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Reported Methods of Abuse for Common Prescription Analgesic Opioids

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Introduction

With the introductory of internet forums, blogs, and social networks, large numbers of individuals are connected together in ways previously deemed difficult or impossible. These outlets can be used as a means of asking questions or freely displaying personal experiences, viewpoints, and anecdotal accounts. Once posted, these questions and remarks are open for other individuals to read, comment and respond. Through these dialogues, a vast electronic database has been created which is instantly retrievable and contains new content on a daily basis [1]. In the healthcare field, this can be beneficial to certain patients or can be used in ways leading to detrimental effects. For example, computer-mediated forums can help patients, such as those with cancer, cope with their diseases states [2]. Likewise, web-based interventions can also help those with alcohol, tobacco, and substance use disorders [3,4]. However, internet discussions can also be used by those seeking to abuse drugs, particularly those interested in recreational use of prescription opioids. Internet forums have become a source of information on how abusers can administer and defeat different prescription drug containing formulations [5]. They can also be used as a means of estimating abusers' preferences for certain products [6]. The information contained in online drug abuse databases are of particular interests to those who are developing abuse-deterrent formulations, since the purpose of these products is to defeat common and upcoming methods of abuse.

The purpose of this paper was therefore to compile a reliable, crowd-sourced database listing the self-reported methods of tampering and abuse of prescription opioid medications. More particular, the information collected was specific to currently marketed formulations having abuse-deterrent properties and the methods detailing ways to bypass their technologies.

Searches were conducted in various online drug-user based forums, which contained personal entries and discussions at different lengths. The generic and trade names of five currently marketed opioid analgesics having abuse-deterrent capabilities were used as the search terms. The products and generic forms searched are as follows: Exalgo® (hydromorphone), Oxycontin® and Oxecta™ (oxycodone), Nucynta® ER (tapentadol), and Opana® ER (oxymorphone).

Reported Administration Methods

This section lists the administration methods abusers listed from all search terms. In general, the methods appeared well-known to the abusing community and appeared easy to recreate. The more popular methods of delivery were those that could effectively deliver a drug quickly into the body and at a high dose. Listed below are the methods individually addressed and contain common as well as novel methods of delivery that were self-reported for each drug. The results are categorized according to the route of delivery:

Oral delivery

This is the most common form of administration, though often at the cost of slower drug onset or lower bioavailability versus other routes. This approach was primarily listed by prescription users for pain management, and is largely immune to abuse because of how much control is exerted over the volume of formulation introduced into the body. Some users reportedly allowed the drug to accumulate in the body over the course of a few days by continuous, measured ingestion. Single and multiple doses were taken by mouth with either an intact or crushed dosage form. Another method reported for oral delivery was "parachuting." This is a novel way of swallowing a drug by rolling it in paper or plastic to slow release of the drug [7]. This method can also be used as a means of taste masking. Tablet dosage forms were also reported to be taken sublingually, where the medication was allowed to dissolve in the saliva and was said to amplify the effects of the drug [8].

Parenteral delivery

Intravenous injection, also known as "shooting up", can be a potent and dangerous form of administration. For tablets, the dosage form is crushed (when possible) into a fine powder before suspending in water or other suitable solutions for extracting the drug. This mixture was then said to be filtered multiple times using common household items, typically a piece of rolled up cotton. For thoroughness and to reduce adverse effects, some users invested in purchasing micron-filters to effectively remove more un-dissolved particulates from the solution. Improper filtration was reported to have caused undesired consequences such as blood clots and other potentially lethal effects [8]. Once a clear drug solution is obtained, it is injected intravenously using a needle and syringe on an isolated vein. If done correctly, the rapid delivery of drug into the bloodstream results in a powerful, euphoric feeling.

Intramuscular delivery was also mentioned as a parenteral method of delivery using similar preparation techniques as intravenous injection. However, these injections are administered deep into a large muscle, with the quadriceps muscle near the hip being reported frequently. Although not as potent as intravenous delivery, it was preferred by some users because it left less physical evidence on the skin after injection and lowered the risk of circulatory disruption [9].

