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Review

Abuse of Dextromethorphan, Carbamazepine, and Naphazoline

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Abstract: The misuse and abuse of over-the-counter (OTC) and prescription medications pose significant public health concerns. Among these, Dextromethorphan (DXM), Carbamazepine, and Naphazoline have gained attention due to their increasing non-medical use. DXM, a common cough suppressant, is abused for its dissociative and euphoric effects, leading to dependency and severe health risks. Carbamazepine, typically prescribed for epilepsy and bipolar disorder, has also shown potential for abuse due to its euphorigenic properties. Similarly, Naphazoline, an ophthalmic vasoconstrictor, has been reported as a substance of misuse, with users seeking its psychoactive effects. Factors contributing to this trend include the widespread availability, affordability, and perceived safety of these medications. Additionally, the lack of regulation and monitoring in pharmacies exacerbates the issue. This review highlights the patterns, risks, and implications of the abuse of these medications, calling for stricter regulations, increased awareness, and better pharmacovigilance practices. Addressing these concerns requires a multi-faceted approach, including policy changes, improved pharmacist training, and public education on the dangers of OTC and prescription drug abuse.

Keywords: dextromethorphan abuse; carbamazepine misuse; naphazoline dependence; OTC drug abuse; pharmacovigilance

Introduction

When a prescription or over-the-counter (OTC) drug is used for purposes other than those listed in the prescribing information or on the packaging label, it is said to be used nonmedically (DuPont, 2006). Abuse of these drugs is a widespread problem in different countries. Prescription drugs are those that a pharmacist is allowed to dispense after receiving a prescription from a doctor, dentist, or other healthcare professional who is legally permitted to write prescriptions. OTC drugs are pharmaceuticals available on the shelves of pharmacies that do not need a prescription (G. B. Collins & McAllister, 2006) {Shaqfeh, 2024 #1635}.

Over the years, there has been a steady increase in the intentional drug abuse of OTC and prescribed medications. OTC medicine abuse has become more widely recognized in recent years among patients, particularly teenagers and young adults (Volkow, 2010). The use of a medicine for psychotropic effects rather than for its prescribed use is known as abuse. OTC drugs have no age restriction or quantity limit and are generally accessible, affordable, and legal, which makes them easy to abuse. Many patients believe that OTC pharmaceuticals are safer than illegal or prescription drugs (America, 2005). OTC pharmaceuticals can be abused by those who abuse prescription drugs or illicit substances. In situations where other substances are not available, OTC drugs can be substituted (Abbott & Fraser, 1998).

It is important to distinguish between terminology used to describe prescription or OTC drug misuse and abuse.

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Misuse was previously described as the improper use of OTC medication for a legitimate medical purpose, such as taking a higher dose than advised or using it for an extended period of time (Shei et al., 2015). On the other hand, the definition of abuse is "any intentional, non-therapeutic use of a drug product or substance, even once, with the goal of attaining a desired psychological or physiological effect " (Al-Khalaileh, Abu-Farha, Wazaify, & Van Hout, 2019).

The frequent use of a medication with the desire to continue using it despite its harmful effects and the effort to voluntarily stop using it or change how you use it are further definitions of dependence and addiction (Organization, 1994). It should be noted that abusing medications, like opiates, can lead to dependence for both legal and illegal reasons (Nielsen & Van Hout, 2017). Additionally, some people have documented a link between the usage of illegal substances and OTC medication consumption (Levine, 2007). Research demonstrates that the improper use of OTC medications can have negative effects on users and their families that might be physical, psychological, or financial (Cooper, 2013b).

Over the previous ten years, there has been growing concern about the diversion and non-medical use of OTC medications. Most likely a result of OTC medicines' perceptions as "safer," less stigmatizing, and more socially acceptable than illegal substances. Medications that can be purchased OTC and used recreationally include cough syrups with codeine or dextromethorphan, some decongestants (like pseudoephedrine), antidiarrheal medications (like loperamide), and specific antihistamines (like promethazine, chlorphenamine, and diphenhydramine). These usage patterns are usually linked to alcohol and illicit drug use (Zaremba, Serafin, & Kleczkowska, 2023).

