The Attitudes, Beliefs and Knowledge of Adult Psychiatrists and Child and Adolescent Psychiatrists About Methylphenidate and its Indicated, Off-Label, and Nonmedical Use

Erişkin Psikiyatri ve Çocuk Psikiyatrisi Hekimlerinin Metilfenidat ve Metilfenidatın Endike, Endikasyon Dışı ve Tıbbi Olmayan Kullanımı Konusundaki Tutum, Bilgi ve İnançları

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ABSTRACT

Objective: Psychostimulants including methylphenidate (MPH) constitute first-line pharmacotherapy for attention-deficit/hyperactivity disorder (ADHD). MPH is only indicated for ADHD and narcolepsy but its off-label use is common. The nonmedical use is also on rise especially among students and physicians, because of the popular opinion that MPH provides cognitive improvement. However, to our knowledge, there is no previous study evaluating the off-label and nonmedical use of MPH among adult psychiatrists and child and adolescent psychiatrists. In this context, the study aimed to evaluate the attitudes, beliefs, and knowledge of adult psychiatrists and child and adolescent psychiatrists about MPH and its indicated, off-label and nonmedical use among this population. Thus, in this particular population, it will be possible to identify realistic or unrealistic beliefs about MPH and to plan training for residents and specialists. Non-indications also will be identified and will contribute to the literature on the identification of new indications.

Material and Methods: Data for this study were collected via an Internet-based survey designed by the researcher using Google forms®. Invitations to participate were shared in adult psychiatrists and child and adolescent psychiatry occupational groups on social media platforms. Data were collected during August 2019.

Results: Of the participants, 39.2% were adult psychiatrists and 60.8% were child and adolescent psychiatrists. All physicians reported that they prescribed MPH at varying rates. The rate of prescribing off-label MPH was 71.8%. The cases most commonly prescribed off-label MPH were autism, mental retardation, and/or ADHD with uncontrolled hyperactivity and agitation under the age of 6 in the children and treatment-resistant depression in the adults, respectively. Nonmedical use was also high at 59.4%. The most common reason for nonmedical use was determined as cognitive improvement for academic activities, followed by reducing sleep and increasing attention during night shifts. Their knowledge about MPH and ADHD was sufficient in general. However, there were some doubts about the diagnostic process.

Conclusion: All participants had been prescribing MPH, both for indicated and off-label cases. They all had substantial knowledge about MPH. However, the adult psychiatrists were more concerned about misuse and the probable adverse effects. The nonmedical use of MPH was also higher among participants than the previously reported rates. New and more comprehensive studies are needed in this context.

Key Words: Methylphenidate, Adult psychiatry and child and adolescent psychiatry, Prescribing, Off-label, Non-medical use

ÖZ

Amaç: Metilfenidat (MPH)'ın da dahil olduğu psikostimülanlar, dikkat eksikliği/hiperaktivite bozukluğu (DEHB) tedavisinde birinci basamak ilaçlardır. MPH sadece DEHB ve narkolepsi için endike olmakla birlikte; endikasyon dışı kullanımı yaygındır. Tıbbi olmayan kullanımı ise, özellikle

MPH'nin bilişsel becerileri artırdığı şeklindeki popüler görüş nedeniyle özellikle öğrenciler ve hekimler arasında artış eğilimindedir. Ancak, bildiğimiz kadarıyla, şu ana kadar erişkin psikiyatristleri ve çocuk ve ergen psikiyatristleri arasında MPH'nin endikasyon dışı ve tıbbi olmayan kullanımını değerlendiren bir çalışma bulunmamaktadır. Bu bağlamda, bu çalışmada erişkin psikiyatristlerinin ve çocuk ve ergen psikiyatristlerinin MPH'ın endike, endikasyon dışı ve tıbbi olmayan kullanımı hakkındaki tutum, bilgi ve inançlarını değerlendirmek amaçlanmıştır. Böylelikle bu özel popülasyonda MPH hakkında gerçeğe uygun ya da gerçek dışı inançları belirleyip asistanlıkta ve asistanlık sonrası eğitimler planlamak mümkün olacağı gibi; endikasyon dışı kullanım alanları da saptanacak ve yeni endikasyonların belirlenmesi konusunda literatüre katkı sağlayacaktır.