Nasal delivery

Administration by the nasal route, or "snorting" as it is commonly referred, appears to produce potent effects second to injection techniques. This was the most popular route mentioned among all user posts. To produce a fine powder, abusers used various objects for grinding while being very careful to preserve as much of the powder as possible. Once ground, a narrow hollow apparatus such as a straw or rolled-up bill is often used to facilitate snorting via a short, intense

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inhalation. The Drug is then absorbed through the nasal mucosa and into systemic circulation. Depending on the drug, this process can be anything from relatively painless to excruciatingly painful. Users also reported snorting powder that was suspended in a liquid solution, allowing for less nasal clogging and more active ingredient being introduced into the body [8].

Rectal delivery

In this type of administration, a drug is inserted into the rectum to produce a fast onset while avoiding first-pass metabolism of the drug. This method is also referred to as "plugging" and is done often by first mixing a crushed a tablet in a liquid solvent and then loading the mixture into an oral syringe. The syringe is then inserted partially into the anus, where the contents are delivered by pushing on the syringe plunger. Users typically report lying down before insertion which supposedly ensures equal absorption of the drug into the body. In most cases, this method was reported to be less potent than snorting or intravenous delivery, but is commonly more potent and popular than oral delivery.

Product-Specific Abuse

This section outlines the individual abuse methods, if any, of the five abuse-deterrent products searched. These methods take into account modern abuse-deterrent technologies and attempt to bypass them.

Exalgo®

Exalgo is currently being manufactured under the OROS (Osmotic (Controlled) Release Oral (Delivery) System. The drug is contained in the center of a hard tablet and is slowly released through a laser-drilled hole in the outside semi-permeable coating. This coating surrounds the entire tablet and is intended to prevent release of the drug while allowing fluid to enter the tablet core. The osmotic pressure of the fluid entering the center portion of the tablet forces the drug to leave via the drilled hole. As such, Exalgo® is very effective in its abuse deterrence, as the drug is protected within the central portion of the physically hard tablet and otherwise inaccessible. This making snorting (specifically), chewing, and intravenous delivery largely ineffective [10]. However, hydromorphone in other products is a popular recreational narcotic known for its characteristic, initial rush of euphoria.

Oxycontin®

Abuse-deterrent tablet formulations of Oxycontin® are thermally treated to produce a hard plastic-like effect making crushing hard to achieve. Furthermore, the tablet forms a thick and viscous solution when abusers attempt to dissolve it in an aqueous fluid. This controlled-release formulation is largely immune to general abuse and tampering methods. Nonetheless, several novel methods have been implemented by users to extract pure oxycodone from the tablets. The following demonstrated some of these methods:

- Use of metal pliers to physically crush the tablet. Swallowing the results rarely produced desired effects [11].
- Method of oxycodone extraction using acetone as a solvent at room temperature. Users reported that this extracted up to 78% of the active ingredient from extended-release tablets using only household products. This method was very popular for the 80 mg tablets [12].
- Extraction by crushing tablets into small pieces using a sharp object and then immersing the product in Coca-Cola or other conventional soft drink. Next, the mixture is microwaved several times in succession with a 3 to 4 minute cooling period in between each period [13].
- The most successful abuse method reported was to slightly crush the tablet while keeping the pill intact to produce a cracked pattern on the tablet similar to a spider web. According to users, this keeps the pill intact while speeding up the digestive process, enhancing bioavailability [14].
- Snorting was reported to be effective once the outer coating of the pill was removed by an abrasive, but this is at the cost of insufflating components that are not meant to be inhaled. However, users reported that snorting this formulation was moderately to intensely painful [15].

Nucynta® ER

The use of hot-melt extrusion technology was used to create this hard to crush and dissolve abuse-deterrent product. Oral ingestion was the most popular method reported for Nucynta® administration. However, rapid absorption is likely stunted by the extended-release nature of the formulation. Anal delivery was reported as being relatively ineffective when compared to other administration methods. Snorting the drug was said to produce immediate effects, but users report that resultant nasal pain and burning sensation is almost unbearable. Users report that the drug has a low effect on tolerance with withdrawal symptoms being intense and uncomfortable compared to other drugs. However, a large amount of users reported that the effects of the drug radically decrease with increased tolerance, making the drug unpopular for high-tolerance users and overtly popular for low-tolerance ones [16]. Therefore, feasibility of abusing this formulation was said to be largely dependent on the tolerance of the user, making this drug an unpopular candidate for abuse [17].

