

Review Article

The effects of trade names on the misuse of some over-the-counter drugs

Luai Z. Hasoun, Heba A. Khader, Ahmad R. Alsayed, Mariam I Shaqfeh, Anas Samara, Malek A. Zihlif

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Abstract

Self-medication and healthcare accessibility depend on over-the-counter (OTC) drugs; nonetheless, their abuse seriously compromises health. The components causing over-the-counter drug abuse—including analgesics including ibuprofen, diclofenac, and acetaminophen—are investigated in this paper. Lack of knowledge of suitable dosages, self-medication practices, and brand names causes confusion which results in negative health effects including gastrointestinal, hepatic, renal, and cardiovascular problems. Because of increased self-medication and false information, the COVID-19 outbreak worsened the abuse of over-the-counter medications. The study highlights the need of patient education, legislative actions, and pharmacist participation to reduce the risks by defining the variations among misuse, abuse, dependence, and addiction. Advocacy for safe and moral use of over-the-counter drugs depends on an all-encompassing approach including legislators, doctors, and public awareness campaigns.

Keywords: OTC drugs; self-medication; drug abuse; patient education; COVID-19; adverse health effects; pharmacist involvement

Luai Z. Hasoun. Biopharmaceutics and Clinical Pharmacy Department, Faculty of Pharmacy, Al-Ahliyya Amman University, Amman-19328, Jordan.

Heba A. Khader. Department of Clinical Pharmacy and Pharmacy Practice, Faculty of Pharmaceutical Sciences, The Hashemite University, Zarqa, Jordan.

Ahmad R. Alsayed*. Department of Clinical Pharmacy and Therapeutics, Applied Science Private University (ASU), Amman, Jordan. a.alsayed.phd@gmail.com

Mariam I Shaqfeh. Department of Pathology Microbiology and Forensic Medicine, School of Medicine, the University of Jordan, Jordan.

Anas Samara. Department of Software Engineering, Bethlehem University, Bethlehem, Palestine.

Malek A. Zihlif. Department of Pharmacology, School of Medicine, The University of Jordan, Amman, Jordan.

INTRODUCTION

Over-the-counter (OTC) medications including analgesics, cold and cough medicines^{1,2} are critical component of Jordanian healthcare system³, and the pharmaceutical market has progressively increased their use⁴. OTC drugs can be bought without a prescription, and have been judged safe and fit for use unlike prescription medicines by health care providers⁵. Millions of people believe that over-the-counter medications are safer than prescribed drugs because if you want them, all you have to do is walk into a drugstore^{6,7}. This misconception leads patients to inadequate self-medication and erroneous self-diagnoses of their diseases⁸. The safety profile of OTC DRUGS is comforting. However, the misuse of medications, which happens when these medications are used incorrectly but for medical purposes despite good intentions, can have negative clinical results⁹. Misuse or abuse of OTC medicines by utilizing an excessive amount of one medication or a wide variety of medications to treat severe illnesses¹⁰ has led to misdiagnosis^{11,12}.

Confusion resulting from similar pharmaceutical names is a major contributing cause of prescription mistakes and possible side effects. Medication names with similar look or phonetics might not always cause brand confusion. This could result from different generic ingredient brands, patients not knowing their medicinal names, or patients not understanding the components of combination drugs¹³.

Drug name confusion can arise from the same medication's availability under several names and formulations¹⁴. Different formulation types may be misinterpreted by the several names used in modified-release formulations, including MR, XL, LA, SR, and Retard¹⁵. Furthermore, uncertainty might result from two different brand names for the same medicine¹⁶.

MISUSE, ABUSE, DEPENDENCE, AND ADDICTION

It is crucial to quickly identify and understand the differences between the concepts of misuse, abuse, dependence, and addiction. There are significant public health issues associated with misuse, abuse, dependence, and addiction. Since they all relate to illegal and inappropriate use of legal drugs including tobacco, alcohol, and prescription medicines, these terms are sometimes used synonymously. Treatment approaches for any problem differ greatly.

Misuse

The term "misuse" refers to the use of an OTC medication for a valid medical reason, albeit in too high dosages or for a length of time longer than advised, as shown by the consumption of painkillers in quantities beyond the indicated amount to cure a headache⁹ or the use of a drug for legitimate medical purposes, but in an incorrect manner, i.e., its use for longer duration than prescribed or in a higher dose than recommended¹⁷.