Gereç ve Yöntemler: Bu çalışma için veriler Google forms® kullanılarak araştırmacı tarafından tasarlanan İnternet bazlı bir anket aracılığıyla toplanmıştır. Katılım davetleri erişkin psikiyatri ve çocuk ve ergen psikiyatrisi meslek gruplarında sosyal medya platformları üzerinden paylaşılmıştır. Veriler 2019 Ağustos ayında toplanmıştır.

Bulgular: Katılımcıların %39.2'sinin erişkin psikiyatristi, %60.8'inin çocuk ve ergen psikiyatristi olduğu saptandı. Tüm hekimler MPH'yi değişen oranlarda reçete ettiklerini bildirdi. Endikasyon dışı MPH reçeteleme oranı %71.8 idi. MPH'nin endikasyon dışı en çok reçete edildiği olgular çocuklarda kontrolsüz hiperaktivite ve ajitasyon ile seyreden otizm ve/veya zihinsel gerilik ile 6 yaşın altında DEHB'si olan çocuklar iken, yetişkinlerde tedaviye dirençli depresyon oldu. Tıbbi olmayan kullanım da %59.4 ile yüksek bulundu. Tıbbi olmayan kullanımın en yaygın nedeni, akademik aktiviteler için bilişsel becerileri artırma iken, ardından gece nöbetleri esnasında dikkati artırma ve uykuyu azaltma olarak bildirildi. Hekimlerin MPH ve DEHB hakkındaki bilgileri genel olarak yeterliydi, ancak tanı süreci hakkında bazı şüpheleri olduğu saptandı.

Sonuç: Tüm katılımcılar hem endike hem de endikasyon dışı durumlar için MPH reçete etmektedir. Tüm hekimlerin MPH hakkında yeterli bilgisi olmakla birlikte, erişkin psikiyatristlerinin ilacın kötüye kullanımı ve olası yan etkileri hakkında daha fazla kaygılı oldukları görüldü. MPH'nin tıbbi olmayan kullanımı, katılımcılar arasında önceden bildirilmiş olan oranlardan daha yüksek bulundu. Bu bağlamda yeni ve daha kapsamlı çalışmalara ihtiyaç vardır.

Anahtar Sözcükler: Metilfenidat, Erişkin psikiyatri ve çocuk psikiyatrisi, Reçete etme, Endikasyon dışı, Tıbbi olmayan kullanım

INTRODUCTION

Psychostimulants, including methylphenidate (MPH) and amphetamines, constitute first-line pharmacotherapy for the treatment of attention-deficit/hyperactivity disorder (ADHD), which is one of the most common psychiatric disorders in children (1). Both MPH and amphetamines act by increasing central dopamine and norepinephrine activity, thereby improving executive and attentional functions. MPH actions include dopamine and norepinephrine transporter inhibition, redistribution of the VMAT-2, and agonist activity at the serotonin type 1A receptor (2).

MPH is a relatively old drug as it was first registered almost sixty years ago, under the brand name Ritalin®. In Turkey, MPH is listed as a narcotic and has restrictive conditions of prescription and dispensing. All prescriptions must be written electronically on a special medical database and all records must be kept. The prescription must be signed by a child and adolescent psychiatrist or a an adult psychiatrist. Despite the limited indications and prescription conditions, off-label use of methylphenidate is common.

The main off-label indications of MPH were autism, ADHD, and psychomotor activity in children under the age of 6; autism, instability, behavioural disorders, and intellectual disability in the 6-18-year-old group; and ADHD, narcolepsy-hypersomnia, depression, and Parkinson's disease in adults (3).

At the same time, it seems that the "nonmedical" use of MPH is also on the rise mainly because of the popular opinion that MPH provides cognitive improvement (4). Yet, its general affects on healthy individuals are not clear, and its neuroenhancement effect has not been proven. Even so, nonmedical MPH use is particularly evident among academics, where many students attempt to obtain MPH. Studies have estimated that the prevalence of MPH off-label use of students is about 1.5-8% (5,6). Even a higher rate of the use was reported among medical and dental students in the USA with up to 20% reported to take a stimulant medication (7-10). To our knowledge, there is no previous study evaluating the off-label and nonmedical use of MPH among adult psychiatrists and child and adolescent psychiatrists, although they are the ones who most frequently prescribe MPH and have easy access to MPH among all physicians.

In this context, we aimed to evaluate the attitudes, beliefs and knowledge of adult psychiatrists and child and adolescent psychiatrists about MPH and its indicated, off-label and nonmedical use among this population.

