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The Rising Trends in the Misuse and Abuse of Over-the-Counter Medications: A Comprehensive Review

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Abstract

Background: Over-the-counter (OTC) medications are widely perceived as safe and accessible, yet their misuse and abuse are rising concerns. While these medications are designed for common ailments, their potential for dependency and harmful effects is often underestimated. This review examines the trends in OTC medication misuse, particularly focusing on substances like dextromethorphan (DXM), diphenhydramine (DPH), and codeine.

Methods: A systematic review was conducted from 2020 to 2023, utilizing databases such as PubMed, Scopus, and Web of Science. The review analyzed existing literature on the misuse patterns of specific OTC medications, associated psychopathological effects, and molecular mechanisms that facilitate their recreational use.

Results: The findings indicate a significant prevalence of misuse among adolescents and young adults, often characterized by unconventional administration methods and concurrent use with other substances. Key substances implicated in misuse include DXM, DPH, and codeine-based cough preparations. The demographic most affected includes males with a history of substance use disorders and psychiatric conditions. The study highlights the complexities of OTC misuse, including the social acceptability of these substances compared to illicit drugs.

Conclusion: The misuse of OTC medications poses a critical public health challenge, with implications for drug-related toxicity, addiction, and mortality. The COVID-19 pandemic has exacerbated these trends, necessitating the development of targeted prevention strategies and public health interventions to mitigate misuse. Increased awareness and monitoring are essential to address the growing problem of OTC medication abuse.

Keywords: Over-the-Counter Medications, Misuse, Dextromethorphan, Substance Abuse, Public Health

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1. Introduction

Over-the-counter (OTC) medications, usually regarded as safe, are obtainable without a prescription and may be immediately acquired from pharmacies or shops (1, 2). Over-the-counter medications are designed to address a range of ailments and symptoms, such as pain, coughs, colds, diarrhea, and nausea. The availability of OTC medications, although promoting self-care, has fostered a public impression of safety and a diminished understanding of their potential for abuse, dependency, and injury (3–6). Certain OTC medications include active components that may be misused when taken in doses beyond the permitted levels and are gaining popularity for their potential to be diverted for the attainment of central psychoactive effects. At now, there is little evidence about the incidence of over-the-counter usage, abuse, and dependency (8–10, 12).

The existing deficiency in information may be partially attributed to inadequate sales monitoring resulting from the advantageous legal position of over-the-counter products. The practice known as "pharming" necessitates attention at several levels due to a rise in treatment admissions, hazardous behaviors, increased emergency department visits, drug-related fatalities, and overdoses. The most implicated substances include specific cough suppressants, sleep aids, and antihistamines, which may sometimes be used in conjunction with other recreational psychotropics, prescription medications, and/or alcohol (17, 18).

The abuse of OTC medications is seen as more socially acceptable, less stigmatizing, and safer than the consumption of illegal narcotics, partly owing to its probable undetectability in conventional drug screenings. The use of OTC medications may include snorting or injecting the powdered form of crushed tablets to enhance the drug's effects or eating these substances for non-therapeutic purposes. Dextromethorphan (DXM) and codeine-based cough mixtures may be abused at elevated doses for recreational or euphoric effects; in contrast, loperamide is sometimes consumed to self-medicate withdrawal symptoms. The abuse of OTC medications is linked to major drug interactions, physical and mental health consequences, individual variability in responses, and considerable socioeconomic implications on users, their families, and the broader society (13–15). At now, the majority of data about OTC misuse is derived from clinical records (such as case reports and case series) and surveys.

The present review sought to (i) analyze the existing literature on the misuse of over-the-counter (OTC) medications, specifically focusing on antihistamines such as diphenhydramine (DPH), promethazine, chlorpheniramine, and dimenhydrinate (DH); cough preparations containing DXM and codeine; and the nasal decongestant pseudoephedrine; (ii) delineate patterns of OTC misuse, associated psychopathological effects, and resultant harms; and (iii) enhance comprehension of the psychotropic molecular mechanisms that facilitate their recreational use.

