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Perini, Edson; Rezende Garcia Junqueira, Daniela; Gomes Cunha Lana, Lorena; Chama
Borges Luz, Tatiana

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Edson Perini^IDaniela Rezende Garcia
Junqueira^{II}Lorena Gomes Cunha Lana^{III}Tatiana Chama Borges Luz^{IV}

Prescription, dispensation and marketing patterns of methylphenidate

Padrões de prescrição, dispensação e comercialização de metilfenidato

ABSTRACT

OBJECTIVE: To analyze the patterns and legal requirements of methylphenidate consumption.

METHODS: We conducted a cross-sectional study of the data from prescription notification forms and balance lists of drugs sales – psychoactive and others – subject to special control in the fifth largest city of Brazil, in 2006. We determined the defined and prescribed daily doses, the average prescription and dispensation periods, and the regional sales distribution in the municipality. In addition, we estimated the costs of drug acquisition and analyzed the individual drug consumption profile using the Lorenz curve.

RESULTS: The balance lists data covered all notified sales of the drug while data from prescription notification forms covered 50.6% of the pharmacies that sold it, including those with the highest sales volumes. Total methylphenidate consumption was 0.37 DDD/1,000 inhabitants/day. Sales were concentrated in more developed areas, and regular-release tablets were the most commonly prescribed pharmaceutical formulation. In some regions of the city, approximately 20.0% of the prescriptions and dispensation exceeded 30 mg/day and 30 days of treatment.

CONCLUSIONS: Methylphenidate was widely consumed in the municipality and mainly in the most developed areas. Of note, the consumption of formulations with the higher abuse risk was the most predominant. Both its prescription and dispensation contrasted with current pharmacotherapeutic recommendations and legal requirements. Therefore, the commercialization of methylphenidate should be monitored more closely, and its use in the treatment of behavioral changes of psychological disorders needs to be discussed in detail, in line with the concepts of the quality use of medicines.

DESCRIPTORS: Methylphenidate, administration & dosage. Drugs of Special Control. Psychotropic Drugs. Drug Utilization. Pharmacoepidemiology.

^I Centro de Estudos do Medicamento. Faculdade de Farmácia. Universidade Federal de Minas Gerais. Belo Horizonte, MG, Brasil

^{II} Faculty of Health Sciences. The University of Sydney. Sydney, Australia

^{III} Programa de Pós-Graduação em Medicamento e Assistência Farmacêutica. Universidade Federal de Minas Gerais. Belo Horizonte, MG, Brasil

^{IV} Laboratório de Educação em Saúde e Ambiente. Centro de Pesquisa René Rachou. Fundação Oswaldo Cruz. Belo Horizonte, MG, Brasil

Correspondence:

Edson Perini
Centro de Estudos do Medicamento
Faculdade de Farmácia – UFMG
Campus Pampulha
Av. Antônio Carlos, 6627 Sala 1050-B2
31270-901 Belo Horizonte, MG, Brasil
E-mail: eperini@ufmg.br

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RESUMO

OBJETIVO: Analisar padrões e requisitos legais do consumo de metilfenidato.

MÉTODOS: Estudo transversal realizado em Belo Horizonte, MG, em 2006. Foram analisados dados de notificações de receitas de metilfenidato e de balanços de vendas de medicamentos – psicoativos e outros – sujeitos a controle especial. Determinou-se a dose diária definida, a dose diária prescrita, o período médio de prescrição e de dispensação, bem como a distribuição regional das vendas desse medicamento no município. Foram estimados, ainda, os gastos com a aquisição do medicamento e analisado o perfil de consumo individual do fármaco por meio da Curva de Lorenz.

RESULTADOS: Os dados dos balanços mensais de comercialização de psicotrópicos cobriram toda a comercialização notificada do fármaco, enquanto aqueles coletados nas notificações de receita cobriram 50,6% das farmácias que o comercializaram, incluindo aquelas de maior volume de venda. O consumo de metilfenidato foi 0,37 DDD/1.000 habitantes/dia. As vendas concentraram-se em áreas mais desenvolvidas e as formulações farmacêuticas de liberação não controlada foram as mais prescritas. A prescrição e a dispensação com dosagens > 30 mg/dia e período de tratamento > 30 dias apresentaram valores em torno de 20,0% em algumas regiões da cidade.