MATERIAL and METHODS

Survey Instrument, Sample Recruitment, and Data Collection:

Data for this study were collected via an Internet-based survey designed by the researcher using Google forms® (Available at: https://docs.google.com/forms/d/1KwWhf5MmNm1nKaQuZNMjFjKQmLDOVWYX6uq8g0_N2cE/edit). An Internet-based survey method was chosen, based on the research showing that this method of data collection correlates with traditional paper-based surveys

for reliability and validity (11), and also to ensure the anonymity of the participants and therefore the reliability of the study. The survey consisted of 3 parts: The first part was about sociodemographic data about age, specialty, academic title and time spent in the profession. The second part was about MPH prescribing habits, off-label use of MPH in patients and nonmedical use for themselves and/or prescribing for a colleague. The last part consisted of beliefs and knowledge about MPH and ADHD.

Invitations to participate were shared in adult psychiatry and child and adolescent psychiatry occupational groups on social media platforms such as Whatsapp and Facebook. Participation in the study was on a voluntary basis and people who completed the form were deemed to have given consent to participate in the study. To be a resident of adult psychiatry or child and adolescent psychiatry was accepted as sufficient for participation. Data were collected during August 2019.

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) 18.0 version was used for data analysis. Results were recorded as arithmetical mean, Standard deviation and percentages. Chi-squared analysis or Fisher's exact tests were used to analyze categorical variables. Numeric variables were analyzed using independent t-tests.

The study was approved by the Institutional Ethics Committee of Akdeniz University on 28.08.2019, with decision number 770. Research and publication ethics were followed during the planning, data collection and writing of the manuscript.

RESULTS

A total of 255 physicians completed the survey. Of the participants, 39.2% were adult psychiatrists and 60.8% were child and adolescent psychiatrists. The most commonly stated academic title was specialist (59.6%) followed by resident (29.4%), assistant professor (5.5%), associate professor (3.9%) and professor (1.6%).

Methylphenidate prescribing habits, and the off-label and nonmedical use of methylphenidate

When looking at MPH prescribing habits, all physicians reported that they prescribed MPH at varying rates. Whereas 53.7% of the physicians reported that they prescribed MPH almost daily, the others reported prescribing a few times a week (24.3%), a few times a month (14.5) and less frequently (7.5%). MPH was preferred as a first-line drug in the pharmacotherapy of ADHD. OROS MPH was the most preferred form with 48.2%, followed by the modified-release capsules and short acting MPH.

Cardiac side effects were reported to be the most worrisome by the physicians at 56.1%, followed by the risk of abuse (32.2%) and epilepsy (5.1%). Irritability, weight loss, sleep problems and loss of appetite were the other mentioned side effects.

Considering the cases physicians prescribed off-label MPH, it was seen that children with autism and/or mental retardation with uncontrolled hyperactivity and agitation were the leading ones with 71.8%. The other cases were the children under the age of 6 with serious attention and/or behavioral problems (42%), patients with persistent depression (as an adjuvant treatment) (33.3%), obese children with uncontrolled eating episodes (27.1%), and children with some attention problems but not diagnosed with ADHD (23.5%) (Table I).

Off-label use by child and adolescent psychiatrists was higher in children with ADHD under 6 years of age and in children with autism/mental retardation (p=0.001 and 0.024, respectively); whereas it was significantly higher in adult psychiatrists in patients with persistent depression and

Table I: Cases prescribed off-label MPH.

	Adult Psychiatrists	C&A Psychiatrists	p
Autism and/or mental retardation with uncontrolled hyperactivity and agitation	64.4%	77.3%	**0.024**
Children under the age of 6 with serious attention and/or behavioral problems	23.8%	54.5%	**0.001**
Patients with persistent depression	51.5%	20.8%	**0.001**
Obese children with uncontrolled eating episodes	20.8%	31.2%	0.068
Children with some attention problems but not diagnosed with ADHD, preparing for a challenging exam	31.7%	18.2%	**0.013**

in children preparing for a challenging exam (p=0.001 and 0.013, respectively).

In terms of nonmedical use, 59.4% reported that he/she had used MPH at least once in their lifetime, and 39.6% had recommended MPH to a colleague for nonmedical use. The most common reason for nonmedical use was determined as increasing attention during academic activities, followed by reducing sleep and increasing attention during night shifts. Increasing attention during hobbies and social interactions, feeling better, and appetite control were less often reported. There was no significant difference between adult psychiatrists and child and adolescent psychiatrists in terms of the reasons for nonmedical use, except for usage to increase attention during hobbies, which was found to be more common in psychiatrists (p: 0.027) (Table II).