Previous studies conducted in Jordan reported that cold and cough preparations, especially those containing Dextromethorphan, systemic nasal decongestants, analgesics, antihistamines like chlorphenamine and diphenhydramine, laxatives such as Loperamide, and ophthalmic products that include drugs that a community pharmacist prescribes to treat minor conditions (such as sympathomimetics like naphazoline for itchy red eyes or antihistamines like antazoline for allergic conjunctivitis) are the most common OTC medicines that abused in Jordan (Al-Khalaileh et al., 2019; Albsoul-Younes, Wazaify, Yousef, & Tahaineh, 2010).

Recently, the demand for some products that contain Carbamazepine as an active ingredient has been increased. This medicine is used to treat medical conditions related to seizures, epilepsy, neuropathic pain. This review will discuss the abuse of Carbamazepine, Dextromethorphan, and Naphazoline and the documentation of information about suspected abuse of these drugs.

Most people who abuse the drug typically do so in combination with an addictive drug or alcohol. In some cases, when Carbamazepine is misused, users become addicted to it is addictive. After being reported often in case reports, though, these people have some success in controlling their own behavior {Soyka, 2006 #1637}. A drug that can cause dizziness, drowsiness and a sense of mild euphoria at high doses is sure to appeal to people for recreation. In addition, young adults and adolescents have reportedly been known to experiment with Carbamazepine, usually in conjunction with another substance, all in search of its tranquilizing or psychoactive properties. However, excessive consumption carries great health risks including toxicity, respiratory depression and life-threatening neurologic effects. There are reports that some individuals intentionally take many tablets of carbamazepine when the object is self-harm or for recreational use, making the situation worse {Kumar, 2017 #1638}. The misuse potential of Carbamazepine is not recognized by healthcare professionals and pharmacists. The government needs to conduct public education and do a better job of monitoring pharmacists, so as to prevent abuses of growing numbers.

Dextromethorphan

DXM was approved as an OTC antitussive by the Food and Drug Administration (FDA) of the United States in 1958. After the FDA evaluated the available safety and efficacy information on the medication in the 1970s, it was widely believed to be both safe and effective (Spangler, Loyd, & Skor, 2016). The Drug Enforcement Administration requested in 2007 that the FDA hold a meeting of its advisory committee to discuss whether dextromethorphan should be recommended for scheduling

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under the Controlled Substances Act. The meeting was held in order to provide a scientific and medical evaluation of dextromethorphan and its potential for abuse.

Naphazoline

Over the last five years, Jordan has seen an increase in the abuse of ophthalmic medicines, many of which can be purchased over the counter and used to experience mind-altering effects. Ophthalmic preparations including anticholinergics, antihistamines, and/or decongestants, such as cyclopentolate, naphazoline, and antazoline, are the most frequently reported ones (Al-Khalaileh et al., 2019; Al-Khalaileh, Wazaify, & Van Hout, 2018; Wazaify, Alali, Yousef, & Qammaz, 2017). Many reported cases of Naphazoline abuse. This is because Naphazoline is a peripherally acting alpha-adrenergic agonist, which probably has some addictive potential.

Carbamazepine

The FDA licensed carbamazepine for the treatment of trigeminal neuralgia, psychomotor and grand mal seizures, as well as manic and mixed episodes of bipolar I disorder (Post, Ketter, Uhde, & Ballenger, 2007). Data on carbamazepine addiction and abuse are limited in the prior literature, and the medication is not recognized as having the potential for abuse. However, many case studies mentioned in the literature review alert us to the possibility of carbamazepine abuse {Shaqfeh, 2024 #1635}.

