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Association between non-medical and prescriptive usage of opioids

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Abstract

Understanding and managing prescription opioid abuse is one of the major challenges in pain management worldwide. The relationships between prescriptive usage of opioids and reported morbidity at the national level, using data from the Drug Abuse Warning Network (DAWN), were examined. When the major prescription opioids were evaluated, the association between prescriptive medical use in kilograms and reported morbidity, as measured by a ratio between the two, was similar for the intermediate-potency opioids (hydrocodone, methadone, oxycodone, and morphine). This rate was much lower for low-potency opioids (codeine, meperidine, pentazocine, and propoxyphene) and much greater for high-potency opioids (hydromorphone and fentanyl). When the drugs were adjusted by potency (relative to morphine), the rates of reported morbidity per kilogram of morphine equivalent opioid in prescriptive usage were similar among the opioids. Using the potency-adjusted total kilograms of opioid in prescriptive use for all the opioids evaluated, there was a statistically significant association ($r^2 = 0.9791$) with the reported morbidity for prescription analgesics as a class, as measured in the DAWN system. These data suggest that non-medical use of opioids is predictable based on potency and extent of prescriptive use.
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1. Introduction

While the use of opioids in the treatment of pain is recognized as one of the mainstays of pain management, their utilization has always been tempered with concerns about abuse, addiction, and diversion of medicinal supplies into illicit channels of trade (American Academy of Pain Medicine and American Pain Society, 1997; Federation of State Medical Boards of the United States, 1998). The cultivation, manufacture, distribution, and dispensing of opioids are subject to international control, with the intent of assuring access for legitimate medical and scientific purposes while minimizing diversion and abuse (Single Convention on Narcotic Drugs, 1961). The international obligations continue to influence national control programs. There are significant differences among nations both with respect to utilization of abusable pharmaceuticals and the degree of concern over diversion of such drugs to illicit use (Costa e Silva, 2002).

The United States reports one of the highest levels of per capita consumption of opioids for legitimate purposes in the world (United Nations, 2004). The United States also has a high level of public concern with the non-medical use and abuse of prescription and illicit drugs. While this paper addresses non-medical use of prescription opioids in the United States, it is hoped that the experience in the United States may serve to inform policy in many countries which will need to address this issue as international efforts to expand access to treatment continue.

Non-medical use of prescription drugs, drug abuse, and addiction are complex and covert disorders and none of the world's nations can be certain of the exact prevalence of drug abuse within its borders. On a national level, the United States government has tried to address this problem through federally sponsored information sources intended to provide data on the prevalence of non-medical use of pain relievers and other pharmaceuticals subject to abuse and the health consequences of such abuse. These databases include the National Survey on Drug Use and Health (NSDUH), which provides prevalence data based on a population survey, and the Drug Abuse Warning Network (DAWN), which provides information on the extent of

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drug abuse-related harm, as suggested by emergency department admissions due to non-medical use of prescription and illicit drugs. These surveys consistently suggest a significant increase in both the prevalence and adverse consequences of prescription opioid abuse and diversion in the United States since the early to mid 1990s (Substance Abuse and Mental Health Services Administration, 2002a,b, 2003a,b).

Unlike illicit drugs, there are reliable estimates of the amounts of prescription drugs available for legitimate and illicit uses. Data on prescription sales have been used as a tool for exploring abuse of prescription opioids (Joranson et al., 2000; Zacny et al., 2003; Gilson et al., 2004; Novak et al., 2004). These data have been used in conjunction with data from DAWN as an indicator of non-medical use (Zacny et al., 2003; Novak et al., 2004). This paper builds on this previous work by expanding the concept that abuse of prescription opioids is a predictable consequence of the amount of prescriptive use of any given opioid. It further explores the types of relationships initiated by others (Joranson et al., 2000; Zacny et al., 2003; Gilson et al., 2004; Novak et al., 2004), by testing the fundamental relationships between non-medical use, potency, and level of prescriptive use for opioids in the outpatient treatment of pain.