CONCLUSÕES: O consumo de metilfenidato apresentou-se elevado no município, maior em áreas mais favorecidas economicamente e predominando o consumo de formulações com maior risco de abuso. Tanto a prescrição quanto a dispensação apresentaram características não compatíveis com as recomendações farmacoterapêuticas e determinações legais. O controle de venda do fármaco deve ser monitorado e a farmacoterapia das alterações comportamentais amplamente rediscutida em concordância com os conceitos do uso de medicamentos com qualidade.

DESCRIPTORIOS: Metilfenidato, administração & dosagem. Medicamentos de Controle Especial. Psicotrópicos. Uso de Medicamentos. Farmacoepidemiologia.

INTRODUCTION

Methylphenidate is a central nervous system stimulant recommended for the treatment of attention-deficit/hyperactivity disorder (ADHD), a neurobehavioral disorder affecting school-going children and adolescents. It is also prescribed for narcolepsy, depression, obesity, and cognitive disorders.¹⁴ Methylphenidate is the most common psychostimulant medicine worldwide, with production increasing from 2.8 tons (t) in 1990 to 63.2 t in 2012.^{a,b} Commercialization of methylphenidate began in Brazil in 1998, and its production increased almost 3-fold between 2009 and 2011.^c

The consumption of methylphenidate, as measured by defined daily doses (DDD) per 1,000 inhabitants/day, increased between 2009 and 2012.^{14,19} In 2009, the levels were 0.39 in the United Kingdom, 1.49 in Spain, and 9.30 in the United States (US) and 0.68 in the United Kingdom, 2.82 in Spain, 7.94 in the US, and 14.72 in Switzerland by 2012, showing a distinguished pattern of increased consumption. In Denmark, consumption increased in the period of 1995 to 2011 recording up to 6.7 DDD per 1,000 inhabitants/day according to a national survey.¹⁹ However, information regarding methylphenidate consumption in Brazil is

^a International Narcotics Control Board. Comments on the reported statistics on psychotropic substance for 2009. Vienna; 2010.

^b International Narcotics Control Board. Comments on the reported statistics on psychotropic substance for 2012. Vienna; 2013.

^c Agência Nacional de Vigilância Sanitária. Panorama dos dados do Sistema Nacional de Gerenciamento de Produtos Controlados: um sistema para o monitoramento de medicamentos no Brasil. *Bol Farmacoepidemiol SNGPC*. 2012 [cited 2014 Jun 23];1(2). Available from: http://www.anvisa.gov.br/sngpc/boletins/2011/boletim_sngpc_2edatualizada.pdf

scarce, although it is now available nationally following the implementation of an electronic system to record prescription and sales data for narcotic or psychotropic substances. Although the consumption of methylphenidate has increased nationally, trends in the pattern of its consumption are unclear in Belo Horizonte, in Southeastern Brazil.²⁰

The consumption of methylphenidate for the treatment of ADHD is controversial in the literature. Different diagnostic criteria, with narrower or broader definitions of ADHD, increases the possibility of misdiagnoses, which may in turn result in excessive prescription and consumption.^{2,18,20} In addition, the pharmacological approach for the treatment of ADHD without educational and psychotherapeutic intervention has been questioned,^{3,13,25} including its relationship to methylphenidate misuse among children.⁴ Higher frequencies of methylphenidate consumption in privileged socioeconomic environments⁵ may also hide sociocultural issues of underuse and overuse in disadvantaged and privileged populations, respectively. Over a decade ago, an article in the Brazilian literature argued that less rigorous control of the sales of methylphenidate was necessary to improve access and lower the risk of stigmatization of the patient, on the basis of the conclusion that there was a low risk of dependency and that adverse reactions to this medicine were nonserious.¹⁰ However, in another scenario, the nonmedical (off-label) use of methylphenidate for recreation or to improve academic performance has highlighted the possibility of abuse.^{7,17}

