LONG- AND SHORT-ACTING METHYLPHENIDATE CONSUMPTION IN SOUTH AFRICA

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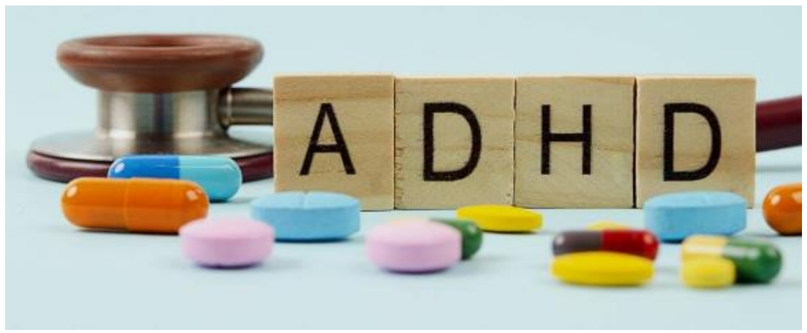

(Source: https://healthlifeandstuff.com/intuniv-for-adhd/)

BACKGROUND

Methylphenidate is used for conditions such as narcolepsy, depression, obesity and cognitive disorders, but nowadays most commonly prescribed for Attention-Deficit/Hyperactivity Disorder (ADHD) [1]. Based on its half-life, dosing of 2-3 times daily up to a maximum dose of 60 mg/day for adults and paediatrics is required [2]. To improve the overall effectiveness, long-acting formulations allowing for once daily dosing are available. Long-acting formulations such as modified-release capsules, including Ritalin LA® (10, 20, 30 and 40 mg) and extended-release tablets, Concerta® (18, 27, 36 and 54 mg), are given once daily in the morning [2]. The use of methylphenidate has increased in various countries. For example, in Israel the consumption of methylphenidate doubled in 2012 compared to 2005, also the cost of medication reduced by an average 20%-25% in the same period [1].
Data from 1994 to 1996 indicated that the DDDs/1000 inhabitants/day for South Africa was 0.12, which was the lowest when compared to other countries [3].

PRIMARY AIM

The primary aim of the study was to analyse the consumption patterns of methylphenidate in South Africa by means of a drug utilisation study using the Defined Daily Dose (DDD) methodology.

METHODOLOGY

- The Intercontinental Marketing Service (IMS) database, containing the private healthcare sector medication sales per month for South Africa, was used to review the sales data of methylphenidate from 2013 to 2016, to establish trends.
- All the available short- and long-acting methylphenidate-containing products in South Africa were included in the study.
- Consumption of methylphenidate was expressed as DDDs per 1000 inhabitants per day and per 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 Defined Daily Dose. The DDD/1000 inhabitants/day for methylphenidate was calculated using the following formula [4]:

"***Number of DDDs/1000 inhabitants/day = (number of packages dispensed x number of doses (tablets or capsules) per package x number of mg per dose x 1000 inhabitants)/(DDD in mg x number of inhabitants in South Africa per day)***"

- Similarly, the number of DDDs per 1000 inhabitants per month was calculated.
- Ethical approval was obtained from the Research Ethics Committee (Human) of the Nelson Mandela University (Ethics clearance number: H17-HEA-PHA-001).

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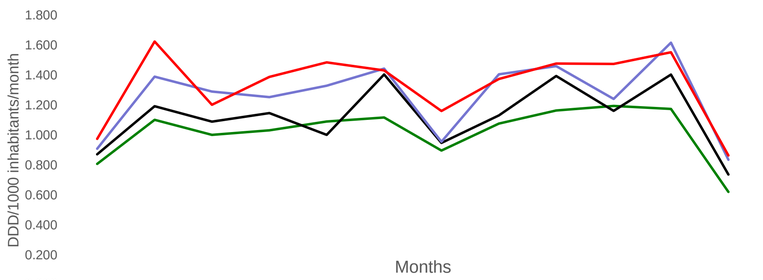
RESULTS AND DISCUSSION

The monthly consumption of methylphenidate showed slight increases over the study period. In October 2013, the highest consumption for the year was 1.194 DDDs/1000 inhabitants/month followed by November (1.174 DDDs/1000 inhabitants/month). In 2014, the highest consumption was in June followed by November (1.405 and 1.404 DDDs/1000 inhabitants/month, respectively). In 2015, the months with the highest consumption were November and September with the DDDs/1000 inhabitants/month being 1.617 and 1.460, respectively. In 2016 the highest consumption was in February followed by November with the number of DDDs/1000 inhabitants/month being 1.625 and 1.552, respectively.



	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC
2013	0.808	1.102	1.002	1.032	1.091	1.118	0.897	1.077	1.164	1.194	1.174	0.621
2014	0.872	1.193	1.090	1.147	1.002	1.405	0.948	1.131	1.394	1.161	1.404	0.737
2015	0.909	1.390	1.291	1.253	1.329	1.444	0.956	1.406	1.460	1.241	1.617	0.836
2016	0.975	1.625	1.202	1.389	1.485	1.432	1.161	1.375	1.477	1.474	1.552	0.865

Figure 1 Methylphenidate consumption expressed as DDDs/1000 inhabitants/ month during 2013 to 2016

