DOI: 10.5455/bcp.20140131023347

A Patient With Dimenhydrinate Dependence: A Case Report

Fatma Duygu Kaya[1]

ÖZET:

Dimenhidrinat bağımlılığı gelişen bir hasta: Olgu sunumu

Taşıt tutması, vertigo ve emezisde kullanılan dimenhidrinat, madde bağımlıları ve psikiyatri hastaları tarafından kötüye kullanımı olan bir antihistaminiktir. Antihistaminiklerin bağımlılık yapıcı potansiyelleri ile ilgili literatürde olgu bildirimleri yer almaktadır. Türkiye literatürüne geçmiş, dimenhidrinat bağımlılığı olan bir olgu bildiğimiz kadarıyla bulunmamaktadır. Burada ikinci bebeğine hamile olduğu ilk ay içinde emezis tedavisi için doktor tarafından önerilen dimenhidrinat 50 mg/gün tedavisini kontrolsüz bir şekilde kesintisiz 12 sene boyunca doz artırarak kullanmayı sürdüren, en son 300 mg/gün dozunda kullanmakta olan 33 yaşında bir kadın olgu ve tedavi süreci sunulmaktadır. Ayrıca bu olgu bağlamında dimenhidrinat bağımlılığı tartışılmaktadır.

Anahtar sözcükler: dimenhidrinat, antihistaminik, bağımlılık

Klinik Psikofarmakoloji Bulteni 2014;24(2):184-7

ABSTRACT:

A patient with dimenhydrinate dependence: a case report

Dimenhydrinate, an antihistamine that is used for motion sickness, vertigo and emesis, is abused by drug addicts and psychiatric patients. In the literature, there are case reports about the addictive potential of antihistamines. To our knowledge, in the Turkish literature there have been no previous case reports of dimenhydrinate dependence. The case of a 33 year-old female, who was advised to use dimenhydrinate 50 mg/day for emesis early in her second pregnancy by her primary care physician and who continued to use the drug for 12 years at a daily dose of 300 mg without a prescription, is presented here. In addition, dimenhydrinate dependence is discussed by the author in the context of this case.

Keywords: dimenhydrinate, antihistamine, dependence

Bulletin of Clinical Psychopharmacology 2014;24(2):184-7

[1]M.D., Dr. Hulusi Alatas Elmadag State Hospital, Psychiatry Clinic, Ankara - Turkey

Address reprint requests to:
Dr. Fatma Duygu Kaya
Dr. Hulusi Alataş Elmadağ Devlet Hastanesi, Psikiyatri Kliniği, Ankara - Türkiye

E-mail address:
fduygukaya@hotmail.com

Date of submission:
August 19, 2013

Date of acceptance:
January 31, 2014

Declaration of interest:
F.D.K.: The author reported no conflict of interest related to this article.

INTRODUCTION

Dimenhydrinate (DH), a drug that is used for motion sickness, vertigo and emesis, contains both the antihistamine (AH) diphenhydramine as the active metabolite and methylxanthine 8-chlorotheophylline. DH is predominantly an H1 receptor antagonist, although it also interacts with other neurotransmitters especially acetylcholine (Ach) and dopamine (DA)[1]. In high doses anticholinergic effects such as urinary retention and confusion become evident and the drug gains an emetic-anorexic property[2]. Its hallucinatory and euphoric effects lead drug addicts to abuse DH and similar AHs in combination with other substances[1]. Such a combination of diphenhydramine and heroin called "cheese" is being sold on the street abroad[3]. On the other hand, the sedative and anxiolytic effects may lead psychiatric patients to abuse or misuse AHs[1].

Case reports of DH dependence are rather scarce in the literature. In 1988 two cases were reported who experienced withdrawal symptoms after drug cessation[4]. Three more cases were reported 1990

who were using high doses up to 3750 mg/day and showed withdrawal symptoms that improved within 7-10 days[5]. AH abuse also occurs among schizophrenic patients, because of its anticholinergic and sedative effects. A schizophrenic patient, who was taking 800 mg/day of diphenhydramine, the active metabolite of DH for his insomnia was reported to have experienced some withdrawal symptoms such as irritability and increased defecation that improved within 10 days[6]. Other two schizophrenic patients, who were taking very high daily doses of DH were reported to have less cravings and decreased need for DH after initiation of clozapine treatment[7]. There are also some publications about children having chronic hematologic and oncologic diseases, who exhibited drug-seeking behavior with use of diphenhydramine as an antiemetic[8]. Two cases of pheniramine dependence have been reported from Turkey, who were using the drug intravenously at doses of 450-600 mg/day and showed withdrawal symptoms after drug cessation[9,10].