2. Methods

An organized electronic search was performed from2020 to 2023, using the following scientific databases without a specified timeframe: PubMed, Scopus, and Web of Science (WoS).

3. Themes And Data About the Misuse and Abuse of Certain Over-The-Counter Medications

This systematic review has shown several themes and data about the misuse and abuse of certain over-the-counter medications, including DXM, DPH, DH, codeine-based cough syrups, promethazine, and pseudoephedrine. Their potential for abuse may be more pronounced in teenagers and young adults (10, 12). OTC recreational use was correlated with elevated dosages (16-29); unconventional methods of administration (e.g., snorting; IM; IV; 30-32); and the concurrent consumption of both legal (e.g., alcohol, prescription opioids, benzodiazepines, other OTCs; 25, 33-36) and illegal (e.g., cannabis, cocaine, ketamine, etc.) substances (30, 31, 34, 35). OTC medications were acquired via different channels, including family and friends, multiple physician prescriptions, illicit internet pharmacies, and theft from hospitals, houses,

and pharmacies. DXM tablets branded as “Snurf” were reportedly obtained online and advertised as a legal high (37).

Two primary populations of OTC misusers were identified: (a) individuals with pre-existing health conditions and/or psychiatric disorders who developed dependence on their prescription/OTC medications due to prolonged or excessive use, such as DXM-based cough mixtures initially prescribed for sinusitis, cough, or nasal congestion, which were subsequently used for extended periods at elevated dosages. Additional instances encompass DH prescribed for emesis during pregnancy, subsequently maintained for 12 years at an elevated dosage without a prescription (38), DPH usage commenced to alleviate initial insomnia and then persisted for 6 months at doses reaching 1,600 mg daily (39), and pseudoephedrine self-administered for weight loss, ultimately leading to addiction (40); (b) individuals, including substance abusers, not undergoing treatment for a medical disorder or illness, who may have initiated misuse or abuse of OTC medications for recreational purposes (36, 40-42).

Among the n = 185 OTC misusers documented in case reports and series surveys (24, 25, 43-47), males were the predominant demographic (F/M = 51/134), with a history of substance use disorder noted in 53 individuals (53/185 = 28.6%). A variety of psychiatric diagnoses were identified (45/185 misusers, 24.3%), encompassing mood disorders (e.g., bipolar disorder, depression, dysthymia; N = 26), anxiety disorders (e.g., adjustment disorder, anxiety; N = 5), psychotic disorders (e.g., schizoaffective disorder, schizophrenia, psychosis, delusional disorder; N = 11), attention deficit hyperactivity disorder (ADHD; N = 1), eating disorders (e.g., bulimia; N = 1), and personality disorders (e.g., dependent personality disorder; N = 1). Concerning the results, the majority of documented cases exhibited complete recovery post-hospitalization, with interventions being either supportive (32, 44–46) or symptomatic, the latter involving benzodiazepines and antipsychotics (25, 27, 28, 43, 47, 48). A comprehensive detoxification protocol was documented in instances of dependence and withdrawal (17); notable examples included buprenorphine at 2 mg/day for the management of acute opiate (codeine) withdrawal symptoms, naltrexone utilized as a relapse prevention strategy for DXM dependence, and topiramate administered for alleviating DXM cravings. Certain patients need particular interventions in the Emergency Unit (49). It has been proposed that drug use treatment would be enhanced by counseling, behavioral therapy support, and rehabilitation to more effectively address drug cravings. OTC-related deaths were associated with either instances of very high doses (24, 31) or with suicide/self-harm (31).