Abuse

The term "abuse" refers to the non-medical use of a drug⁹, the use



of illegal drugs, or the overuse or inappropriate administration of prescription, over-the-counter, or other drugs for uses other than its intended use. Abuse of substances can cause problems with physical health, mental health, emotional stability, and occupational performance¹⁸. The term “abuse” is used to describe the use of drugs for non-medical purposes, i.e., to experience their mind-altering effects¹⁷.

Dependence

Drug dependence is a long-term, progressive illness marked by severe impairment that is caused by repeated, excessive use of a psychoactive substance. Physiological, psychological, or social dysfunction can all be signs of impairment¹⁹.

Addiction

Addiction is described as a persistent, recurring condition marked by compulsive substance seeking and usage despite negative effects. It is regarded as a brain condition because it involves functional abnormalities in brain circuitry related to reward, stress, and self-control. After a person stops using drugs, the alterations could last for a very long time²⁰.

BRAND NAMES AND OTC ANALGESICS MISUSE

All medications have a generic name as well as perhaps one or more brand names. The pharmaceutical manufacturer chooses the brand name. Having various names for the same drug has occasionally led to mistakes.

Medication misuse can have a significant negative influence on a number of health-related outcomes, including lowered quality of life, problems with public health, and increased financial burdens associated with medical care²¹.

Though generally safe, analgesics are among the most often used and abused medications. Multiple people using different brand analgesics at once causes analgesic nephropathy²². Many children use over-the-counter painkillers, yet many still find it confusing about the differences between brand-name and generic drugs. Particularly with acetaminophen, there were significant information gaps about OTC use, side effects, and contraindications²³.

The Misuse of OTC analgesics

The Misuse of OTC NSAIDs

Non-steroidal anti-inflammatory drugs (NSAIDs) sold over the counter are among the most popular analgesics. The patient is typically unaware of the misuse of these medications, which happens regularly. Acute NSAID overdoses or other major negative consequences might result from improper use²⁴.

Among the most often used treatments worldwide are NSAIDs, which have analgesic, antipyretic, and anti-inflammatory action.

Because of their general safety and efficacy, many NSAIDs—including aspirin and ibuprofen—are available over-the-counter in different countries²⁵. Although NSAIDs are safe and effective when taken in line with medical guidelines, incorrect use may have many negative effects²⁶. Although NSAIDs are safe and effective when used according to medical guidelines, inappropriate use can have a variety of negative effects²⁷⁻³¹ including overdosing, mortality, gastrotoxicity, hepatotoxicity, nephrotoxicity, cardiotoxicity, and nephrotoxicity. This puts a burden on healthcare systems³².

Essential is bettering patient education, pharmacovigilance, and prescriber and pharmacist knowledge of non-medical and extra-medical NSAID use and associated health consequences³³.

Ibuprofen

A common analgesic, antipyretic, and anti-inflammatory medicine today is ibuprofen. Although the patterns of usage of these analgesics vary greatly from country to country, it likely ranks third in non-prescription OTC use for the alleviation of acute pain, inflammation, and fever. This is true even though aspirin and paracetamol are the most commonly used OTC medications worldwide. Ibuprofen, which is available as an OTC drug, is probably the least dangerous of these three analgesics because it rarely causes fatalities from accidental or intentional intake or other major side effects³⁴.

Ibuprofen comes in tablet form in dosages of 200 to 800 mg. Peak plasma concentrations are attained in one to two hours and it is well absorbed orally. It takes between 30 and 60 minutes for analgesia to start working after oral consumption³⁵. Less than an hour in adults and up to three hours in children marks the beginning of antipyretic activity, which varies with age^{36, 37}. A half-life of 1.8 to 2 hours indicates that it is rapidly digested. In 24 hours the entire metabolized and excreted amount of ibuprofen is gone³⁸, and Protein binding is 99%³⁹.

Mechanism of Action

Classed as a non-steroidal anti-inflammatory drug (NSAID), ibuprofen acts as a non-selective inhibitor of cyclooxygenase, an enzyme facilitating the synthesis of prostaglandins (mediators of pain and fever) and thromboxanes (promoter of blood clotting) via the arachidonic acid pathway⁴⁰. Ibuprofen is a non-selective COX inhibitor hence it reduces the activity of both COX-1 and COX-2. Suppression of COX-1, which reduces the synthesis of prostaglandins that help to moderate inflammation, discomfort, fever, and edema, is blamed for the side effects of ibuprofen, including gastrointestinal ulcers⁴¹.