Brazilian legislation restricts the prescription and dispensation of narcotic or psychotropic substances.^e Prescriptions require special documentation prior to dispensation. The prescription notification form is used to authorize the commercialization of substances on specific lists of medicines that are subject to special control: List A (yellow), for narcotic and psychotropic substances that are most restricted, followed by Lists B (blue) and C (white). The yellow and blue notifications are retained by pharmacies at the time of the purchase. The prescription notification form for methylphenidate belongs to List A, and has a recommended maximum treatment of 30 days, consistent for this substance class. Additionally, balance lists of drugs – psychoactive and others – subject to special control (BMPO) is used to record all purchases and sales controlled by the municipal surveillance bureau information, including the pharmacy, the responsible pharmacist, and the medicine prescribed and dispensed. Each pharmacy is required to submit this information to the county health authorities periodically and the process has been controlled by an

online record system through the national surveillance bureau since 2007.

Considering that the assessment of clinical conditions that justifies methylphenidate prescription is difficult, and that the drug also has abuse potential, concerns have been raised regarding the rationality of methylphenidate consumption. This study aimed to analyze the patterns and legal requirements of methylphenidate consumption in the fifth most inhabited city of Brazil. Specifically, we assessed the prescription, dispensation, and commercialization of methylphenidate, exploring the patterns of use according to established indicators. This is the first study to consider the commercial patterns of the prescription and dispensation of methylphenidate in a city in a large and heterogeneous country like Brazil.

METHODS

We conducted a cross-sectional study regarding the data for methylphenidate prescription and dispensation extracted from BMPO and the prescription notification forms in Belo Horizonte between January 1 and December 31, 2006. The city, which is the capital of Minas Gerais, is located in the most economically developed region of the country, with approximately 2.4 million people (12.0% of the state and 1.3% of the national population). It has a high rate of literacy and piped water, and the average monthly income is about 10.0% higher than the national average. The municipality is divided into nine districts: Barreiro, Central-South, East, Northeast, Northwest, North, West, Pampulha, and Venda Nova. Each district represents a health sector responsible for the planning and implementation of different healthcare interventions.

The Prometheus Project is a research line of the *Centro de Estudos do Medicamento* (CEMED – Center of Medicines Studies in English) of the *Universidade Federal de Minas Gerais*, which focuses on the clinical, epidemiological, social, and anthropological perspectives of methylphenidate consumption. The project was created following published scientific and legal recommendations for the prescription and dispensation of methylphenidate in Brazil.

We extracted the following information from BMPOs for methylphenidate: brand name, formulation and package, dose unit, and the amount sold/dispensed. We calculated the totality of methylphenidate commercialization in total milligrams and in Defined Daily Doses (DDD) in milligrams/1,000 inhabitants/day.

^d European Medicines Agency Press Office. European Medicines Agency makes recommendations for safer use of Ritalin and other methylphenidate-containing medicines in the EU [press-release]. London; 2009 [cited 2014 Aug 11]. Doc. Ref. EMEA/22315/2009. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/Press_release/2009/11/WC500014589.pdf

^e Agência Nacional de Vigilância Sanitária. Portaria nº 344, de 12 de maio de 1998. Aprova o Regulamento Técnico sobre substâncias e medicamentos sujeitos a controle especial [Approves the Technical Regulation on substances and medicinal products subject to special control]. Brasília (DF): 1998 [cited 2014 May 27]. Available from: http://bvsms.saude.gov.br/bvs/saudelegis/svs/1998/prt0344_12_05_1998_rep.html

The recommended DDD of methylphenidate by the World Health Organization is 30 mg/day for adults, but DDD for children has not been established. Commercialization of methylphenidate was characterized by pharmaceutical formulation (regular-release tablets *versus* controlled-release tablets) and treatment costs were estimated by assessing the number of commercialized units on the basis of the average unit price for the corresponding prescriptions, using prices informed by ANVISA (Brazilian National Surveillance Bureau) for 2006. All costs in the study are indicated in US dollars (USD).