The most common reason for recommending MPH to a colleague was found to be academic studies. Whereas 66% of nonmedical MPH users reported moderate to good benefit, 34% reported little or no benefit.

The attitudes, beliefs and knowledge about methylphenidate

Although most of the physicians agreed that the diagnosis and treatment of ADHD had been supported by many scientific studies for many years and the main treatment of ADHD was pharmacotherapy; nearly half of them believed that there was an overdiagnosis of ADHD among children and many children were prescribed MPH unnecessarily. In a similar manner, half of the physicians reported that in case their child was diagnosed with ADHD and drug treatment was started, they would use the drugs unwillingly because of their side effects, or would seek a second physician's opinion before using them.

Among physicians, while 49.8% stated that MPH can be used as a pleasure-inducing substance, 32.1% answered the statement "methylphenidate is addictive" as yes or not sure. However, the ones that agreed with the statement "methylphenidate increases the risk of developing substance abuse in children at older ages" remained at 7.5%.

Agreement with the statements "methylphenidate is addictive", "methylphenidate can be used as an pleasure-inducing substance", and "methylphenidate increases the risk of developing substance abuse in children at older ages" was significantly higher in adult psychiatrists (p: 0.001, 0.0038 and 0.001, respectively). However, there was no significant difference between the 2 groups in terms of agreement with the statements "The diagnosis and treatment of ADHD have been supported by many scientific studies for many years", "there is an overdiagnosis of ADHD among children", and "many children are prescribed MPH unnecessarily".

Whereas 89.6% of child and adolescent psychiatrists believed that the main treatment of ADHD was pharmacotherapy, the rate was 72.3% among adult psychiatrists (p=0.001).

DISCUSSION

This is the first study evaluating the frequency of off-label and nonmedical MPH use and the knowledge, attitudes and beliefs about MPH among adult psychiatrists and child and adolescent psychiatrists to our knowledge.

The rate of prescribing off-label MPH was 71.8% in this study. Off-label use is defined as "use in non-authorised paediatric age categories, and use in other (non EU-authorised) indications outside of the clinical trial setting" (12). Actually, MPH is only indicated as a part of a comprehensive treatment programme for ADHD in children aged 6 years and over, and for narcolepsy both in children and adults; however, it is widely prescribed for children with autism and/or mental retardation with uncontrolled hyperactivity and agitation, children under the age of 6 with serious attention and/or behavioral problems, and patients with persistent depression (3). There are also some case reports reporting benefit from MPH for uncontrolled eating episodes (13-14). Indeed, although atypical antipsychotics, especially risperidone, are the first-line treatment option for children under 6 years of age

Table II: Reasons of psychiatrists and child and adolescent psychiatrists for nonmedical use of MPH.

	Adult Psychiatrists	C&A Psychiatrists	p
Increasing attention during academic activities	47.5%	56.5%	0.16
Reducing sleep and increasing attention during night shifts	12.9%	6.5%	0.082
Increasing attention during hobbies and social interactions	9.9%	3.2%	**0.027**
Feeling better	3%	2.6%	0.85
Appetite control	4%	3.2%	0.76

with autism, mental retardation and/or ADHD (15), MPH may be necessary when antipsychotics are not sufficient to control the symptoms. In case of depression, patients who experience partial or no response to antidepressant treatment are considered to have treatment-resistant depression (TRD) and are candidates for treatment options such as augmenting with another agent or switching to a different class of antidepressant. In these cases, some studies have reported that psychostimulants might be effective as an augmentation therapy for TRD, especially in adults (16).

In accordance with the literature, the conditions most commonly prescribed off-label MPH were autism, mental retardation and/or ADHD with uncontrolled hyperactivity and agitation under the age 6 in children, and TRD in adults, respectively, in this study.