Misuse and Toxicity

Ibuprofen is often used and easily accessible OTC. Ibuprofen toxicity may occur if the drug is consumed in excess; unreported side effects of ibuprofen misuse include renal tubular acidosis, which can cause fatal hypokalemia⁴². Despite



the fact that NSAIDs, like ibuprofen, are typically well tolerated, they can have rare but very harmful side effects, such as upper GI bleeding and perforation, renal failure, and heart failure⁴³. Ibuprofen is toxic, mutagenic, teratogenic, and genotoxic agent in various organisms. In human cases mostly overdose or misuse was found to be toxic⁴⁴.

Ibuprofen use is known to cause stomach bleeding, which can result in gastritis, ulcers, hemorrhages, or perforations. Ibuprofen use inhibits COX isoforms, which lowers prostaglandin levels, which affects the release of gastroprotective mucus⁴⁵. Ibuprofen is used more frequently than other NSAIDs due to its relative safety compared to other medications in its class. The risk of excessive dosage levels and short-term interval dosing, which may trigger gastrointestinal issues, is also increased when using ibuprofen OTC without seeking medical advice⁴⁶.

Ibuprofen use is associated with decreased renal function, and a recent surveillance study found that NSAIDs can be nephrotoxic even in patients who have normal kidney function⁴⁷.

Various organ systems' biological functions can be affected by ibuprofen toxicity due to cyclooxygenase pathway decrease. Even at therapeutic doses, ibuprofen can elicit gastrointestinal and renal adverse effects because prostaglandins and thromboxanes maintain the stomach mucosal layer and renal blood flow. Ibuprofen, alone or with other analgesics, causes 29% of NSAID overdoses. Overdose typically causes ibuprofen toxicity⁴⁸.

Diclofenac

Diclofenac (phenylacetic acid) is an anti-inflammatory analgesic that is frequently used and works similarly to morphine to relieve pain following coronary artery bypass graft surgery⁴⁹. It is frequently used as an analgesic and an antipyretic to relieve pain in people who have rheumatoid arthritis, osteoarthritis, and other conditions⁵⁰.

Diclofenac is an NSID that is frequently used to treat a range of rheumatic conditions, including Ankylosing spondylitis, osteoarthritis, rheumatoid arthritis, and sudden muscle pain. Diclofenac can, in rare circumstances, lead to hepatic damage in patients, just as other NSAIDs⁵¹.

Diclofenac is available as either the sodium salt or the potassium salt, with the sodium version being the most popular form. Diclofenac sodium has a propensity to cause the body to retain salt and water, which increases the risk of cardiovascular events. When treating patients with cardiovascular problems, potassium diclofenac is preferable⁵².

Mechanism of action

Diclofenac is a member of a class of NSAIDs that block COX-1 and COX-2 enzymes. Prostacyclin [PGI₂], thromboxane [TX] A₂, and prostaglandin [PG]-E₂ are examples of prostanoids that

are inhibited by the binding of NSAIDs to COX isozymes⁵³⁻⁵⁵. The fundamental mechanism by which NSAIDs exert their powerful analgesic and anti-inflammatory effects is thought to be the suppression of PGE₂, which is the predominant prostanoid generated in inflammation^{54,56,57}. Diclofenac has a greater ability to inhibit COX-2 isoenzymes than COX-1 isoenzymes^{54,58,59}.

Misuse and Toxicity

One of the most significant risks that can result from the misuse of drugs is idiosyncratic drug-induced liver injury (DILI). Such a problem has long been linked to diclofenac⁶⁰. The formation of the quinoneimine metabolite was found to be responsible for this idiosyncratic toxicity. Quinoneimine is an over-oxidized metabolite of diclofenac⁶¹. Diclofenac therapy causes various negative side effects^{62,63}. Patients may experience an asymptomatic rise in plasma transaminase⁶⁴ indicating that it can cause hepatotoxicity. Additionally, it has been observed that diclofenac causes a small number of cases of severe hepatotoxicity⁶³. However, it is unknown how diclofenac harms the liver⁶⁵. According to reports, they may be connected to the hazardous metabolites formed during diclofenac's biotransformation, which may cause the development of oxidative stress, or, in certain situations, they may be connected to immune reactions^{64,66}.

Acetaminophen (paracetamol)

Acetaminophen, or paracetamol, is one of the most popular and frequently used drugs for the relief of pain and fever. Among analgesics, it holds a distinctive place. It is virtually universally acknowledged that, in contrast to NSAIDs, it has no anti-inflammatory activity, does not cause gastrointestinal harm, and has no unfavorable effects on the heart and kidneys⁶⁷.