Prescription notifications were used to characterize prescription and dispensation patterns of methylphenidate (amount per user and per gender, the total cost of the treatment per year, the medical specialty of the prescribers, the total amount of methylphenidate prescribed and dispensed in the number of packages and in terms of the pharmaceutical formulation, and the duration of treatment in days, both prescribed and dispensed). We estimated the prescribed daily dose (PDD) using the average doses.

We used the Lorenz curve, an analytical technique described by Hallas & Støvring¹¹ to study the skewness of methylphenidate consumption. The curve was expected to be diagonal line if all users took similar doses, while a skewed pattern would cause the curve to skew toward the upper left corner.^{10,11} Users were ranked in descending order by methylphenidate consumption (obtained by multiplying the PDD by the treatment duration) to estimate the Lorenz curve. The cumulative percentage of methylphenidate used was then calculated and plotted on the y-axis, against the cumulative percentage of persons on the x-axis, and skewness analyzed by calculating the cumulated first percentile (1-percentile) and fiftieth percentile (50-percentile). The cumulated 1-percentile and 50-percentile for methylphenidate consumption is defined as the share of total methylphenidate consumed by 1.0% and 50.0%, respectively, of the most heavily consuming users. High values for any of these measures, assumed at levels of 15.0% and 90.0% for the 1-percentile and 50-percentile respectively, suggest skewed consumption. Thus, a Lorenz 1-percentile of > 15.0% implied the existence of heavy users, whereas a Lorenz 50-percentile of > 90.0% indicated widespread occasional or sporadic consumption.^{10,11}

We used three indicators to assess the quality of prescription and dispensation according to previously reported parameters and on the basis of Brazilian sanitary legislation, as follows: the proportion of prescriptions with a dosage of > 30 mg/day (number of prescriptions with dosage of > 30 mg/day/total prescriptions); the proportion of prescriptions with duration of treatment longer than the recommended period (number of prescriptions lasting > 30 days/total prescriptions), and, the proportion of prescriptions dispensed that are for more than the

recommended treatment duration (number of prescriptions dispensed for > 30 days of treatment/total prescriptions). These indicators were dichotomized, as follows: daily dosage (> 30 mg; ≤ 30 mg), prescribed treatment duration (> 30 days; ≤ 30 days), and dispensed treatment duration (i.e., > 30 days; ≤ 30 days). The indicators were compared according to administrative districts using the Pearson Chi-square test with significance values of P value < 0.05.

Stata software version 10.1 (Stata Corp, College Station, TX) was used for all statistical analyses.

The study was approved by the Research Ethics Committee of the *Universidade Federal de Minas Gerais* (ETIC147/06). Managerial personnel of the participating pharmacies (pharmaceutical or commercial) received a document containing project details before signing an informed consent form.

RESULTS

Of the 79 pharmacies that commercialized methylphenidate in Belo Horizonte in the year of 2006, 5 contributed to 97.1% of all sales, and 1 pharmacy was responsible for 36.8% of total sales. More than 85.0% of methylphenidate commercialized was concentrated in the East, Central-South, and West regions, accounting for 27,157 packages or 8,456,860 mg, which was equivalent to 657,230.37 USD (Table 1).

In total, 31,869 drug packages were sold (9,611,280 mg, 725,078.58 USD). The more frequently commercialized pharmaceutical formulation was regular-release tablets (84.4%). Total methylphenidate consumption was 0.37 DDD/1,000 inhabitants/day.

In total, 6,611 methylphenidate prescriptions were analyzed from 40 participating pharmacies. These accounted for 50.6% of all pharmacies reporting on the commercialization of methylphenidate in 2006, and comprise the five that were responsible for the largest volume of sales. It was possible to identify the medical specialty of the prescribing physicians in 92.7% of the cases. The majority were neurologists (48.4%), followed by psychiatrists (42.4%), and pediatricians (5.2%). The remaining (4.0%) prescriptions were from professionals of other medical specialties.