Consumption of low-dose and high-dose methylphenidate

Figures 2 and 3 represent the portions of low-dose and high-dose methylphenidate tablets and capsules consumed over the study period. The trend was consistent over the four years. The long-acting formulation comprised of Concerta® sustained release tablets at various strengths (18/27/36/54 mg). The long-acting formulation consists of Ritalin LA® capsules at differing strengths (10/20/30/40 mg) and the short-acting formulation includes Methylphenidate® and Ritalin® 10 mg tablets. The short-acting methylphenidate tablet consumption was 14.99%, for 2013. Ritalin LA® capsules (10/20/30/40 mg) was at 20.70%. In each subsequent year there was a decrease in consumption of Ritalin® LA and in 2016 this reduced to 18.64%. The most popular choice from the four strengths of long-acting Ritalin® was the 20 mg capsule. The highest methylphenidate consumption was observed with Concerta® tablets (18/27/36/54 mg), which are sustained release and require once daily dosing. In 2013, the consumption of Concerta® was 64.30% and this gradually increased in 2016 to 66.29%. The most popular dosage strength in this product range was the 36 mg tablet, followed closely by the 54 mg dosage strength.

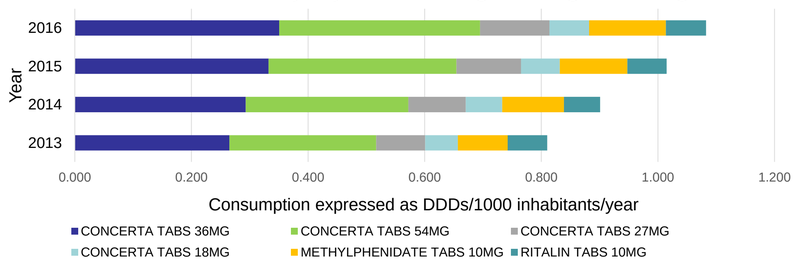


Figure 2 Consumption of methylphenidate tablets according to trade names from 2013 to 2016

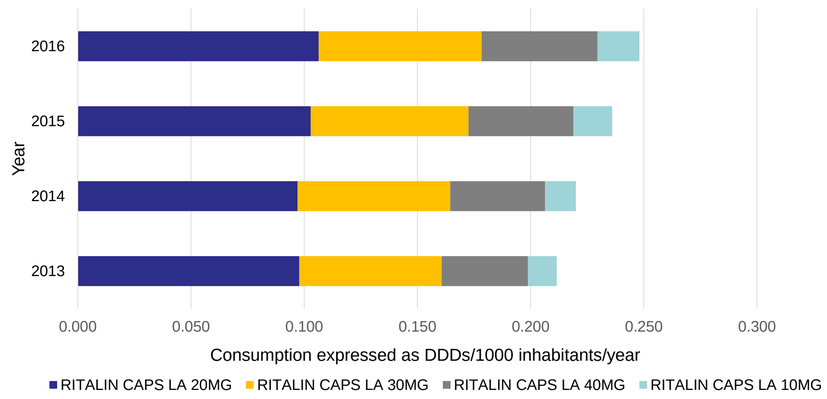


Figure 3 Consumption of methylphenidate capsules from 2013 to 2016

The UN Narcotics Control Board [3] reported that the DDD/1000 inhabitants/day for South Africa during 1994-1996 was 0.12 DDDs/1000 inhabitants/day. There has therefore been at least a 10-fold increase in methylphenidate consumption based on the results from this study. The consumption in 2013 was calculated to be 1.066 DDDs/1000 inhabitants/day, which increased to 1.380 DDDs/1000 inhabitants/day in 2016. This is lower when compared to other countries such as Israel which 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 [1].

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, short-acting formulations [1]. Total methylphenidate consumption in Brazil was 0.37 DDDs/1000 inhabitants/day which is lower when compared to South Africa.

Whilst the dose in most cases was below the DDD, with 20 mg per day being commonly prescribed, methylphenidate was used to treat ADHD in children and adolescents. Increased consumption was attributed to the confidence in therapeutic value of methylphenidate. However, it may also be due to over-diagnosis of ADHD due to diagnostic difficulties and failure to adhere to established diagnostic criteria [5]. This could suggest that the diagnosis rate in South Africa is lower when compared to other countries such as Israel and more awareness is required and the cost of treatment should be further evaluated. This could possibly be so since treatment of ADHD in South Africa has been mainly focused on children. The South African guideline for the treatment of adults was only published in 2017 [6], thereby limiting the number of adults seeking diagnosis and treatment. An alternative explanation for not seeking treatment could be the stigma and myths surrounding ADHD and stimulant medication [7].

The higher consumption observed for methylphenidate in November is possibly due to examinations for South African patients that are studying at schools or tertiary institutions. Evidence of drug holidays, where the amount of medication consumed was lower, was noticeable in the months of July and December. The occurrence of drug holidays is in keeping with other South Africa studies [8,9]. The drug holiday is a consequence of methylphenidate treatment being recommended for school and removal of treatment resulted in improved appetite and sleep; allow child growth to catch up; assess the continuous need for treatment and remedy any disagreements between child and parent about continuing treatment [8-10].

CONCLUSION AND RECOMMENDATIONS

- The higher consumption observed for methylphenidate in November is possibly due to examinations for South African patients that are studying at schools or tertiary institutions.
- Long acting sustained release methlyphenidate tablets showed the highest consumption during the study from 2013 to 2016.
- Evidence of drug holidays, where the amount of medication consumed was lower, was noticeable in the months of July and December. The occurrence of drug holidays is in keeping with other South Africa studies.

ACKNOWLEDGEMENTS

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