The cough suppressant DXM emerged as the most often abused over-the-counter medication owing to its dose-dependent sedative, dissociative, and stimulant effects (16, 118–120). DXM's psychotropic effects primarily stem from its active metabolite, dextrorphan, which, when administered in high doses, antagonizes N-methyl-D-aspartate (NMDA) receptors, thereby modulating excitatory neurotransmission; this leads to the manifestation of distinct dissociative, ketamine-like experiences (19, 25, 31). The effects are contingent upon various factors, including an individual's CYP2D6 subtype, body weight, tolerance to DXM, and the concurrent administration of other CYP2D6 substrates, such as antidepressants (fluoxetine, fluvoxamine, nefazodone, paroxetine, sertraline, venlafaxine), antipsychotics (clozapine, haloperidol, risperidone, thioridazine), β-blockers (atenolol, metoprolol, propranolol), antiarrhythmics, and opioid analgesics (codeine, tramadol, and methadone), which may attenuate the rate of DXM metabolism, leading to DXM intoxication.

Chronic DXM usage has been associated with folate deficit due to the recurrent demethylation of DXM, which may result in aberrant folate requirements for methyl group transfer (26, 39). Furthermore, instances of dental caries were linked to the elevated syrup content in cough preparations (26). Despite DXM's lack of perceived addictive qualities, susceptible people may swiftly acquire tolerance, dependence, and withdrawal symptoms with prolonged usage. Interactions with other medications may provide synergistic effects; indeed, OTC cough formulations sometimes include, with DXM, other pharmacological medicines such as chlorpheniramine, acetaminophen, or pseudoephedrine, each demonstrating distinct effects. Individuals misusing chlorpheniramine-containing DXM formulations may have anticholinergic signs and symptoms. Conversely, the antipyretic and analgesic acetaminophen induces delayed liver

damage (29). Interactions between DXM and selective serotonin reuptake inhibitors (SSRIs) or monoamine oxidase inhibitors (MAOIs) may increase the risk of serotonin syndrome (50,51).

Despite being often used and usually regarded as harmless, instances of antihistamine misuse and dependency have been documented (52). These compounds were first promoted for their antiallergic effects and are now used as sleep aids. The toxicity of antihistamines seems to be clinically associated with antagonism of acetylcholine in both central and peripheral systems. Moreover, owing to many possible modes of action, DPH (e.g., the antihistamine component of DH) might abruptly inhibit the cell membrane pump mechanism of central 5-hydroxytryptophan and peripheral noradrenaline neurons, resulting in the euphoria experienced by some users. At elevated doses and in conjunction with other substances (e.g., alcohol, cannabis, and stimulants), DPH and DH may be used to elicit a stimulant effect. Documented instances of DPH dependency have emerged from prolonged use of substantial dosages (often exceeding 1,000 mg/day).

Gradual tapering has been reported to mitigate withdrawal symptoms (17). In contrast, promethazine is used in cough syrups for its antihistaminic, antiemetic, and sedative properties, sometimes combined with codeine in prevalent cough suppressants; its potential for misuse seems linked to its tranquilizing and sedative effects, as well as the amplification of other concurrently taken medications. The recreational use of promethazine combined with a soft drink and/or alcohol, sometimes referred to as "purple drank," is now favored by adolescents for its euphoric effects and widespread availability. Promethazine has been documented among substance use disorder clients and is misappropriated as a replacement for another drug or to enhance the effects of insufficient dose (i.e., to postpone the beginning of opioid withdrawal or to amplify the sedative effects of benzodiazepines/Z-drugs) (13, 19, 20). An overdose of promethazine is linked to antimuscarinic delirium, agitation, and neuroleptic malignant syndrome (33). Scott et al. (53) documented a promethazine-induced delirium that was managed with intravenous physostigmine, which counteracted both central and peripheral anticholinergic effects, akin to a polydrug overdose resulting from DPH consumption (48). Chlorpheniramine serves as an economical sleep aid and/or anxiolytic owing to its antimuscarinic characteristics; its misuse has been associated with euphoric sensations, which perpetuates habitual use and the potential for drug dependency. It may, however, be linked to psychotic symptoms in susceptible persons, such as those with mental problems or those concurrently misusing other substances.