The prescription corresponded to 3,068 users. They received 1-15 drug prescriptions during the period of the study, each equivalent to 240.00 USD/user/year, or approximately 1.5 times the minimum wage. The majority of the users were men (72.6%). Treatment doses lower than the DDD were observed in 66.9% of prescriptions: 20 mg/day in 46.7% and 10 mg/day in 20.2%. In 15.6% of the cases, 30 mg/day was the prescribed dose, whereas doses of > 30 mg/day were prescribed in 17.6% of the cases. Of the total

Table 1. Methylphenidate commercialization by administrative district according to the balance list of sales of psychoactive and other drugs subjected to special control (BMPO). Belo Horizonte, MG, Southeastern Brazil, 2006. (N = 79)

Region	Amount (mg)	%	Packages (units)	%
East	3,952,720	41.1	12,744	40.0
Central-South	2,790,240	29.0	9,571	30.0
West	1,713,900	17.8	4,842	15.2
Northeast	745,500	7.8	2,902	9.1
Northwest	215,020	2.2	968	3.0
Barreiro	114,100	1.2	516	1.6
Venda Nova	71,900	0.7	294	0.9
Pampulha	7,900	0.1	32	0.1
Total	9,611,280		31,869	

BMPO: balance lists of sales of psychoactive and other drugs subjected to special control

of all prescriptions, 0.8% had a recommended dose of > 60 mg/day. Lorenz curve analysis (Figure) did not show the presence of a significant proportion of heavy users or sporadic users (1-percentile = 7.8%; 50-percentile = 82.9%; respectively).

PDD was estimated to be 23.9 mg/day [standard deviation (SD) 12.8; range 10-240 mg/day] with an average treatment period of 31 days. The maximum prescribed treatment period was 600 days. The dispensation was conducted for an average 29 days, and for a maximum of 540 days. Approximately 85.0% of the prescriptions were dispensed for up to 30 days (Table 2). The distribution of PDD by administrative district showed a similar pattern of approximately 20 mg/day. Exceptions were noted in the East and Northeast districts where PDDs was slightly higher and equal to 26.1 mg/day (SD = 13.6) and 25.4 mg/day (SD = 12.5), respectively (Table 3).

Significant regional differences between the daily dosage and dispensation were observed. The East, Northeast, and Central-South districts showed higher proportions of prescriptions with a daily dosage of > 30 mg (Table 4). The pattern of prescribed treatment duration did not vary among regions, but significant differences were noted in the Pampulha and the Central-South districts showing higher prescription rates of notifications with > 30 days of treatment.

DISCUSSION

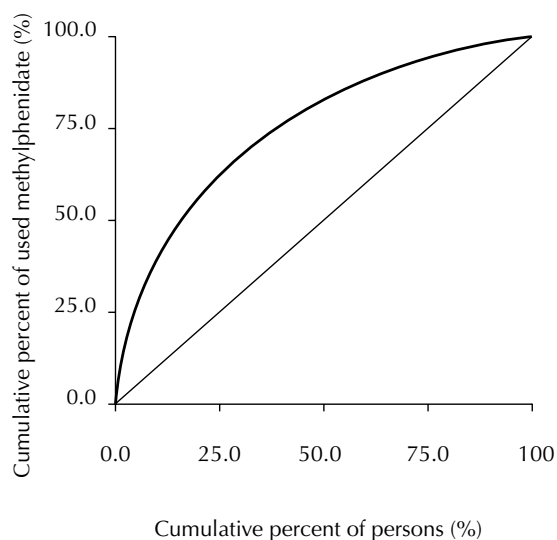
The estimated consumption of methylphenidate in Belo Horizonte in 2006 was comparable with two European countries, i.e., Spain (1.26 DDD/1,000 inhabitants/day) and Ireland (0.65 DDD/1,000 inhabitants/day), and one Latin American country, i.e., Chile (0.53 DDD/1,000 inhabitants/day also in 2006).^f In general, most prescriptions recommended a dose below the DDD, with 20 mg/day being the most commonly prescribed.

