

# Assessment of Methylphenidate Prescriptions Written for the Treatment of Attention-Deficit/Hyperactivity Disorder

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## ÖZET:

Dikkat Eksikliği Hiperaktivite Bozukluğu tedavisi için yazılan metilfenidat reçetelerinin değerlendirilmesi

**Amaç:** Metilfenidat, dikkat eksikliği-hiperaktivite bozukluğu (DEHB)'nin tedavisinde kullanılan ve kontrole tabi olan bir ilaçtır. Bu çalışmada metilfenidatın reçetelenmesine ait detayların araştırılması amaçlandı.

**Gereç ve Yöntem:** İstanbul Sağlık Müdürlüğü arşivindeki 2009 yılı Ocak-Aralık dönemine ait seçilen örneklem üzerinden DEHB tanılı toplam 5681 metilfenidat içeren kırmızı reçete (MİKR) retrospektif olarak incelenerek ilaç kullanımının detayları değerlendirildi. İstatistiksel karşılaştırmalarda Ki kare testi kullanıldı ve  $p < 0.05$  olduğunda, istatistiksel olarak anlamlılıktan söz edildi.

**Bulgular:** DEHB tanılı, MİKR'lerin büyük kısmında (%85.4) yaş bilgisinin bulunmadığı; bu bilgiye sahip olan reçetelerin ise %78.5'inin 18 yaş altı çocuklara ait olduğu saptandı. MİKR'lerin %73.7'si erkek hastalara aitti. MİKR'lerin %63'ünü çocuk ve ergen psikiyatri uzmanları ile çocuk sağlığı ve hastalıkları uzmanlarının yazmış olduğu görüldü. Çocukları tedavi eden hekimlerin yazdığı reçetelerin daha çok üniversite hastanelerinde (%64.5), erişkinleri tedavi eden hekimlerin yazdığı reçetelerin ise daha çok özel hastanelerde (%36.6) yazıldığı saptandı. Çocukları tedavi eden hekimler metilfenidat'ın doz bilgisini diğer hekimlerden daha fazla yazmışlardı ( $p < 0.01$ ). MİKR'leri çocuk yaş grubunu tedavi eden hekimler en çok kış, diğer hekimler ise en çok yaz mevsiminde yazmıştı ( $p < 0.01$ ).

**Sonuç:** Metilfenidat, daha çok çocuk hastalara reçete edilmekle birlikte bu tedaviyi alan erişkin hasta oranının hiç de az olmadığı dikkati çekmektedir. Erişkinler için yazılan reçetelerde daha belirgin olmak üzere, MİKR'leri yazan hekimlerin bazı reçeteleme alışkanlıkları ile ilgili eksiklikleri önemsenmeli ve düzeltilmeye çalışılmalıdır.

**Anahtar sözcükler:** Metilfenidat, dikkat eksikliği hiperaktivite bozukluğu, ilaç tedavisi, ilaç reçeteleri

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## ABSTRACT:

Assessment of methylphenidate prescriptions written for the treatment of Attention-Deficit/Hyperactivity Disorder

**Objective:** Methylphenidate is a medication used for the treatment of attention deficit hyperactivity disorder (ADHD). In this study, we aimed to investigate the details of methylphenidate prescriptions.

**Materials and Methods:** A total of 5681 methylphenidate prescriptions written for the treatment of ADHD were collected from the archives of the Provincial Health Directorate of Istanbul between January and December 2009 and were retrospectively evaluated regarding the details of drug usage. Statistical comparisons were based on the Chi-square test at a  $p < 0.05$  level of significance.

**Results:** The ages of the patients were not mentioned in most of the methylphenidate prescriptions (85.4%). Out of those prescriptions with age information, 78.5% were written for patients younger than 18 years old. Methylphenidate prescriptions were mainly written for male patients (73.7%). Sixty three percent of methylphenidate prescriptions were written by pediatric and adolescent psychiatrists as well as pediatricians. Methylphenidate prescriptions for pediatric patients were more often written in university hospitals (64.5%), whereas those for adult patients were more often written in private hospitals (36.6%). Doctors treating pediatric patients more often mentioned dosage information than doctors treating adult patients ( $p < 0.01$ ). Methylphenidate prescriptions for pediatric patients were more often written in winter, whereas the majority of those for adult patients were written in summer ( $p < 0.01$ ).