Codeine was identified in the context of misuse involving codeine-based cough and cold medications and/or co-ingested with other drugs, such as DXM, DPH, ephedrine, pseudoephedrine, methyl ephedrine, chlorpheniramine, promethazine, and caffeine (26, 27, 34). Codeine is a natural isomer of methylated morphine and, like DXM, functions as a prodrug, necessitating metabolic activation by O-demethylation to morphine by CYP2D6. Consequently, the effects of codeine are linked to CYP2D6 metabolism; for instance, ultrarapid CYP2D6 metabolizers generate an excessive quantity of morphine, leading to potentially fatal opioid poisoning. The recreational usage is associated with mu receptor agonism and the subjective experiences of pleasure, exhilaration, analgesia, and "liking" (54). Codeine poisoning manifests as respiratory depression and profound somnolence, potentially advancing to stupor or coma; in instances of severe overdose, fatality may ensue. Unique codeine administration methods have been documented, such as a misuser discovering online how to extract the codeine base using a technique known as cold water extraction (CWE) for subsequent injection. The habitual use of codeine is outlined, along with the development of tolerance and dependency (49).

Ephedrine and its stereoisomer pseudoephedrine, documented as substances of abuse both independently and in conjunction with coingestants, are classified as sympathomimetic agents that stimulate alpha- and beta-adrenergic receptors. Ephedrine is shown to facilitate weight reduction and improve athletic performance; both pseudoephedrine and ephedrine have been noted for their illegal usage in methamphetamine manufacturing (55). The abuse was linked to large dosages and intravenous administration (56). Dependence difficulties have been documented (57).

4. Constraints

The literature on prescription drug misuse presents challenges due to its heterogeneity and the difficulties in identifying misuse practices; interpretation was more straightforward for cases reported by healthcare professionals requiring intervention, as well as information from the National/Regional Poison Data System (57), among others. The UNODC defines the misuse of medicines as "the problematic consumption outside of acceptable medical practice or medical guidelines, involving self-medication at excessive doses and for prolonged durations, for intoxicating purposes, and when the risks and adverse consequences surpass the benefits" (8–11). Nonetheless, variations and inconsistencies in terminology regarding the OTC phenomenon were noted; this usage was termed non-medical use, problematic use, harmful use, recreational use, self-medication, or inappropriate use, raising doubts about the existence of a consensus on the adverse effects (i.e., problems, harm) associated with OTC use. Indeed, various phrases may not necessarily pertain to the same topic (8).

5. Conclusions

The recent comprehensive analysis indicated that the abuse of over-the-counter medications is an increasingly significant health concern linked to possible effects, such as drug-related toxicity, addiction, and mortality. Currently, the CoViD-19 pandemic has probably contributed to the prevalence of these misuse activities, since an increasing number of users have shifted from illicit narcotics to prescription and over-the-counter medicines. OTC medicines are readily available and seen as reasonably safe due to their favorable legal position, therefore embraced in a "pill-popping culture" (11). There is a need for both the formulation of ad hoc treatment recommendations and the strategizing of prophylactic actions. These efforts should focus on implementing several related concerns, including schedule modifications, adequate monitoring, improved detection of abuse in clinical and pharmacy practices, and the promotion of public health awareness programs (9, 11, 16). For instance, in response to the recent increase in opioid misuse and associated overdose fatalities globally, initiatives are concentrating on enhancing public health monitoring and restricting opioid prescriptions.

The misuse of codeine-containing goods may be exacerbated by their broad availability; thus, upscheduling and pharmacy-based interventions aimed at consumers might restrict the acquisition of codeine products without a prescription. The recent launch of novel over-the-counter combinations with non-opioid ingredients may provide a safer alternative to these often abused drugs (58). The antidiarrheal loperamide, identified as being misused at elevated dosages and linked to cardiotoxicity, prompted the Food and Drug Administration (FDA) to endorse modifications to its packaging. These changes restrict each carton to a maximum of 48 mg of loperamide and mandate that tablets and capsules be packaged in individual doses (59).