Prescribed and OTC Drugs

Prescription drugs are those that a pharmacist will dispense after receiving a prescription from a doctor, dentist, or other healthcare professional with the legal authority to provide them (Lessenger & Feinberg, 2008). Non-prescription drugs (NPDs), commonly referred to as OTC drugs, are drugs that are available from licensed medical professionals without a prescription (Nomura, Kitagawa, Yuda, & Takano-Ohmuro, 2016). OTC medications are accessible without a prescription and can be obtained directly from associated pharmacies/stores because they are typically regarded as safe (Cohen et al., 2020; Schifano et al., 2021). To treat a variety of minor disorders, OTC medications are widely used (Algarni, Hadi, Yahyouche, Mahmood, & Jalal, 2021).

OTC medications are intended for treating a range of conditions and symptoms, such as pain, colds and flu, diarrhea, nausea, and more (Cooper, 2013a). OTC medications encourage self-care, which benefits patients as well as the healthcare system by decreasing the financial burden on other healthcare facilities (Nomura et al., 2016). On the other hand, prescription and nonprescription (or so-called OTC) pharmacological preparations are now more widely available, which has led to a significant rise in their nonmedical usage (McCabe, Teter, & Boyd, 2006).

In Jordan, OTC medications are recognized as an essential component of healthcare (Albsoul-Younes, Tahaineh, & Moumani, 2011). and the pharmaceutical industry has seen a steady rise in the usage of OTC products (Ravichandran & Basavareddy, 2016). In Jordan, community pharmacies are the primary healthcare facilities that are the most reachable (Wazaify, Shields, Hughes, & McElnay, 2005).

The accessibility to OTC drugs has impacted the public's perception of safety and a lack of information regarding their potential for abuse, dependence, and injury while encouraging self-care (Cooper, 2013b). Therefore, a risk could be obtained from utilizing OTC medications (Wazaify et al., 2005). These include inaccurate self-diagnosis, insufficient dosage, problems with addiction after long-term use, unfavorable drug reactions, and drug interactions (Bond & Hannaford, 2003; Hughes, McElnay, & Fleming, 2001). Furthermore, the active components in certain OTC medications have the potential to be abused at doses higher than those advised (Abuse, 2017). The National Institute on Drug Abuse (NIDA) reports that prescription and OTC medicines are the most frequently abused substances among Americans aged 14 and older, followed by alcohol and marijuana ((NIDA). 2014).

Abuse of OTC drugs

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The use of non-prescription drugs for purposes other than those listed on the label or in the prescribed information is a broad definition of non-prescription drug abuse (Lessenger & Feinberg, 2008). The use of stimulants like caffeine and nicotine, as well as drugs that may have hallucinogenic effects when taken in high doses, like antihistamines and cough suppressants, as well as self-medication for non-label indications and intentional overdose, are examples of behaviors that fall under this category (Conca & Worthen, 2012).

OTC abuse has also been linked to notable drug combinations, impacts on physical and mental health, individual variations in reactions, and considerable socioeconomic consequences on users, their families, and the larger community (Chiappini & Schifano, 2020). Also, the abuse of OTC drugs and the usage of illicit substances have been linked in some people, according to reports (Levine, 2007). Health-related quality of life (HRQoL) was generally reduced, hospitalization was required, and mortality was a common consequence of misuse, abuse, and dependency on OTC medications (Algarni et al., 2021). However, Problematic use of OTC medications can increase the risk of suicide overdose deaths (Algarni et al., 2021). For example, Loperamide, dextromethorphan, and codeine-based analgesics have been associated with fatalities in those who ingested high dosages on purpose (Hopkins, Dobbin, & Pilgrim, 2018; Karami, Major, Calderon, & McAninch, 2018; Schifano & Chiappini, 2018). According to a study by (Abazid, Abu-Farha, Alsayed, & Barakat, 2023) when participants in a Syrian rehabilitation center were asked the reason they abuse drugs, they said that it helped them deal with everyday issues, gave them the delusion that they were living in a dream world, and allowed them to work for extended periods time without getting tired. Additionally, participants thought that drug usage does not result in addiction (Abazid et al., 2023).