Although the notifications included no information on the clinical indications, others studies suggest that the drug is mainly used to treat ADHD in children and adolescents.^{15,23,24} The confidence in the therapeutic value of methylphenidate in this treatment has resulted in a significant increase in its consumption over recent years. However, this increase may also be a consequence of over-diagnosis due diagnostic difficulties and failure to comply with established diagnostic criteria.^{1,9,12,21}

The Lorenz curve indicated that there was not a significant prevalence of either heavy or sporadic users, which is similar to that observed by others authors.^{15,19} This correlates with the values for the use of methylphenidate for ADHD in Denmark between 2010 and 2011 (1-percentile = 6.1% and 50-percentile = 84.4%).¹⁹ However, we found significant differences in the daily dose prescribed and dispensed between districts, with more prescriptions of > 30 mg/day in the East, Northeast, and Central-South districts. These districts include markedly wealthier city areas, and the observed differences may represent social determinants of methylphenidate consumption, reinforcing the need to investigate diagnostic aspects related to methylphenidate prescription and dispensation. Furthermore, these higher doses raise the risk of adverse effects, such as anxiety, headache, insomnia, tachycardia, and anorexia.

Prescription and dispensation of methylphenidate was concentrated in the East and Central-South administrative districts. The association between increased dispensing and better quality of life in those regions indicates two possible interdependent factors: a regional concentration of pharmacy networks dominating the drug market and socioeconomic issues of access to health care services and medications. Although we cannot exclude differences in diagnostic criteria adopted by physicians in different areas, it was noticeable that the percentage of pharmacies commercializing methylphenidate was low, with just five being

^f International Narcotics Control Board. Statistics on psychotropic substance for 2006. Vienna; 2007.



^a The straight line indicates the hypothetical scenario of homogenous prescriptions among users; the curved line indicates the real prescribed drug proportion (1-percentile = 7.8% and 50-percentile = 82.9%)

Figure. Lorenz curve for methylphenidate prescription,^a according to the prescription notification forms. Belo Horizonte, MG, Southeastern Brazil, 2006. (N = 3,068 users).

responsible for most sales. This identifies an alarming pharmacoepidemiological reality that deserves the attention of health authorities.

It is important mentioning that methylphenidate is not currently incorporated by the Brazilian Unified Health

System (SUS). Therefore, a court order is required for this medicine be provided free of charge. This may explain the concentration of sales in the East and Central-South districts where the household income *per capita* is higher. These results reinforce the relevance of the role of socioeconomic factors in the prescription and use of methylphenidate, as was also reported in the US.⁸ Inequitable access to methylphenidate may therefore affect diagnosis and treatment, linking poverty with poorer mental health care.

Regular-release tablets were the most frequently commercialized pharmaceutical formulation, which is similar to the results of other studies.²³ This type of formulation has the disadvantage of a more complex medication regimen that can compromise treatment adherence. Moreover, regular-release tablets may also facilitate drug abuse since methylphenidate has the capacity of methylphenidate to induce euphoric effects similar to cocaine.¹⁶ In this context, controlled-release formulations offer lower abuse potential and a more convenient dosing schedule, despite being more expensive.⁶

The prescribed and dispensed methylphenidate treatment durations did not agree with national legislation. Approximately 20.0% and 15.0% of the total of the prescribed and dispensed methylphenidate, respectively, exceeded the acceptable treatment period of 30 days. There was a regional difference in drug dispensation, which should alert drug-regulatory agencies when planning drug control activities, especially when consolidating information on a computerized

Table 2. Prescribed daily dose, average prescribed treatment duration and dispensation of methylphenidate, according to the Prescription Notification Form Belo Horizonte, MG, Southeastern Brazil, 2006. (N = 6,611)

Variable	PDD (mg)	Average duration of the treatment (days)	Dispensation (average, in days)
Average (standard deviation)	23.9 (12.8)	31.4 (19.0)	29.1 (16.0)
Minimum	10	4	3
Maximum	240	600	540

PDD: prescribed daily dose

Table 3. Distribution of dispensed prescriptions and of prescribed daily doses by administrative district, according to the Prescription Notification Forms. Belo Horizonte, MG, Southeastern Brazil, 2006.