A diverse array of professionals must engage in addressing the issues of OTC misuse, particularly physicians, notably general practitioners (GPs), who can assist OTC misusers in the early identification of drug-related problems and refer them to suitable services (e.g., mental health or addiction services). They should also monitor rapid increases in medication requirements or frequent, unscheduled refill requests, as well as detect potential "doctor shopping" behaviors. Medical practitioners will persist in their responsibility to educate patients on the proper use of pharmaceuticals, adhering to prescribed guidelines, and recognizing possible interactions with other legal or illegal substances (11, 16, 18). Pharmacists must be vigilant for prescription falsifications or changes, since they are at the forefront of identifying prescription drug misuse problems. Furthermore, prescription drug monitoring tools may aid healthcare workers in recognizing individuals obtaining prescriptions from various sources (11, 13, 16–18).

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الاتجاهات المتصاعدة في إساءة استخدام الأدوية التي تُصرف دون وصفة طبية: مراجعة شاملة

الملخص

الخلفية :تُعتبر الأدوية التي تُصرف دون وصفة طبية (OTC) آمنة وسهلة الوصول بالنسبة للجمهور، ومع ذلك، فإن إساءة استخدامها وإدمانها أصبحت مصدر قلق متزايد. وعلى الرغم من أن هذه الأدوية مخصصة لعلاج الأمراض الشائعة، إلا أن احتمالية التبعية والآثار الضارة لها غالبًا ما يتم التقليل من شأنها. تستعرض هذه المراجعة الاتجاهات المتعلقة بإساءة استخدام الأدوية التي تُصرف دون وصفة طبية، مع التركيز على مواد مثل ديكستروميثورفان(DXM) ، وديفينهيدرامين(DPH) ، وكوديين.

الطرق :تم إجراء مراجعة منهجية للفترة بين 2020 و2023، باستخدام قواعد بيانات مثل PubMed و Scopusو .Web of Scienceحللت المراجعة الأدبيات الموجودة حول أنماط إساءة استخدام بعض الأدوية التي تُصرف دون وصفة طبية، والآثار النفسية المرتبطة بها، والآليات الجزيئية التي تُسهل استخدامها الترفيهي.

النتائج :تشير النتائج إلى انتشار كبير لإساءة استخدام هذه الأدوية بين المراهقين والشباب، وغالبًا ما يتسم ذلك بطرق غير تقليدية للإعطاء واستخدامها مع مواد أخرى. تشمل المواد الرئيسية التي يتم إساءة استخدامها DXM و DPHومستحضرات السعال التي تحتوي على الكوديين. وتُظهر النتائج أن الفئات الديموغرافية الأكثر تأثرًا تشمل الذكور الذين لديهم تاريخ من اضطرابات تعاطي المخدرات والحالات النفسية. وتسلط الدراسة الضوء على تعقيدات إساءة استخدام الأدوية التي تُصرف دون وصفة طبية، بما في ذلك القبول الاجتماعي لهذه المواد مقارنةً بالمخدرات غير القانونية.

الاستنتاج :تشكل إساءة استخدام الأدوية التي تُصرف دون وصفة طبية تحديًا خطيرًا للصحة العامة، مع آثار تتعلق بالتسمم الدوائي والإدمان والوفيات. وقد تفاقمت هذه الاتجاهات خلال جائحةCOVID-19 ، مما يتطلب تطوير استراتيجيات وقائية محددة وتدخلات صحية عامة للحد من إساءة الاستخدام. يُعد تعزيز الوعي والمراقبة أمرًا ضروريًا لمعالجة المشكلة المتزايدة لإساءة استخدام الأدوية التي تُصرف دون وصفة طبية.

الكلمات المفتاحية :الأدوية التي تُصرف دون وصفة طبية، إساءة الاستخدام، ديكستروميثورفان، تعاطي المخدرات، الصحة العامة.