A person who wants to abuse an OTC drug may visit multiple pharmacies for the same drug or get it from the same pharmacy at various periods. Additionally, the absence of proactive steps from pharmacists to monitor patients' usage of OTC medications has created numerous potentials for abuse (Sansgiry, Bhansali, Bapat, & Xu, 2016). Pharmacists are frequently overworked, and the ongoing, stressful workload of filling prescriptions lessens their capacity to become pharmacovigilant.

Commonly Abused OTC Medications

The most often reported non-prescription medications of abuse were generally cough and cold remedies, followed by systemic nasal decongestants. Other drugs in decreasing order included basic analgesics, antihistamines, laxatives, and alcohol (Albsoul-Younes et al., 2010).

Pregabalin (an anti-epileptic medicine), various ophthalmic preparations (cyclopentolate, naphazoline, and antazoline), anticholinergic anti-Parkinson pharmaceuticals, and misoprostol were the least cited prescription drugs on the list of drugs reported as being abused (Albsoul-Younes et al., 2010).

Another study conducted in Saudi Arabia at Saudi University among female students by (Dabbagh et al., 2021), showed that Decongestants (like pseudoephedrine and chlorpheniramine), cough suppressants (like Dextromethorphan), OTC sedatives (like diphenhydramine), and antiemetics (such as dimenhydrinate) are some of the frequently abused OTC medications with an addictive potential (Dabbagh et al., 2021).

Other studies showed that the most commonly abused OTC products include cough and cold treatments with dextromethorphan, sympathomimetic drugs like pseudoephedrine, and first-generation antihistamines like diphenhydramine and chlorpheniramine (Cooper, 2013b).

The most commonly reported OTC drugs abused in Jordan are cough and cold remedies such as Dextromethorphan, ophthalmic solutions such as Naphazoline, and antiepileptic drugs such as carbamazepine which are the top OTC products reported to be abused in many previous studies. The abuse of Carbamazepine has been noticed recently; therefore, this study will investigate the abuse of each of these OTC medications.

In Jordan, it is possible to purchase ophthalmic products without a prescription that contain drugs used to treat minor conditions that can be identified in a community pharmacy, such as

 doi:10.20944/preprints202504.0542.v1

antihistamines for allergic conjunctivitis like antazoline or sympathomimetics for itchy red eyes like naphazoline (Al-Khalaileh et al., 2019).

On the other hand, Dextromethorphan which is a cold and cough suppressant remedy, is at the top of abused products and one of the most popular OTC drugs that can be purchased without a prescription in Jordan to be abused.

Dextromethorphan DXM

The most common cough medicine in the United States and other areas of the world is dextromethorphan hydrobromide (DXM, or "robo"), an ingredient in more than 125 OTC cough and cold treatments. DXM is most frequently found in "extra-strength" cough syrup, with a dosage of 3 mg per 1 ml of syrup. The suggested dosage for treating coughs is 1/6 to 1/3 of an ounce of medication containing 15 mg to 30 mg of DXM. Similar to phencyclidine and ketamine, it has a dissociative effect at larger doses (NATIONALINSTITUTEONDR, 2001). Thus, it can result in a false-positive phencyclidine screening test in a urine sample. DXM is the methylated dextro-isomer of levorphanol. Also, it is a semi-synthetic morphine derivative and a codeine analog.

The toxic effects of an overdose are added to those of DXM by itself. Unknown numbers of teenagers in the United States and Europe take acute megadoses of dextromethorphan, which are doses 5 to 10 times higher than those advised for treating irritating nonproductive coughs (Schwartz, 2005). DXM has surprisingly few side effects at recommended dosages and when taken within four-hour intervals, and it is a powerful cough suppressant. However, people who take large doses of the medication or take it more frequently than advised may experience various physical and psychoactive side effects depending on the dosage taken (AmiricanAddictionCenter).

Mechanism of Action of DXM

DXM's activity on multiple channels and receptors results in a variety of pharmacologic consequences. It is thought that DXM's well-known antitussive actions come from its stimulation of sigma-1 receptors (r1R) and antagonistic effects on N-methyl-D-aspartate (NMDA) (Brown, Fezoui, Selig, Schwartz, & Ellis, 2004).