**Conclusion:** It was interesting to note that a remarkable percentage of adult patients get methylphenidate treatment although these prescriptions are written most often for pediatric patients. The findings of this study point out that methylphenidate treatment in adult patients should be more thoroughly evaluated and resolved.

**Key words:** Methylphenidate, attention deficit hyperactivity disorder, drug therapy, drug prescriptions

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## INTRODUCTION

Attention deficit hyperactivity disorder (ADHD) is one of the most common childhood psychiatric disorders worldwide (1). According to the American Psychiatric Association, the percentage of children with ADHD is estimated to be between 3-7% (2). Many adults with ADHD are diagnosed in childhood; one third of them recover in time and the rest progress with mild or serious consequences (3). When the current data are compared with that the findings of studies conducted in the 1990's, the use of psychostimulants in the diagnosis and treatment of ADHD has markedly increased, despite a recent downward trend (4-9).

In the treatment of children with ADHD, stimulant agents have proven to be more effective than non-stimulant agents (10). Among orally administered stimulants methylphenidate, dextroamphetamine and amphetamine-dextroamphetamine combinations are the first line agents used in treatment (11). In Turkey methylphenidate HCl is the drug available for the treatment of ADHD. Short acting (10 mg tablet) and long acting extended release (18, 27, 36 and 54 mg tablets) forms are available, which are subject to red coloured prescriptions (RCP); in other words, methylphenidate is a controlled medicine (CM) and one of three copies of a methylphenidate prescription (MP) must to be sent monthly to the Provincial Health Directorate, where it is stored for a period of 5 years (12,13).

There is insufficient data in Turkey with regards to the number of patients on methylphenidate as well as their age distribution. Small scale studies as well as statistical data produced by the International Narcotic Control Commission (the amount of methylphenidate imported increased from 2 kg in 1998 to 23 kg in 2002) give insights about the subject (4). However investigating this subject in a metropolitan city such as Istanbul can make contributions to the current literature at both the national and international level. In this study, among RCPs sent to Provincial Health Directorate of Istanbul, those for methylphenidate were examined to determine the details of

methylphenidate prescribing and to compare how these details showed differences between adults and children.

## MATERIALS AND METHODS

In this study, among RCP that were issued between the 1st of January 2009 and the 31st of December 2009 and archived in the Provincial Health Directorate of Istanbul, 5681 MPs written for the treatment of ADHD were examined retrospectively. Data of the MPs, which was provided from the database of a comprehensive drug utilization study that assessed controlled prescriptions in 2009, was analyzed (14).

All the controlled prescriptions from all the districts of Istanbul are forwarded monthly to the Provincial Health Directorate in accordance with national legislation (13). After being given permission from the directorate and obtaining ethical approval, copies of the CM prescriptions were accessed from the archives. Care was taken that data be representative of all the months of the year 2009. In order to represent 10% of the archived controlled prescriptions in the city, 4.000 prescriptions per month, adding up to a total of 48.000 prescriptions, were selected randomly. Prescriptions were coded, the patients' personal details were removed and the data was entered into the computer (Microsoft Excel® and SPSS® programs). A total of 48.000 prescriptions, of which 5681 were MPs (11.8%), were identified from the database. These prescriptions were carefully studied for certain parameters that would influence drug utilization. No additional intervention was performed for the validation of diagnosis and medicinal content of the prescriptions. Data from the MP was recorded, including date of issue, patient demographics (age and gender), health insurance status, specialty and institution of the prescribers, brand name and strength (amount of the active substance) etc. The data was then carefully reviewed.