To our knowledge this is the first reported case of dimenhydrinate dependence from Turkey. Here a patient, who had been using DH continuously for 12 years including during her three pregnancy and lactation periods, is presented.

CASE

A 33-year old married female patient with four children was referred to our outpatient psychiatry clinic by an emergency physician with withdrawal symptoms after stopping DH for three days that she had been using for 12 years at a daily dose of 300 mg. She was unable to obtain DH anymore due to new health regulations that ban medication use without a prescription. She complained about nausea, vomiting (20 times a day), hand tremors, irritability, perspiration, drowsiness, headache, poor appetite and hypersomnia and her physical examination was positive for mydriasis and mild hand tremor. She met the ICD-10 criteria of "sedative, hypnotic or anxiolytic dependence with withdrawal (F13.23)". The criteria for drug dependence, including drug tolerance, withdrawal, increased use, unsuccessful efforts to cut down use and continued use despite knowing that it caused significant physical problems, were positive for the patient. Her electrocardiogram showed sinus rhythm with a heart rate of 88 beats/min, her blood pressure was 130/80 mmHg and axillary temperature was 36.5°C. Laboratory tests were done including complete blood count, renal and liver function tests, thyroid function tests, serum ferritin, folate and vitamin B12 levels. All values were within normal limits except for low vitamin B12 level (83 pg/mL) (laboratory reference range was 120-883 pg/mL). The blood level of DH was not measured due to inadequate laboratory equipment in our hospital. After a motivational interview with the patient, DH was started again with a decreased dose (250 mg/day) because of her severe withdrawal symptoms.

Three days after her initial visit, her withdrawal symptoms were completely relieved. Written informed consent was obtained from the patient allowing her medical data to be used for academic purposes. A detailed psychiatric history was taken; the Beck Depression Inventory (BDI) and Addiction Profile Index (API) clinician-administered version were administrated[11]. The API total score was 6.7 indicating severe addiction and the BDI score was 39, which indicate severe depression. Her history was negative for current and past use of nicotine, alcohol, illicit substances and chronic diseases.

She was married when she was 16 and had her first child at the age of 19. Two years later, when she was two weeks pregnant with her second child, she presented to a primary care physician because of emesis. He prescribed DH 50 mg/day and she increased the dose up to 150 mg/day during her pregnancy and lactation period. The baby was breastfed for 3 months and had febrile convulsions once at the age of two. In that year, she got pregnant again and increased the dose up to 300 mg/day in the second trimester. She developed depressive symptoms such as insomnia and loss of interest when her husband left town for business. Because of the desirable sedative effects of the drug, she couldn't quit and gave birth to a healthy boy who was breastfed for two years. When the baby was

nine months old, her husband returned home, but their marital problems were not solved. At the age of 28, when she was pregnant again, she went to her routine pregnancy follow ups, but didn't tell her doctors about her drug dependence. In that period, her husband had to leave home again for business and that triggered a new depression episode. The unborn baby was detected to have a diaphragmatic hernia and underwent surgery immediately after birth without any complications. Three years ago, she decided to quit the drug but her mother developed cancer and died, so she couldn't. When the patient was referred to our clinic, she had been using DH 300 mg/day continually for 12 years with a history of three or four unsuccessful quitting attempts accompanied by similar withdrawal symptoms with no hospital admissions. Escitalopram 10 mg/day, mirtazapine 15 mg/day and vitamin B12 tablets were started because of her depression and vitamin B12 deficiency. The DH dose was gradually tapered down (50 mg/day per week) and stopped within five weeks and the only withdrawal symptom was mild nausea. At follow ups at 3 months, her BDI scores had decreased and she didn't take any DH.