Psychosis, dependency, and physical withdrawal can all be brought on by DXM. It possesses particular sigma-1 opioidergic and serotonergic characteristics (Lessenger & Feinberg, 2008). Cytochrome P450 (isoenzyme CYP2D6) is principally responsible for the metabolism of DXM. The active metabolite of DXM, dextrorphan, has comparable qualities but is a stronger N-methyl-D-aspartic acid receptor antagonist and a weaker sigma opioid receptor agonist. DXM and its metabolite, dextrorphan, exhibit particular biological characteristics of addiction, such as tolerance, and can cause particular psychological consequences. Even at greater levels, there are more severe effects that could be fatal. Drug abusers seek out the dissociative state that dextrorphan's intoxication effects, which have pharmacodynamic features (Lessenger & Feinberg, 2008). Withdrawal is manifested by a profound depression (Miller, 2005). DXM has a half-life (t1/2) of 1.4-3.9 hours as a parent molecule and 3.4-5.6 hours as dextrophan, with an average onset of action of 15 to 30 minutes (S. R. Collins, 2018). The CYP2D6 enzyme activity of the individual affects the duration of action, which is 5–6 hours (Brown et al., 2004).

Abuse of DXM

Between 2004 and 2010, the Substance Abuse and Mental Health Services Administration (SAMHSA) reports an increase in the frequency of admissions to emergency rooms related to antitussive medications like DXM; however, rates leveled off in 2011.

Euphoria and dissociative hallucinations are just a couple of the clinical signs and symptoms that DXM has the potential to produce. These effects are likely mediated by a rather nonselective action on serotonin reuptake inhibition and r1 opioid, a3b4 nicotinic, and NMDA receptors (Logan, 2009; Logan, Goldfogel, Hamilton, & Kuhlman, 2009; Logan et al., 2012).

 doi:10.20944/preprints202504.0542.v1

According to the American Addiction Center, when people consume 100–200 mg of DXM, they reach the first plateau of usage, also known as the first level. Users will start to feel stimulant effects at this dosage.

At doses of 200–400 mg, the second level, or second plateau, appears. People will experience euphoria and visual hallucinations at this dosage.

When people take 300–600 mg of DXM, the third plateau of abuse's consequences take place. Along with feelings of euphoria and hallucinations, people with this condition often struggle with balance, motor coordination, and visual perception, which increases the risk of accidents.

The fourth plateau, which happens when people consume more than 600 mg of DXM, represents the highest level of abuse. At this concentration, users suffer intense sedation, considerable hallucinations, and dissociation effects resembling those of extremely dangerous substances like phencyclidine PCP, and ketamine. People may start to feel as though they are leaving their bodies and that everything is not real, which can cause serious problems with judgment.

Young adults and teenagers are both frequently mentioned in allegations of abuse (Spangler et al., 2016). A total of 72,260 calls were reported as purposeful abuse of a DXM cough and cold product between 2000 and 2015, with a peak in 2006, according to data from the American Association of Poison Control Centers (Karami et al., 2018).

Side Effects of DXM Abuse

A DXM overdose can result in euphoria, hallucinations, disorientation, confusion, poor coordination, and dissociative sedation (Karami et al., 2018; Schwartz, 2005). Also, symptoms of the central nervous system and the autonomic nervous system, such as ataxia, somnolence, mydriasis, tachycardia, respiratory depression, and hypertension, are common manifestations of adverse events (Paul et al., 2017; Romanelli & Smith, 2009). Serotonergic effects can occur from agonist effects at serotonin receptors, whereas adrenergic effects (such as diaphoresis and hypertension) can result from dose-related suppression of catecholamine reuptake (Ritter et al., 2020). DXM-containing medications were discovered to induce a psychotic condition (Martinak, Bolis, Black, Fargason, & Birur, 2017; Price & Lebel, 2000).