The original aim of our study was to compare pediatric, adolescent and adult prescriptions for methylphenidate, however due to missing age information in the majority of prescriptions (only

828 prescriptions had age information) the analysis was instead conducted between two different groups of physicians prescribing methylphenidate. MPs written by child and adolescent psychiatrists and pediatricians were grouped together. Accordingly, the comparisons were made for MPs prescribed for children by physicians caring for children (PCC) and those prescribed for adults by physicians caring for adults (PCA). Statistical comparisons were based on the Chi square test at a  $p < 0.05$  level of significance.

## RESULTS

The majority of 5681 the RCPs for methylphenidate for the treatment of ADHD (85.4%) had no age information. Prescriptions with age information were written for patients with an average age of  $15.1 \pm 11.1$  years (1-55 years) with the average age being  $10.1 \pm 3.8$  years in children and  $19.5 \pm 13.4$  years in adults. A total of 805 (14.1%) MPs contained both age and gender information and 78.6% of these were for patients under the age of 18 (74.1% male), with 21.4% written for adults (64.5% male). Among children, most prescriptions (51.9%) were for the 6-12 year age group (Table 1).

The majority of MPs were prescribed by pediatric psychiatrists (61.7%), psychiatrists (34.7%), neurologists (1.6%), pediatricians (1.3%) and other physicians (0.7%), respectively. Accordingly, 63% of MPs was prescribed by PCCs.

MPs were mostly prescribed in university hospitals (44.6%), private hospitals (18.3%), private

offices (14%), training and research hospitals (13.9%) and state hospitals (7.5%), respectively. MPs written by PCCs were prescribed mostly at university hospitals (64.5%) and training and research hospitals (17.4%) whereas prescriptions by PCAs were prescribed at private hospitals (36.6%) and in private practice (28.8%).

to the majority of MPs were reimbursed by the Social Security Institution (86%). MPs generated by PCCs and PCAs were mainly reimbursed by the Social Security Institution (89.6 and 75.9% respectively). A significant number of prescriptions by PCAs had no insurance coverage (13.5%); this percentage was considerably lower in PCC prescriptions (1.8%).

Visual evaluation of the MPs revealed that the strength of the drug was indicated in 95.8% of the prescriptions and this was significantly higher in prescriptions written by PCCs (96.8%) when compared to those written by PCAs (94.1%) ( $p < 0.01$ ) (Table 2).

Concerta® and Ritalin® are the brand names for methylphenidate available on the market in Turkey and are marketed by two different companies in tablet form at different strengths. The majority of prescriptions were for Concerta® tablets (62.7%) and this brand was prescribed more frequently by PCCs than by PCAs ( $p < 0.01$ ) (Table 2).

In contrast to patient age information, patient gender information was featured in most of the MPs (94.6%) and 73.7% of the MPs were for males. PCCs prescribed more methylphenidate for males than PCAs ( $p < 0.01$ ) (Table 2).

**Table 1: Classification of methylphenidate prescriptions based on age groups and gender**

Age groups of patients <sup>†</sup>	Total <sup>#</sup> n (%)	Female		Male		Male/Female Ratio n
		n	%	n	%	
<b>&lt;18 years</b>						
< 6 years	35 (4.4)	10	28.6	25	71.4	2.50
6-12 years	418 (51.9)	122	29.2	296	70.8	2.43
13-17 years	153 (19.0)	25	16.3	128	83.7	5.12
Other*	27 (3.3)	7	25.9	20	74.1	2.86
Subtotal	633 (78.6)	164	25.9	469	74.1	2.86
<b>18-44 years</b>	131 (16.3)	49	37.4	82	62.6	1.67
<b>45- 55 years</b>	41 (5.1)	12	29.3	29	70.7	2.42
<b>Total</b>	805 (100.0)	225	28.0	580	72.0	2.58

\*Patients labeled as 'under the age of 18' by health insurance.

<sup>†</sup>Only data containing age and gender were reviewed.

<sup>#</sup>Totals are given in the columns as a percentage with male-female patients percentages given in the lines.