Oxecta™

Of all the drug products searched, Oxecta™ was the only immediate-release formulation. It is produced using a mixture of ingredients that create a gelled mass in small amounts of liquid. Additionally, it also has a nasal irritating surfactant in the formulation to discourage nasal administration. Due to its tamper-resistant nature and low amount of drug in each tablet (when compared to an extended-release product), the dose is well below the threshold for most serious abusers. Oxecta™ was not a popular candidate for abusers based on the lack of personal entries regarding its existence. However, this could also be due to its recent release on the market in 2011. With oxycodone being the active ingredient, the drug is highly desirable for abusers but more effectively achieved by means of tampering with long-acting formulations (e.g., Oxycontin®). There were a small amount of users reporting ingestion via "parachuting," or delivering the drug directly into the throat via a conventional tube in order to prevent its bitter taste.

Opana® ER

This is another tamper-resistant product using hot-melt extrusion technology to produce a rigid tablet that gels in solution. As such, the product is hard to crush by conventional means and therefore prohibits nasal and parental abuse. However, several posts listed various tampering techniques including:

- Tablets being cut-up into several pieces and then suspended in an alcohol solution to release the active ingredient. Solution was then drawn into a conventional sprayer which is used to

disperse the mixture in air which evaporates the solvent leaving behind the pure drug. This technique was reported to amplify the effects of oral delivery [18].

- Use of a Dremel® rotary tool to slowly shave away the tablet outer coating. A barrier mechanism is then placed around the tool to collect more shavings from the whole tablet. The resultant powder was collected and used for snorting, reportedly amplifying its effects [18].
- Vitamin B12 was reported to be effective in stopping the gelling process once the product was ground down for snorting. Users report that this was significantly effective in bypassing the abuse-deterrent technology.
- The extended-release formulation was circumvented by first creating a solution of similar pH to that of the gastric environment. The tablet was then added to the solution inducing drug release into the solvent over time. An extraction process of the resultant solution yielded a material with high bioavailability. Alternatively, the drug can be extracted from the tablet in an alcohol solution over time with the entire liquid contents then ingested [19].

Conclusion

This study illustrated the prevalent use of blogs and other online media to discuss methods of abuse and tampering of prescription drug products. Through this investigation, it was interesting to find most recreational drug abusers were not those pioneering and posting alternate delivery methods. Instead, methods being propagated were mostly by individuals with painful, chronic illnesses whose pain therapies were reportedly not being properly managed. These individuals then sought to increase their doses or seek alternate and unconventional methods of administration to achieve proper analgesia. Based on this finding, it is unlikely that a patient being properly treated for pain management would seek to tamper and misuse their pain medication.

The findings of our search also indicated that abuse-deterrent formulations have varying degrees to which they are discussed. This may be based on factors such as how long they have been on the market and the prevalence of their use in the clinical setting. However, the postings revealed that most formulations having some resistance to abuse were more complicated to abuse or were less desirable. Continued monitoring of blogging platforms sharing prescription drug abuse related content may help define weaknesses in abuse-deterrent formulations and lead to more robust designs in the future.

Last but not least, this research displays how abusers are desperately using very aggressive physical and chemical methods to change the nature of the dosage form in order to obtain maximum concentration of the drug. Pharmaceutical companies are obligated to show safety and toxicity of any traces of impurities in the final product (if existed) that may generate for instance during processing, through drug-excipient interactions, and upon storage over time. This required tests that involved lengthy time periods and the spending of millions of dollars in research and development. However, no studies are performed to show how a dosage form may react, or what harmful and toxic byproducts may be produced, when placed under the various tampering techniques used by abusers. For example, the use of various solvents (acetone, alcohol, soda) high shear grinding, microwaving, freezing, and other processes subject the active drug and its excipients to extreme conditions. There is little evidence to know what may generate out of such dangerous manipulates and if the nature of the drug or excipients change to more monstrous entities. This can be dangerous to abusers, particularly when administering directing into the body by various routes.

We recognize this study to be small and preliminary in its results which are based on a selected population. Additionally, the information it contains is based on user self-submissions and at times can be bias, exaggerated, or even fabricated. Nonetheless, this type of research gives insight into how abuse-deterrent formulations are being viewed by those it is intended to stop. Furthermore, the desire to manipulate opioid based dosage forms may start out of desire to achieve better analgesia or for recreational use, but in the end it is unwise, unsafe, and subjects the abuser to immense risk.

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