Mechanism of action

In general, and especially in vulnerable groups, paracetamol is still the first-line treatment of choice for mild to severe acute pain. Despite being widely used, there remains disagreement over paracetamol's analgesic mechanism of action. The idea that paracetamol produces its analgesic effect via a COX-dependent inhibitory effect is being called into question by a growing body of research. The production of the bioactive AM404 metabolite in the central nervous system (CNS) is a key mediator in the various mechanisms through which paracetamol analgesia works. TRPV1 is a key factor in the brain's and dorsal horn's neuronal response to pain, and AM404 is a powerful activator of this receptor. The bioactive metabolite AM404 stimulated the signaling cascade involving the TRPV1 channel, mGlu5 receptor, PLC, DAGL, and CB1 receptor in the periaqueductal grey⁶⁸.

Misuse and toxicity

Paracetamol is sold under a variety of brand names. This can be confusing and lead to you taking more paracetamol



than advised. It is typical for people to misunderstand the correct dosage and active ingredient for OTC drugs containing acetaminophen. Particularly for frequent acetaminophen users and individuals with low language skills, the unintentional usage of these drugs raises a significant risk of mistakes and negative effects. There is increasing concern regarding the possibility of consumers accidentally misusing OTC drugs containing acetaminophen, which could result in abrupt liver failure⁶⁹.

Since it has mild analgesic and anti-inflammatory effects, paracetamol (acetaminophen [APAP]) is a regularly recommended over-the-counter drug. Sadly, it is the leading cause of people presenting with severe liver failure in many hospital emergency rooms, usually connected to purposeful or unintentional over dosage. Acute liver damage from APAP is dose-dependent and made worse by malnutrition and other liver conditions⁷⁰. In addition to other etiological factors, misuse of drugs is the main cause of acute hepatic failure⁷¹⁻⁷³. One of the most often used medications for treating mild to moderate pain, fever, and inflammation is acetaminophen⁷⁴. On the other hand, acetaminophen overdose is listed as one of the main causes of AHF in North America and Europe^{75,76}. In the event of an overdose, acetaminophen may be responsible for roughly 50% of AHF globally^{77,78} which may affect 60,000 people each year⁷⁹.

The most common cause of abrupt liver failure in the United States is APAP overdose, and the drug's hepatotoxicity is caused by the production of the reactive metabolite N-acetyl-p-benzoquinone imine (NAPQI). While therapeutic doses of APAP primarily undergo glucuronidation and sulfation and only a small portion (10%) undergoes oxidation⁸⁰. Excessive doses of APAP during an overdose cause the cytochrome P450 system to significantly increase drug metabolism, resulting in elevated levels of NAPQI^{80,81}. Although the liver has large amounts of reduced glutathione to scavenge the modest amounts of NAPQI produced after a therapeutic dose of APAP, this is overpowered by an overdose, where NAPQI first depletes liver GSH and then forms adducts with cellular proteins. The mitochondria, which are a key factor in mediating liver damage after APAP, are a prominent target for NAPQI protein adducts production within the hepatocyte⁸².

The misuse of OTC drugs during COVID-19

During the COVID-19 pandemic, OTC medicines sales substantially surged^{83,84}. NSAID drugs belong to a broader group that also includes antipyretics, anticoagulants, and, at higher doses, anti-inflammatory agents. Nevertheless these drugs come with their own potential dangers: greater chances for stomach ulcers and bleeding, heart attack and kidney problems⁸⁵⁻⁸⁷. Aspirin, ibuprofen and naproxen belong to the best-known of NSAIDs, now widely available OTC in many countries⁸⁸. Use of OTC drugs rose from 48.4% before the pandemic to 83.8% after. At a time when the most widely

used OTC medication was NSAIDs, paracetamol also tended to be abused and over-used by some people. More than half of consumers had no understanding about the recommended dosage or possible side effects. While as more OTC medicines are used. There too increase the risk for harmful drug events as well as unknown health conditions. These pandemic conditions facilitated inappropriate self-medication because there were vet no longer any barriers to the availability of medicines as well as the growing influence posed by social media. Self-medication was slightly more than usual in this era, with drug relief and fever reduction drugs most frequently employed. This is consistent to the common complaint of headaches, colds flu-like symptoms that account for so many people in poorer health. The first motive for self-medication was individual experience of the same kind of problem^{71,89}.