2. Methods

2.1. National data on drug abuse

DAWN is an annual report of a nationally representative, geographically weighted sample of emergency department (ED) visits ("episodes" in DAWN terms) related to intentional non-medical use where the patient's reason for using the substance(s) was dependence, suicide attempt or gesture, or psychic effects (recreational use). These data provide an annual estimate of the medical consequences of drug abuse for the 48 coterminous United States. The data are reported at the level of drug substance (generic names) and drug class, and national estimates of the frequency with which different drugs are "mentioned" in DAWN are published. DAWN's estimates of episodes measure ED visits, not unique individuals who visit the ED. For each episode, up to four drugs can be reported; each drug is considered a "mention". There are limitations to the timeliness, breadth and representativeness of coverage in DAWN, as well as the effect of methodological changes on longitudinal analysis of the data inherent in using changing survey methods over time. However, even with these limitations, DAWN data are frequently used in policy decisions as a surrogate measure of the extent of the public health problem posed by a given drug.

2.2. Kilograms of opioid usage

The years 1994 through 2002 had substantial increases in prescription drug abuse as measured by various indicators of prescription drug abuse, including DAWN ED mentions. DAWN ED mentions for the major opioid drugs for this period (codeine, fentanyl, hydromorphone, hydrocodone, meperidine, methadone, morphine, oxycodone, pentazocine, and propoxyphene) were compared with the kilogram amounts of these drugs distributed by prescription in the United States. Prescription opioid sales data were purchased from IMS Health Inc., a commercial vendor of sales data for the pharmaceutical industry.

Information in the National Prescription Audit (NPA) is derived from IMS Health's Xponent service. Xponent captures roughly 70% of all prescriptions sold in the United States, including retail, mail service, long-term care, and managed care outlets and projects them to a national estimate of sales. IMS Health employs a proprietary projection algorithm, based on a stratified and geographically balanced sample, to extrapolate to uncovered areas. IMS Health's NPA is the industry standard for prescription sales data. A limitation of using data on prescriptions is that it does not capture all drug in outpatient use (e.g., drug dispensed from hospitals), nor does it capture drug lost from the supply chain "pre-prescription" (lost in transit, losses at the wholesalers, or pharmacy theft). The IMS Health data do, however, give one of the best publicly available estimates of the amount of drug in prescriptive use in a given year.

Associations between annual DAWN ED mentions and kilograms of drug was assessed for each opioid using a correlation statistic (Pearson's r), with alpha set at less than 0.01. The coefficient of determination (r^2) is a measure of variance and shows, for each drug, the proportion of variability in DAWN ED mentions that is explained by assuming a linear relationship between the two variables in question.

2.3. Equianalgesic kilograms

Conversion of the amounts of the different opioid drugs in kilograms to the equivalent kilograms of morphine was achieved using approximate equianalgesic oral doses compared to morphine. Equianalgesic potency conversion tables are routinely used in the pain management setting when switching patients from one opioid to another. The equianalgesic doses were taken from standard sources (Foley, 1985; Gutstein and Akil, 2001) for all drugs except fentanyl and propoxyphene, where the morphine equivalents are controversial. For fentanyl, the morphine equivalent value was based on the reported potency of fentanyl as 100 times that of morphine (Gutstein and Akil, 2001) with appropriate modification for bioavailability. Since the transmucosal route is a frequently reported mode of abusing available formulations of fentanyl (both the solid matrix and the transdermal patch) and the transmucosal bioavailability of fentanyl is 25% (Actiq® package insert), the multiplier used to determine the morphine equivalent quantities of fentanyl was 25. For propoxyphene, the equianalgesic dose is reported to be one half that of codeine (Foley, 1985). Table 3 summarizes the morphine equivalents used in this analysis for the various opioids and the multiplier used to establish the morphine equivalent quantities.

3. Results

3.1. Relationship between DAWN ED mentions and kilogram usage

Previous work provides evidence that for the years 1997 through 2002, there was a positive relationship between the

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