DISCUSSION

DH, a widely recommended anti-emetic during pregnancy, is in the FDA pregnancy category B, which means that it is unlikely to harm an unborn baby[12], but as with other AHs, there is also a potential dependence risk for DH. The rewarding effects of AHs have been reported to be related to effects on other neurotransmitters but not directly to H1 receptor antagonism[13]. AHs increase DA neurotransmission in mesolimbic areas in rodents and create cocaine-like effects[3]. In addition to this effect, the diphenhydramine content of DH also stimulates opiate receptors and Ach release and inhibits serotonin and norepinephrine reuptake[1]. The other component of DH, 8-chlorotheophylline, increases DA by blocking adenosine receptors[1]. In summary, AHs directly increase DA levels and methylxanthines indirectly have the same effect by adenosine antagonism. Therefore, the two components of DH reinforce each other's rewarding effects and the presence of methylxanthine increases the addictive properties of DH. Lately, quetiapine abuse has been frequently reported. The antihistaminergic and mild dopaminergic effects of quetiapine have been found to be responsible for its abuse potential[14]. It has been shown that pheniramine and diphenhydramine induce conditioned place preference in rats[15] and self-administration in monkeys[16].

DH has been reported to have been taken in doses up to 5000 mg/day, although a daily dose of 800 mg is enough to become high, cause tolerance and withdrawal symptoms such as irritability, loss of appetite, amnesia, agitation, nausea and depression[1].

This case is of particular interest in that although the taken daily dose of DH was not toxic, the duration of DH use (12 years) with the presence of tolerance and withdrawal symptoms is remarkable. In Turkey, recent health regulations that ban medication use without prescription will probably lead such drug addicts to seek help at psychiatry clinics and increase their motivation to recover. Additional attention to the addictive tendencies of patients and awareness of the potential abuse risks of AHs by clinicians would help prevent the abuse of these medications.

References:

1. Halpert AG, Olmstead MC, Beninger RJ. Mechanisms and abuse liability of the anti-histamine dimenhydrinate. Neurosci Biobehav Rev 2002;26:61-7. [CrossRef]
2. Medline Plus. http://www.nlm.nih.gov/medlineplus/druginfo/meds/a607046.html
3. Tanda G, Kopajtic TA, Katz JL. Cocaine-like neurochemical effects of antihistaminic medications. J Neurochem. 2008;106(1):147-57. [CrossRef]
4. Young GB, Boyd D, Kreeft J. Dimenhydrinate: evidence for dependence and tolerance. CMAJ 1988;138(5):437-8.

5. Craig DF, Mellor CS. Dimenhydrinate dependence and withdrawal. CMAJ 1990;142(9):970-3.

6. Feldman MD, Behar M. A case of massive diphenhydramine abuse and withdrawal from use of the drug. JAMA 1986;255(22):3119-20. [CrossRef]

7. Prost E, Millson RC. Clozapine treatment of dimenhydrinate abuse. Am J Psychiatry 2004;161(8):1500. [CrossRef]

8. Dinndorf PA, McCabe MA, Frierdich S. Risk of abuse of diphenhydramine in children and adolescents with chronic illnesses. J Pediatr 1998;133(2):293-5. [CrossRef]

9. Saatcioglu O, Evren C. A case of pheniramine dependence. Subst Abus 2005;26(1):45-7. [CrossRef]

10. Bilici R, Eksioglu S, Tufan E. Pheniramine Dependence: A Case Report. Poster Presentations. Klinik Psikofarmakoloji Bülteni- Bulletin of Clinical Psychopharmacology 2012;22(Suppl. 1):S147.

11. Ogel K, Evren C, Karadag F, Gurol DT. The development, validity, and reliability of the Addiction Profile Index (API). Turk Psikiyatri Derg 2012;23(4):263-75.

12. Suzer O. Suzer Pharmacology, İstanbul: Published by Klinisyen Tıp Kitabevleri; 2005. p. 517. (Turkish)

13. Campbell VC, Kopajtic TA, Newman AH, Katz JL. Assessment of the influence of histaminergic actions on cocaine-like effects of 3alpha-diphenylmethoxytropane analogs. J Pharmacol Exp Ther 2005;315(2):631-40. [CrossRef]

14. Fischer BA, Boggs DL. The role of antihistaminic effects in the misuse of quetiapine: a case report and review of the literature. Neurosci Biobehav Rev 2010;34(4):555-8. [CrossRef]

15. Halpert AG, Olmstead MC, Beninger RJ. Dimenhydrinate produces a conditioned place preference in rats. Pharmacol Biochem Behav 2003;75(1):173-9. [CrossRef]

16. Wang Z, Woolverton WL. Self-administration of cocaine-antihistamine combinations: super-additive reinforcing effects. Eur J Pharmacol 2007;557(2-3):159-60. [CrossRef]