**Table 2: Comparison between PCC and PCA with regards to prescriptions for methylphenidate containing the following parameters: "strength", "brand name" and "gender of the patient".**

Prescriber	Physicians caring for children		Physicians caring for adults		Total	
	n	%	n	%	n	%
<b>Status of prescription writing strength</b>						
Yes	3463	96.8	1977	94.1	5440	95.8
No	116	3.2	125	5.9	241	4.2
Total	3579	100.0	2102	100.0	5681	100.0
Statistics	p <0.01		$\chi^2=23.86$			
<b>Brand name of prescription drugs</b>						
Concerta®	2361	66.0	1200	57.1	3561	62.7
Ritalin®	1218	34.0	902	42.9	2120	37.3
Total	3579	100.0	2102	100.0	5681	100.0
Statistics	p <0.01		$\chi^2=44.6$			
<b>Gender of the patient</b>						
Female	817	24.8	595	28.7	1412	26.3
Male	2484	75.2	1476	71.3	3960	73.7
Total	3301	100.0	2071	100.0	5372	100.0
Statistics	p <0.01		$\chi^2=10.4$			

On detailed analysis of all the MPs, it was noted that the seasonal distribution of prescriptions was as follows: winter (29.6%), summer (28.2%), autumn (24.3%) and spring (17.9%). PCCs prescribed methylphenidate mainly in winter and summer (34.8% and 23.4% respectively) while PCAs prescribed in summer and autumn (36.4% and 27.9%) and there was a statistically significant difference between the two groups (p<0.01).

## DISCUSSION

Based on our findings, 11.8% of prescriptions for ADHD had MP and thus it is important to note that the share of MPs with the corresponding diagnosis of ADHD is not insignificant in our society. ADHD is one of the most common childhood psychiatric disorders while its etiology is still unclear. The disease spectrum consists of varying degrees of hyperactivity, impulsivity and attention deficit (11). It affects 3-7% of school children and has a 3-5 fold male predominance (15). Various studies have showed the ADHD prevalence among children and adolescents in Turkey to be 8% (16,17). In our study on the MPs containing age and gender information, 51.9% were prescribed for the 6-12 year age group, with a male to female ratio of 2.5:1 and a ratio of

5.1:1 in the 13-17 year age group, which was consistent with the literature (18). Methylphenidate has FDA approval for the treatment of ADHD and narcolepsy in both adults and children aged 6 and above (19). In the patient information leaflet of Concerta® and Ritalin®, the drug indications are listed as ADHD and ADHD-narcolepsy in patients over the age of 6 (20). In our study 4.4% of MPs were for children under the age of 6 and it is interesting to note 'the use of the drug in underage patients.

The prevalence of ADHD in adults is reported to be between 1-4% (11,21). However, in adults, the reported persistence of ADHD diagnosed during childhood is 30-70%, an inconsistency which may be due to differences in study methods as well as in diagnosis (1).

In our study on the MPs that had age and gender information, 21% were for the 18-55 year age group with 16% being in the 18-44 year age group. This distribution indicates that adulthood ADHD is rather significant. Differently from children, adulthood ADHD has no clear guidelines with regards to treatment and diagnosis. The comorbidity of other psychiatric disorders in adults further complicates diagnosis and treatment. Drugs used for childhood ADHD are generally effective in adult cases (22) with methylphenidate being listed as the

first line treatment (23-25).

Because of the high risk for abuse of methylphenidate, numerous countries have enforced restrictions in the prescription and distribution of the drug (26,9). In Turkey, the Ministry of Health issued a circular letter listing the specialists, who are authorized to prescribe methylphenidate. In the treatment of ADHD in patients under the age of 18, methylphenidate can be prescribed on a RCP by child and adolescent psychiatrists, child neurologists, neurologists and pediatricians, provided that a medical certificate containing the signatures of a pediatric and adolescent psychiatrist organized by a health board is obtained (27). A circular was published on April 14, 2010, which limited the prescription of methylphenidate. Methylphenidate can only be prescribed in patients under the age of 25 by psychiatrists and child/adolescent psychiatrists. In our study conducted with data from 2009, most of the prescriptions were written by the aforementioned physicians (96.4%), with 61.7 % being by pediatric and adolescent psychiatrists and 34.7% by psychiatrists. It is interesting to note that specialists, who are no longer authorized to prescribe methylphenidate (mostly neurologists and pediatricians) only accounted for 3.6% of the MPs.

