



Consumption of methylphenidate and atomoxetine in the private healthcare sector in South Africa: a longitudinal study

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Abstract

Background Globally Attention-Deficit/Hyperactivity Disorder (ADHD) has been in the spotlight. Despite some controversies, treatment of ADHD remains the cornerstone of patient care. **Objective** To describe the consumption of methylphenidate and atomoxetine in the private healthcare sector in South Africa over a four-year period (2013–2016). **Method** Data were extracted from the Intercontinental Marketing Service (IMS) database for the drug utilisation study. Consumption patterns were expressed as number of Defined Daily Doses (DDDs)/1000 inhabitants/day and number of DDDs/1000 inhabitants/month. **Results** Methylphenidate (95.85%) was the medication of choice when compared to atomoxetine (4.15%) in 2013. The corresponding figures for 2016 were 96.40% and 3.60%. Consumption of ADHD medication showed slight changes over the 4-year period. If only the private healthcare sector population is considered, consumption of methylphenidate was 6.010 DDDs/1000 inhabitants/day in 2013, and 7.827 DDDs/1000 inhabitants/day in 2016. A previous study (1994–1996) reported 0.12 DDDs/1000 inhabitants/day for methylphenidate. Consumption of atomoxetine was 0.044 DDDs/1000 inhabitants/day in 2013 and 0.050 DDDs/1000 inhabitants/day in 2016. **Conclusion** Consumption showed an increase in use of methylphenidate in South Africa, with small changes observed over the study period. Further studies are required.

Keywords ADHD · Atomoxetine · Attention-deficit/hyperactivity disorder · Defined daily dose · Drug utilization · Methylphenidate · South Africa

Impact on Practice

- The consumption of both methylphenidate and atomoxetine have increased in South Africa, but the exact increase cannot be determined due to the absence of data for its use in the public healthcare sector.
- The WHO ATC/DDD methodology is a useful measure to compare drug consumption between regions and countries over time, and further studies on methylphenidate and atomoxetine consumption, also in other African countries, are strongly recommended.

Ashmitha Premchand Munasur-Naidoo and Ilse Truter have contributed significantly to the manuscript.

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Introduction

Attention deficit/hyperactivity disorder (ADHD) initially considered primarily a childhood disorder persists into adulthood, and is described as a chronic psychiatric condition characterised by a triad of pervasive and impairing levels of hyperactivity-impulsivity and/or inattention which affects daily life and the development of an individual [1]. Pharmacological treatment of ADHD remains at the forefront of patient care. Increasing awareness of ADHD, and the use of effective treatment, may lead to improved patient outcomes in children and adults.

The consumption of ADHD medication varies according to the prevalence of the condition and legislation in

the specific country. In South Africa, methylphenidate (MPH) and atomoxetine (ATX) are the only medications approved for ADHD. MPH, a centrally acting stimulant, inhibits the reuptake of norepinephrine and dopamine and is the only stimulant approved in South Africa for ADHD. ATX a ‘non-stimulant’, selective noradrenaline re-uptake inhibitor which also increases prefrontal dopamine release, is stated to be effective in individuals with ADHD and co-morbid mood and anxiety disorders.

The use of MPH has increased worldwide. For example, in Israel the consumption of MPH doubled in 2012 compared to 2005 [2]. Similarly, in Denmark from 1995 to 2011, an increased consumption of 6.7 Defined Daily Doses (DDD)/1000 inhabitants/day was reported [3]. From 2003 to 2012, in Iceland, there was a nearly four-fold increase in adult ADHD because of an upsurge in use of extended-release MPH and also to some extent ATX [4]. Although the consumption of ADHD medication has been studied in various countries, few studies have focused on South Africa to establish the consumption patterns of MPH and ATX.

Aim of the study

The aim was to analyse the consumption patterns of MPH and ATX in the private healthcare sector in South Africa by means of a drug utilisation study using the DDD methodology to establish trends.

Ethics approval

Ethics approval was obtained from Nelson Mandela University Research Ethics Committee (Human) (Reference number H17-HEA-PHA-001).

Method

A retrospective drug utilisation study was conducted over four years (2013 to 2016). The Intercontinental Marketing Service (IMS) database, containing the private healthcare sector medication sales per month for South Africa, was used to analyse the sales data of the main medication for ADHD, namely MPH (ATC code N06BA04) and ATX (ATC code N06B09) [5]. The available short- and long-acting MPH-containing products in South Africa were included, namely Methylphenidate HCl-Douglas® (10 mg tablets), Ritalin® (10 mg tablets), Ritalin LA® (10/20/30/40 mg capsules), Concerta® (18/27/36/54 mg tablets). ATX was only available under the tradename Stratterra® (10/18/25/40/60/80 mg capsules). There was no generic equivalent for ATX.

Consumption of MPH and ATX was expressed as DDDs/1000 inhabitants/day and month, where the number of DDDs was the total amount of the active ingredient sold in a certain time period (day or month) divided by the DDD. The DDD/1000 inhabitants/day for MPH and ATX was calculated using the following formula:

“Number of DDDs/1000 inhabitants/day = (number of packages dispensed x number of doses (tablets or capsules) per package x number of milligram (mg) per dose x 1000 inhabitants)/(DDD in mg x number of inhabitants in South Africa per day)”. Similarly, the number of DDDs/1000 inhabitants/month was calculated.

IMS data report only on private sector medication usage. The South African population was based on the Statistics South Africa mid-year figures [6]. In each year from 2013 to 2016 the population used is indicated in Table 1. It is generally reported that 17% of the South African population belong to a private medical insurance scheme. The population given in Table 1 is therefore the estimated number of patients who belonged to private medical insurance schemes in the respective years.