Only when DXM is utilized appropriately is it safe. However, the primary risk of psychotic symptoms (i.e., mania, psychosis, or hallucinations) should be regarded to be its recreational or recurrent use, especially by teenagers and young adults. In light of this, general practitioners need to advise all patients comprehensively about the possibly severe adverse effects of DXM (Zaremba et al., 2023).

Ophthalmic Solutions

Ophthalmic decongestants sold over the counter are frequently used to treat eye irritation and redness. Alpha-adrenergic, vasoconstrictive amines such as naphazoline, tetrahydrozoline, or phenylephrine are the main active ingredient in these eyedrops; some preparations additionally contain an antihistamine for type 1 histamine-receptor blocking.

In 54 papers from 54 various countries around the world (including Brazil, the USA, Italy, Turkey, etc.), the abuse of topical ophthalmic anesthetics was detailed in a review. It emphasized that allegations of such abuse had been made in case series, case reports, and reviews and had primarily concentrated on the product's toxicity and associated consequences (Al-Khalaileh et al., 2018). In Jordan, it is possible to buy ophthalmic products without a prescription that contain drugs used to treat minor conditions that can be identified in a local pharmacy, such as antihistamines for allergic conjunctivitis like antazoline or sympathomimetics for itchy red eyes like naphazoline (Al-Khalaileh et al., 2019).

Naphazoline

In Jordan, there has been a rise in the abuse of ophthalmic medications, many of which are bought from pharmacies without a prescription and used to experience effects that affect the mental

 doi:10.20944/preprints202504.0542.v1

state (Al-Khalaileh et al., 2019; Al-Khalaileh et al., 2018; Wazaify, Alali, et al., 2017). The ophthalmic preparations that contain anticholinergics, antihistamines, and/or decongestants, such as tropicamide, cyclopentolate, naphazoline, and antazoline, are the most frequently reported ones to be abused (Wazaify, Alali, et al., 2017).

The characteristics of naphazoline are as follows:

(a) it stimulates alpha1- and alpha2-adrenergic receptors;

(b) it causes vasoconstriction (primarily in the kidneys and mucous membranes, which have the highest density of alpha-adrenergic receptors);

(c) it constricts the pupil; and

(d) it has anti-inflammatory (anti-edematous) properties.

Naphazoline (Naphthyzin), a medication used to treat rhinitis, is frequently used orally. Since naphazoline may be purchased over the counter without a prescription, it is not an illegal substance (Skryabin, Vinnikova, Komarov, & Khvan, 2020). Naphazoline, an alpha-adrenergic agonist with peripheral action, has some risk for addiction. The substance causes euphoria, which is similar to the feeling one gets from psychostimulants (Skryabin et al., 2020).

Abuse of Naphazoline

In a case study of Naphazoline abuse reported by (Skryabin et al., 2020) for 23 aged patient who was born in Moscow, he reported that he heard from friends that naphazoline induces happiness and regular sleep and that it is beneficial to "come back to normal" after the "stimulant marathons. The patient tried Naphazoline intravenously but experienced no effects. Then he made the decision to consume it, which resulted in euphoria: "15 cc (1 bottle) was enough to feel high: I felt the unreality of what was happening, relaxation, and odd feelings in the body.

He began ingesting naphazoline. For two months, the dosage was increased to 60 ml (4 bottles) every day. Both by itself and in conjunction with other psychoactive substances, the patient ingested naphazoline. He experienced anxiety, weakness, inner unease, tension, and irritation after stopping Naphazoline (Skryabin et al., 2020). Therefore, according to the case study, Naphazoline, a peripherally acting alpha-adrenergic agonist, probably has some addictive potential.