As of 2005, the number of pediatric and adolescent psychiatrist specialists and residents nationwide was approximately 120 with most of them working at university hospitals, which supports our data that MPs written by PCCs (64.5%) were mostly prescribed in tertiary institutions (4). MPs written by PCAs took place mostly in private hospitals and private offices (64.6%), which shows the marked difference in preferences between children and adults in treatment institutions. "Social Security Institution- The Purchase Agreement for Private Health Services from Health Care Servers" published in January of 2009, enabling patients to receive treatment in private centers, seems to have contributed to these figures, and 75.9 % of prescriptions were reimbursed by the Social Security Institution.

In our study, the number of prescriptions for extended release methylphenidate (Concerta®

tablet) outnumbered those for short acting methylphenidate (Ritalin® tablet). This difference was significant in MPs by PCCs. The ratio of Concerta® tablets to Ritalin® tablets in prescriptions for children was 1.94:1 whereas this ratio was 1.33:1 in adults. Studies for Ritalin® tablets outnumber those for Concerta® tablets; however, the short acting nature of Ritalin and the administration of the drug in divided doses may have led to Concerta® tablets being the drug of choice among school aged children. Moreover, short acting methylphenidate taken 2-3 times a day leads to unstable plasma levels whereas slow release methylphenidate has stable plasma levels and a single dose lasts for 12 hours, which is advantageous in school aged children.

PCCs mainly prescribed methylphenidate in winter (34.8%). The reason for this may be due to the starting of the educational semester and subsequent MPs for ADHD were generated with the intention of improving academic performance. A study by Truter also showed an increase in MPs during the second half of the semester due to final exams (28). In our study, MPs showed a significant increase towards winter compared to autumn, a subsequent decline in spring and a second peak in the summer season. In Turkey, the summer holiday begins in the middle of June, which seems contradictory as we would expect a decrease in prescriptions in this period. It is recommended that methylphenidate should be discontinued on weekends and holidays due to possible adverse effects on growth. In our educational system the major exams for middle and high school, the 'placement exam' and 'graduate placement exam', are conducted in June which could, to some extent, explain our findings. In adults, MPs were predominantly written in summer and spring (36.4 and 27.9% respectively). There is insufficient data for the interpretation of the reasons behind this trend in adults. Further studies and data are needed to determine the relationship between methylphenidate and academic performance as well as the seasonal distribution of MPs.

The art of writing accurate prescriptions is one of the educational outcomes in rational use of medicinal products. Prescriptions should contain

the following information: the prescriber's details, the patient's details, drug details (name, dose, dosage form, amount, strength, instructions for use) and the date (29,30). In our study, we found that patient age information was missing in 14.6% of prescriptions, which leads to our belief that proper prescription education should be focused on and implemented during medical education and continuing medical education. Age information is especially important in young children as well as elderly patients. In our study 76.8% of prescriptions that contained age information belonged to patients under 18, which means that there is a large number of MPs in this age group which lack this information.

Our study has certain limitations; one of them being that the results are not representative of the country. Our study consisted of only 10% of a year's prescriptions from the Provincial Health Directorate

of Istanbul, which also provides a basis for future studies while giving us an idea about the usage of methylphenidate. Secondly, as we did not record patient name information, our records might contain more than one prescription for the same patient. Despite efforts on our part to overcome this by a large sample size, it cannot be claimed that this error did not occur.

In conclusion, while most prescriptions were for children there is also a substantial number of adult prescriptions. According to our study there is a need for further research with regards to utilization of methylphenidate in adults. The fact that, with the exception of the missing age information, the prescription information was almost complete is encouraging; however, in a disorder such as ADHD where age is of great importance, care should be taken to rectify this error.

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