Prescribing in the South African public sector is according to the Essential Medicine Lists, where only MPH at hospital level is included (ATX is not included). The authors

Table 1 MPH and ATX consumption expressed as DDDs/1000 inhabitants/day from 2013 to 2016 [6]

Year	Population of South Africa	Population belonging to the private healthcare sector ^a	DDD/1000 Inhabitants/day (%) (n)	
			MPH	ATX
2013	52,980,000	9,006,600	6.01 (95.85%) n = 827,359	0.26 (4.15%) n = 55,897
2014	54,000,000	9,180,000	6.59 (95.80%) n = 920,920	0.29 (4.20%) n = 61,683
2015	54,960,000	9,343,200	7.36 (96.07%) n = 1,036,293	0.30 (3.93%) n = 65,292
2016	55,910,000	9,504,700	7.83 (96.40%) n = 1,126,558	0.29 (3.60%) n = 57,655

^a17% of the South African population (the estimated population belonging to the private healthcare sector)

know anecdotally that MPH is extensively used in the public sector and despite several attempts, no consumption figures for methylphenidate could be obtained for the public health-care sector. The study therefore reports on the consumption of MPH using only the private sector population (17% of the population) and the whole South African population was used as denominator for ATX (since it is not available in the public sector). Microsoft Excel® was used for statistical analysis.

Results

In 2013, the consumption of MPH represented 95.85% and ATX 4.15% (see Table 1). The corresponding figures for 2016 were 96.40% and 3.60%, respectively, indicating a slightly higher consumption of the stimulant medication.

Consumption of methylphenidate

The DDD for MPH is 30 mg/day as recommended by the World Health Organisation (WHO) for adults (the DDD for children has not been established) [5]. Figure 1a depicts that the monthly consumption of MPH showed slight increases over the study period. Consumption generally peaked in February, June and November. February is the start of the new school year, while June and November are typically examination months in South Africa.

Consumption of atomoxetine

The DDD for ATX is 80 mg/day as defined by WHO [5]. The consumption of ATX demonstrated less variation over the study period (both over the four years, as well as over the different months of the years (see Fig. 1b). Slight peaks

Fig. 1 Drug consumption expressed as DDDs/1000 inhabitants/month from 2013 to 2016



were also observed in February, June and November, but less than for methylphenidate.

Discussion

The first-line treatment for ADHD in South Africa is MPH [9]. If stimulant treatment is not possible, ATX is available. This is in line with studies from other countries. In Denmark, use of ADHD medication in 2012 was 92.6% MPH, 6.8% ATX and 0.6% modafinil [3]. In a study on newly diagnosed adults in the United Kingdom, 14% were on ATX which reduced by half after 2 years, whereas the proportion on MPH remained consistent [7]. Similarly, a study conducted among adults in Iceland increased in 2003 from 2.9 DDDs/1000 inhabitants/day to 12.2 DDDs/1000 inhabitants/day in 2012 [4].

In South Africa, the consumption of MPH in 2013 was 6.01 DDDs/1000 inhabitants/day, which increased to 7.83 DDDs/1000 inhabitants/day in 2016. The United Nations Narcotics Control Board reported that the DDD/1000 inhabitants/day for MPH in South Africa during 1994–1996 was 0.12 DDDs/1000 inhabitants/day [8]. A definite increase in MPH consumption was therefore observed. Various other countries also observed increases. Israel reported a doubling in their consumption of ADHD medication from 4.02 DDDs/1000 inhabitants/day in 2005 to 9.92 DDDs/1000 inhabitants/day in 2012 [2]. These changes have been associated with a reduction in cost and changes in prescribing patterns characterised by an increased prescription of high-dose and long-acting preparations and a decrease in the low-dose and short-acting formulations. An increase in consumption can be attributed to the confidence in the therapeutic value of MPH. However, it may also be due to over-diagnosis of ADHD due to diagnostic difficulties and failure to adhere to established diagnostic criteria. The diagnosis rate in South Africa (estimated at 3–5%) is similar when compared to other countries such as Israel. The South African guideline for the treatment of adults was only published in 2017 [9], thereby historically focussing treatment on children and limiting the number of adults seeking diagnosis and treatment. An alternative explanation for not seeking treatment could be the historical stigma surrounding ADHD and stimulant medication.

The higher consumption observed for MPH in February, June and November was possibly due to examinations and periods of academic stress for South African patients that are studying at schools or tertiary institutions. Evidence of drug holidays when the amount of medication consumed was lower was noticeable in the months of July and December and is in keeping with other South African studies [10]. Drug holidays are a break in treatment of MPH being recommended for school or study, and break in treatment results in

improved appetite and sleep; allowing child growth to catch up, and to assess the continuous need for treatment.

The peaks and troughs observed with ATX differed from some previous South African studies. Drug holidays have not been recommended for ATX. The observed troughs need to be further investigated to understand whether it was not tolerated or if patients responded poorly to it.

A limitation was the population as this covers 17% which represents the private healthcare sector. The private sector has treatment guidelines for children and this was recently published for adults. The public sector has treatment guidelines for children, however, no such guidelines are available for adults. A further limitation was that data did not allow for individual patient, age or gender determination, to confirm whether the dosing instructions were in agreement with standard dosages used for adults and children. It was also not known whether or when the medication was actually taken by the patient.

Conclusion

MPH and ATX remain the cornerstone of ADHD treatment in South Africa. MPH consumption increased over the last two decades, while ATX showed more consistent use in the private sector. With the implementation of adult ADHD guidelines in the private sector in South Africa, it is recommended that trends are monitored and further studies on the cost and prescribing patterns of MPH and ATX be conducted.

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Conflicts of interest The authors have no conflict of interest.

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