However, there is obvious evidence that adrenaline regulates the neuronal activity of the midbrain dopamine system, either directly by activating postsynaptic adrenal receptors or indirectly by controlling inputs at presynaptic glutamatergic or GABAergic terminals (Mejias-Aponte, 2016). The ventral tegmental area (VTA) is the area of midbrain dopamine areas that receives the most attention in terms of adrenergic control (Mejias-Aponte, 2016). Although further research is needed, it is probable that the reward linked with naphazoline use results from the activity of dopaminergic neurons from the VTA and enhanced activity in the ventral pallidum, which increases dopamine release.

Prisoline® and Naphcon® abuse had previously been reported in Jordan from the perspective of pharmacists using the cross-sectional survey approach (Wazaify, Abood, Tahaineh, & Albsoul-Younes, 2017; Wazaify & Scott, 2017). However, community pharmacies were not aware of this tendency (Albsoul-Younes et al., 2010) as a less expensive and authorized substitute for other illegal or controlled drugs (Wazaify, Abood, et al., 2017).

Therefore, a study conducted in Jordan by (Al-Khalaileh, Abu-Farha, Van Hout, & Wazaify, 2021) among ophthalmologists to identify the abuse of ophthalmic medications by Jordanians suggests that Prisoline® was the drug of abuse that more than half of the patients consume (n = 73, 53.3%) (Al-Khalaileh et al., 2021).

Only 5/73 (6.8%) physicians were aware that Prisoline® comprised naphazoline and chlorpheniramine maleate, while 22/73 (30.1%) doctors were aware that Naphazoline was the active component of Prisoline (Al-Khalaileh et al., 2021). There have been some reported cases of Prisoline® abuse, although only six out of 73 ophthalmologists (or 8.2%) reported that the medicine was also being used to support addiction (Al-Khalaileh et al., 2021).

 doi:10.20944/preprints202504.0542.v1

Ophthalmologists also reported that the eye drops Naphcon-A® (naphazoline hydrochloride and pheniramine maleate), Apihist® (antazoline sulphate and naphazoline nitrate), and Ophtazoline® (antazoline sulphate and naphazoline nitrate) were potentially addictive (n = 41, 29.9%, n = 25, 18.2%, n = 24, 17.5%, respectively). Naphcon-A® is not used to feed addiction, according to just one ophthalmologist (0.7%) (Al-Khalaileh et al., 2021).

Because of this, regulatory actions are required to manage the abuse of particular ophthalmic products (Prisoline®, and Naphcon-A®) that contain naphazoline as an active ingredient, through a more proactive role of the pharmacist instead of just denying and refusing sale. Additionally, the JFDA and the Jordan Pharmaceutical Association should establish the best practices for managing drug abuse of all varieties, including ophthalmic drugs, in community pharmacies.

Carbamazepine

With a tricyclic structure resembling that of the antidepressant imipramine, Carbamazepine (CBZ) is an iminosilyl anticonvulsant. CBZ has been used as an anticonvulsant, as well as a treatment for acute mania or depression, as well as a preventive measure for bipolar affective disorder and an episode of dyscontrol or violence.

Among the medication's most frequently mentioned benefits is its comparatively low risk of behavioral and cosmetic adverse effects (Johnston & Freeman, 1981). Also, it has been documented that CBZ has positive effects on mood and cognitive abilities (Dodrill & Troupin, 1977; Sillanpaa, 1979).

Neuropathic pain and seizure disorders are common conditions for which CBZ is prescribed (Alrashood, 2016). Off-label, it is used to treat bipolar illness as a second-line medication and in conjunction with an antipsychotic when standard antipsychotic therapy has not worked (Ceron-Litvoc, Soares, Geddes, Litvoc, & Lima, 2009).

Abuse of Carbamazepine

As a tricyclic medication, CBZ can cause euphoria. Individual reports have shown that this is typically reported as a side effect of long-term use (Hosseini & Ahmadi, 2014; Sullivan & Davis, 1997). Nonetheless, physicians have carefully noted in certain case reports that the drug's euphoric effect may contribute to abuse potential (Degenhardt, Stockings, Patton, Hall, & Lynskey, 2016; Sullivan & Davis, 1997). It is not surprising that CBZ may occasionally cause adverse emotional responses as numerous research have demonstrated that it has beneficial mental effects (Silverstein, Parrish, & Johnston, 1982).