The nonmedical use rate was also considered high in our study group with 59.4%. Nonmedical or illicit use is defined as "use that was not prescribed, or use only for the experience or feelings it causes" (17). A growing body of literature suggests that the non-medical use of MPH is increasing, for reasons of helping with concentration, attention and focusing and improving academic performance, especially by college and university students (18-20). Although the prevalence rates differ from study to study, the results of most studies indicate that the practice is common. Among college students, self-reported rates range from 1.5% to 31% in the various surveys, with the most nationally representative study estimating annual nonmedical MPH use of about 4% (21). As knowledge about the drug increases and access to the drug becomes easier, it will not be wrong to expect these rates to increase. Indeed, Low and Gendaszek reported the prevalence of nonmedical use of MPH or amphetamine as 35% among college students in a psychology class (22). The reported rates among medical students and resident physicians were 17% and 22.2%, respectively (4,23).

From this point of view, the studying process for the medical specialty exam, the laborious and difficult medical and specialty trainings of adult psychiatrists and child and adolescent psychiatrists and the easy access to the drugs may have increased the rate of nonmedical MPH use among these physicians.

Whereas 66% of nonmedical MPH users in our study reported moderate to severe benefit, 34% reported little or no benefit from MPH. Actually, the popular opinion that MPH enhances attention in healthy individuals was not verified through the meta-analyses. Studies could not provide any consistent evidence for neuroenhancement effects of MPH, except for a positive effect on memory (24). However, in most of the studies the use of relatively low doses such as 10-20 mg of MPH was reported and this might be a probable explanation for the lack of a benefit. Unfortunately we did not ask the doses the physicians benefited from but given their drug-related experience, we can assume that they used higher, and consequently more adequate doses.

Looking at the attitudes, beliefs and knowledge of the physicians, it can be said that their knowledge about MPH and ADHD was sufficient in general. However, they had some doubts about the diagnostic process. In fact, nearly half of them believed that there was an overdiagnosis of ADHD among children and many children were prescribed MPH unnecessarily. In a similar manner, half of the physicians reported that in case their child was diagnosed with ADHD and drug treatment was started, they would use the drugs unwillingly because of probable side effects, or would seek a second physician's opinion before using them. In terms of treatment, 89.6% of child and adolescent psychiatrists believed that the main treatment of ADHD was pharmacotherapy. However, 27.2% of adult psychiatrists thought that other methods such as education and cooperation of the family and school, art and sports activities, and organizing the education of the child were effective as the first choice in the treatment of ADHD. In addition, adult psychiatrists had more doubts about MPH, in terms of the risk of abuse, addiction, and increasing the risk of substance abuse in future, compared to the child and adolescent psychiatrists. This may be related to the fact that adult psychiatrists do not prescribe MPH as much as child and adolescent psychiatrists and therefore they have less clinical experience about MPH, although their knowledge was sufficient.

Finally, there are limitations and strengths of the study that should be noted. First, because of the internet-based nature of the study, repeated participations and/or the inclusion of persons not eligible for the study might have occurred. Moreover, some of the participants stated as a comment that they diagnosed themselves as adult ADHD and therefore used MPH. They were a very small group compared to the total, but as this critique came after the data collection, they could not be represented as a separate group, and it would not be possible to exclude them. Despite these limitations, this study also has significant clinical implications. First, this is the first study evaluating the off-label and nonmedical use of MPH among adult psychiatrists and child and adolescent psychiatrists. In addition, due to the nature of the study, we had the chance to reach a large number and variety of participants, and increase the representation value of the study group. And finally, by showing that off-label MPH use is quite high and considering our almost 60 years of experience about MPH, it may pave the way for new arrangements on the indications for MPH.

CONCLUSIONS

In conclusion, all of the adult psychiatrists and child and adolescent psychiatrists had been prescribing MPH, both for indicated and off-label cases. They all had substantial knowledge about MPH. However, the adult psychiatrists were more concerned about its misuse and probable adverse effects. The nonmedical use of MPH was also higher among participants than the previously reported rates. New and more comprehensive studies are needed in this context.

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The study was approved by the Institutional Ethics Committee of Akdeniz University on 28.08.2019, with decision number 770. Research and publication ethics were followed during the planning, data collection and writing of the manuscript.

