,13} To decrease the adverse effects of stimulants, 1 recommendation among clinical practices is to take a planned break from the medication, known as a “drug holiday.”¹⁴ Drug holidays are implemented for 25% to 70% of children with ADHD who receive stimulant treatment throughout a number of countries,¹⁵ and these drug holidays most commonly coincide with school holidays.¹⁶ Nationwide observations may find that drug holiday regimens cause seasonal patterns of stimulant prescriptions. For example, a recent study in Turkey found that stimulant consumption increases and decreases during specific months within a year.¹⁷

ATX is a selective norepinephrine reuptake inhibitor and is classified as a nonstimulant.¹⁸ It is generally

prescribed as a second-line medication in the management of ADHD for children who do not respond to stimulants.^{8,19} Clinical trial data indicate that the widespread adverse effects of ATX include fatigue (25%), headache (20%), and nausea (18%).²⁰ One survey found that ~24% of patients occasionally stopped taking ATX on weekends and during school holidays.²¹ The prevalence of drug holidays for ATX is considerably lower than that for stimulant use.¹⁵ Nevertheless, a significant seasonal effect with regard to ATX prescriptions was also noted in Turkey.¹⁷ Because ATX has pharmacologic properties and adverse effect profiles different from stimulants, the potentially different seasonal effects between stimulants and nonstimulants require further study. Therefore, the present study used Taiwan’s nationwide population-based dataset to determine seasonal patterns of prescriptions for ADHD and to evaluate whether the seasonal effects on stimulants (IR-MPH and OROS-MPH) and nonstimulants (ATX) vary.

MATERIALS AND METHODS

Data Source

Chang Gung Memorial Hospital’s institutional review board approved this study. Data were gathered from the ambulatory claims database of the National Health Insurance Research Database of Taiwan (NHIRD-TW). Implemented in 1995, Taiwan’s National Health Insurance (NHI) program is a mandatory universal health insurance program, for which the Bureau of National Health Insurance is the sole payer for health care services. This bureau has contracted 93% of all health care providers in Taiwan, and at least 96% of all insured people have used health care services from the contracted hospitals or clinics since the beginning of the program. Contracted medical care institutions are required to electronically submit monthly medical expense–related claim documents; these documents cover a patient’s demographic data, the medical institution visited, diagnostic codes and date of any prescriptions, drugs prescribed, and claimed medical expenses.

Defining ADHD Patients and Medications

We included all patients newly diagnosed with ADHD (aged ≤ 18 years) between January 2000 and December 2011 whose records were found in the

Download English Version:

<https://daneshyari.com/en/article/5824970>

Download Persian Version:

<https://daneshyari.com/article/5824970>

[Daneshyari.com](https://daneshyari.com)