To our knowledge, the abuse of CBZ has not been reported so far. Therefore, we can find a limited number of reported cases of CBZ abuse.

One of these cases was reported by (Hosseini & Ahmadi, 2014) for a 43-year-old patient who suffered from bipolar, he was admitted to the hospital many times due to psychological disorders. He has had treatment for the last five years with daily doses of bipyridine TDS, valproate 600, CBZ 1200 mg, and perphenazine 32 mg (Hosseini & Ahmadi, 2014).

With these medications, the patient experienced total remission. Despite being able to regulate his manic symptoms, he raised his CBZ dosage to 1800 mg. For three to four days, he experiences happiness and euphoria, dizziness, and tiredness without any psychotic symptoms or uncontrollable conduct. Three times a day, this mood was experienced. The patient stated that in order to achieve pleasure, he has occasionally taken greater daily doses of CBZ—between 1200 and 1800 mg. On the other hand, he also remarked that the higher dosages made him feel drowsy and disoriented. He claimed to have had a good night's sleep, felt content, and relished his time with his wife and other family members (Hosseini & Ahmadi, 2014).

Another case study was reported by (Xu et al., 2018), in China among Adolescents for CZB abuse. In this study, all available teenage patients who were admitted to the pediatric intensive care unit at Shengjing Hospital, China Medical University, between January 2015 and July 2016 due to CBZ overdose were retrospectively reviewed (Xu et al., 2018). CBZ overdose led to the hospitalization of

 doi:10.20944/preprints202504.0542.v1

all patients. With a medication dosage of at least 1,500 mg, the median dose consumed was 2,000 mg (range 800–5,000 mg) (Xu et al., 2018).

According to self-reported reasons, patients took CBZ for things like being a "cool thing" linked to personal loyalty 41.18% of the admitted cases, a humorous thing which constitutes 23.53% of the cases, and feeling of euphoria after using it repeatedly which involved 23.53% of the reported cases (Xu et al., 2018).

Mechanism of CBZ Euphorigenic Effect

According to Nutt et al., study of the brain mechanisms behind substance abuse and addiction, euphoria is believed to be connected to endogenous release of dopamine and/or opioids (Nutt, Little, Taylor, & Minchin, 1984). There is evidence to suggest that opiate pathways play a role in the euphoric and stimulating effects of ethanol (Shippenberg & Altshuler, 1985). suggesting that endogenous opiate systems may also be influenced by CBZ (Post, 1994; Post, Uhde, & Ballenger, 1984). Thus, it is trustworthy that CBZ enhances ethanol-induced stimulation by means of opiate pathways being activated (Sullivan & Davis, 1997).

It has also been demonstrated that CBZ activates serotonergic and dopaminergic systems, suggesting that the euphorigenic effect may have been caused by CBZ through these mechanisms (Elphick, Yang, & Cowen, 1990).

Conclusion

The problem of misuse and abuse of OTC and prescription drugs, with particular emphasis on Dextromethorphan, Carbamazepine, and Naphazoline, has become increasingly serious, now presenting a major public health challenge. Originally intended for therapeutic use, these drugs have increasingly been diverted into a pop-type high, with particular consequences to health, dependence and, in the worst cases, death. These drugs are easy to get hold due to the lack of regulation and general public unawareness.

The demand for stricter regulatory measures, keener pharmacist vigilance and public education initiatives revealed by this review is what is met by the situation. On the one hand, pharmacists have to be aware of what their responsibility is: by monitoring the pattern of sales, one can identify who might be misusing medications and offer proper counseling. Again, public health campaigns should point out the dangers of self-medication, emphasising that non-medical use of medication may carry serious consequences indeed.

It will take a joint effort by lawmakers, doctors and the public to tackle this issue. By implementing better controls and publicizing warnings to people, the present trend of drug abuse can be slashed. That would be beneficial both for health and lightening the load on health care systems.

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