The impact of self-medication on OTC drug misuse

Self-medication, according by the World Health Organisation (WHO), is "the use of medicinal products by the consumer to treat self-recognised disorders or symptoms, or the intermittent or continuous use of a medication prescribed by a physician for chronic or recurring diseases or symptoms." In reality, it also involves family members using medications, particularly in cases involving the treatment of old people or children⁹⁰.

Globally, prescription drug use is less common than over-the-counter medicine use for self-medication. Usually used to treat conditions not requiring strict medical observation or treatment, OTC drugs are OTC drugs although they are used for self-medication with the goal of preventing diseases and preserving health⁹¹. Many OTC analgesic users are associated to self-medication. The medical consequences of treatment decisions deviating from a doctor's prescription are a major challenge⁹². A lot of OTC analgesic use is related to self-medication. The medical consequences of treatment decisions deviating from a doctor's prescription are a major challenge⁹³. If consumers were more knowledgeable about the dosage when it should be taken and what occurs should they overindulge? Absence of this understanding could lead to skin diseases, allergies, and hypersensitivity⁹⁴.

Self-medication, according to the WHO, is the use of medical products by people to treat self-identified diseases or symptoms or the sporadic or continuous use of a physician-prescribed prescription for chronic or recurrent disorders or symptoms. Actually, it also includes the use of drugs belonging to family members, especially in relation to the treatment of children or the elderly". Globally, patients are looking more and more for unrestricted access to efficient therapies free from prescription or doctor's visit need. As such, more and more prescription-only medications (POM) are moving toward OTC availability. Many more medications are moving to over-the-counter classification so that patients may self-manage their therapy. The idea of self-care empowerment may be undercut when customers lack the knowledge to self-administrate treatment

safely. This could relate to personal choice of analgesic medications. When used improperly, these medications carry serious hazards. NSAIDs show a wide spectrum of side effects, interactions, and contraindications over many patient populations even at over-the-counter dosages. The major analgesic of choice in the elderly is paracetamol since age-related deterioration in renal function, polypharmacy, and gastrointestinal and cardiovascular illnesses call for increased awareness when NSAIDs are being taken. For most people who need over-the-counter analgesics, paracetamol is a better general choice even if overdosing has a risk of hepatotoxicity⁹⁵. SM has grown to be one of the most preferred substitutes since private medical sessions are somewhat expensive. In distant or rural areas, where people suffer with social, financial, and educational disadvantage and have poor access to healthcare services, the conditions may be worsened. Other important elements influencing self-medication are patient satisfaction with healthcare providers, long waiting times, medication costs, educational attainment, age, and gender⁹⁶⁻¹⁰¹.

The misuse of OTC among members of society of different ages

Although many teenagers use over-the-counter painkillers, a lot are confused by the differences between generic and brand-name formulations. Particularly for acetaminophen, there were notable information gaps on the use of OTC medications, their side effects, and contraindications²³. Teenagers' OTC drug abuse raises a major patient safety concern since it increases the incidence of poisonings and emergency department visits. Because OTC medicines are readily available, teenagers can view them as harmless even if taken in too high dosages¹⁰².

Among the most often used non-opioid analgesics (NOAs) among the older population were paracetamol, acetylsalicylic acid, and ibuprofen. Patients given the drugs for tooth pain, pyrexia, general discomfort, and chronic joint problems¹⁰³. Using NSAIDs in elderly is related to a higher risk of numerous side effects^{104,105} such as peptic ulcer disease, gastrointestinal bleeding, increasing blood pressure, heart failure, and acute renal failure^{71,106-109}.

CONCLUSION

Affected by factors like brand name uncertainty, self-medication behaviors, and inadequate knowledge of appropriate intake and accompanying dangers, the incorrect use of OTC medications—especially analgesics—represents a significant public health issue. Although OTC medications are usually judged safe when used as directed, their great availability increases the possibility of abuse and has negative effects on health including gastrointestinal problems, hepatotoxicity, nephrotoxicity, and reliance. The COVID-19 outbreak aggravated the issue since self-medication grew out of more availability and false information. Reducing OTC drug use calls for a whole approach including more patient education, more pharmacovigilance, and more awareness among medical professionals on non-medical medication use. Legislating better, supporting pharmacist interventions, and increasing public awareness campaigns help to reduce the risks associated with over-use of over-the-counter medications. Encouragement of acceptable prescription practices helps the healthcare system to guarantee the correct use of over-the-counter drugs and more effectively guard consumers against inadvertent damage.

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