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REFERENCES

1. Faraone, SV. The pharmacology of amphetamine and methylphenidate: Relevance to the neurobiology of attention-deficit/hyperactivity disorder and other psychiatric comorbidities. Neurosci Biobehav Rev 2018; 87:255-70.
2. Scahill L, Schwab-Stone M. Epidemiology of ADHD in school-age children. Child Adolesc Psychiatr Clin N Am 2000; 9:541-55.
3. Trenque T, Herlem E, Taam MA, Drame M. Methylphenidate off-label use and safety. Springer Plus 2014; 3(1):286-93.
4. Cohen, YG, Segev RW, Shlafman N, Novack1 V, Ifergane G. Methylphenidate use among medical students at Ben-Gurion University of the Negev. Neurosci Rural Pract 2015; 6(3):320-26.
5. Ragan CI, Bard I, Singh I. What should we do about student use of cognitive enhancers? An analysis of current evidence. Neuropharmacology 2013; 64:588-95.
6. McCabe SE, Knight JR, Teter CJ, Wechsler H. Non-medical use of prescription stimulants among US college students: Prevalence and correlates from a national survey. Addiction 2005; 100(1):96-106.
7. Tuttle JP, Scheurich NE, Ranseen J. Prevalence of ADHD diagnosis and nonmedical prescription stimulant use in medical students. Acad Psychiatry 2010; 34(3):220-3.
8. McNiel AD, Muzzin KB, DeWald JP, McCann AL, Schneiderman ED, Scofield J, Campbell PR. The Nonmedical use of prescription stimulants among dental and dental hygiene students. J Dent Educ 2011; 75(3): 365-76.
9. Kudlow PA, Naylor KT, Xie B, McIntyre RS. Cognitive enhancement in Canadian medical students. J Psychoactive Drugs 2013; 45(4):360-5.
10. Webb JR, Valasek MA, North CS. Prevalence of stimulant use in a sample of US medical students. Ann Clin Psychiatry 2013; 25(1):27-32.
11. Denscombe, M. Web-Based questionnaires and the mode effect: An evaluation based on completion rates and data contents of near-identical questionnaires delivered in different modes. Soc Sci Comput Rev 2006; 24(2):246-54.
12. Guideline on good pharmacovigilance practices (GVP). Module V - risk management systems. European Medicines Agency 2012; 17. Available at: https://www.ema.europa.eu/en/documents/scientific-guideline/draft-guideline-good-pharmacovigilance-practices-module-v-risk-management-systems_en.pdf
13. Drimmer EJ. Stimulant treatment of bulimia nervosa with and without attention-deficit disorder: three case reports. Nutrition 2003; 19(1):76-7.
14. Önder A, Sürer Adanir A. Methylphenidate treatment for binge-eating disorder in a 12-year-old boy. Psychiat Clin Psych 2018; 28(2):222-23.
15. Loy JH, Merry SN, Hetrick SE, Stasiak K. Atypical antipsychotics for disruptive behaviour disorders in children and youths. Cochrane Database Syst Rev 2017; 8(8):CD008559.
16. Gwirtsman HE, Szuba MP, Toren L, Feist M. The antidepressant response to tricyclics in major depressives is accelerated with adjunctive use of methylphenidate. Psychopharmacol Bull 1994; 30:157-64.
17. Wu LT, Pilowsky DJ, Schlenger WE, Galvin DM. Misuse of methamphetamine and prescription stimulants among youths and young adults in the community. Drug Alcohol Depend 2007; 89(2-3):195-205.
18. Kroutil L, Van Brunt D, Herman-Stahl M, Heller D, Bray R, Penne M. Nonmedical use of prescription stimulants in the United States. Drug Alcohol Depen 2006; 84:135-43.

19. Weyandt L, Janusis G, Wilson K, Verdi G, Paquin G, Lopes J, Dussault C. Nonmedical prescription stimulant use among a sample of college students relationship with psychological variables. J Atten Disord 2009; 13:284-96.
20. White B, Becker-Blease K, Grace-Bishor K. Stimulant medication use, misuse, and abuse in an undergraduate and graduate student sample. J Am Coll Health 2006; 54: 261-68.
21. Bogle, KE, Bradley HS. "Illicit methylphenidate use: A review of prevalence, availability, pharmacology, and consequences." Curr Drug Abuse Rev 2009; 2(2):157-76.
22. Low KG, Gendaszek AE. Illicit use of psychostimulants among college students: A preliminary study. Psychol Health Med 2002; 7(3):283-7.
23. Bulbul F, Alpak G, Unal A, Kilic OHT, Ermis B, Savas HA. Misuse of methylphenidate and attitudes about methylphenidate among resident physicians. Bulletin of Clinical Psychopharmacology 2014; 24(2):135-38.
24. Repantis D, Schlattmann P, Laisney O, Heuser I. Modafinil and methylphenidate for neuroenhancement in healthy individuals: A systematic review. Pharmacol Res 2010; 62(3):187-206.