Region	N	%	PDD	Standard deviation
Central-South	3,579	54.1	23.8	13.3
East	1,175	17.8	26.1	13.6
Northeast	1,015	15.4	25.4	12.5
Northwest	240	3.6	19.7	7.8
Pampulha	239	3.6	21.0	8.7
Venda Nova	132	2.0	19.6	8.0
Barreiro	126	1.9	19.2	8.9
West	105	1.6	20.1	8.7
Total	6,611	100	23.9	12.8

PDD: prescribed daily dose

Table 4. Prescription and dispensation of methylphenidate by dose and treatment duration in different administrative districts, according to the Prescription Notification Forms. (N = 6,611)

Region	Prescription				Dispensation	
	Dose (%)		Duration (%)		Duration (%)	
	> 30 mg	≤ 30 mg	> 30 days	≤ 30 days	> 30 days	≤ 30 days
Central-South	17.1	82.9	19.7	80.3	16.2	83.8
East	24.3	75.7	19.4	80.6	14.1	85.9
Northeast	21.6	78.4	18.5	81.5	14.2	85.8
Northwest	4.6	95.4	18.8	81.2	6.7	93.3
Pampulha	7.9	92.1	23.0	77.0	19.7	80.3
Venda Nova	2.3	97.7	18.2	81.8	14.4	85.6
Barreiro	7.1	92.9	21.4	78.6	5.6	94.4
West	2.9	97.1	22.9	77.1	12.4	87.6
	p < 0.001 ^a		p = 0.80 ^a		p < 0.001 ^a	

^a Pearson Chi-square test

monitoring system. Indeed, this could readily be monitored by the new online system for the control of psychotropic sales.

Our results are based on commercialization and prescription data, representing estimates of the true consumption of methylphenidate in the investigated population.²² The data were collected in a large city, similar to many others in terms of population and development characteristics. Therefore, our results may be regarded as an important source of parameters for the question investigated. Prescription notifications were analyzed for 50.6% of the commercial pharmacies reporting to dispense methylphenidate in BMPO. According to this data, 70.0% and 60.0% of pharmacies in the East and Central-South districts, respectively, submitted their notifications of prescription for inclusion in this study. These regions accounted for approximately 70.1% of methylphenidate commercialization in the city, including the five highest-dispensing pharmacies (97.1% of sales between them). Thus, we believe our data allows analysis of a representative picture of the prescription and dispensing practices in the area.

The data sources did not provide any diagnosis-related information and precluded assessment of the sociodemographic profile of users, such as education and income, which limited our analyses. However, the study was based on the information required by health legislation in the country, conferring consistency to the data collected. Furthermore, this is the

first study to characterize the patterns of commercialization, prescribing, and dispensation of methylphenidate in Brazil. Our results suggest that there are regional differences in methylphenidate consumption, with higher access in the more economically developed areas. However, these were based in sales data only and did not assess the habitation region at the individual level. Consequently, this evidence should be interpreted with caution.

Methylphenidate was often prescribed in pharmaceutical formulations with higher risk of abuse and less likely to encourage adherence. Furthermore, the regulations regarding the prescription and dispensation of methylphenidate are not consistently applied. Health authorities, physicians, and pharmacists need to exercise greater caution regarding the use of methylphenidate. This drug therapy is nowadays considered a standard treatment for ADHD, but besides the fact that it has a not well-known biological bases, it has relevant psychosocial and cultural components. Therefore, treatment with methylphenidate may be intensely discussed in order to establish the rationality and safety of its use. Authorities must improve the control and supervision of methylphenidate commercialization and implement interventions to promote good prescription practices. We believe that the less strict drug control proposed by Carlini et al⁴ (2003), to facilitate access and avoid stigmatization, is highly questionable given our findings.

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