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Trends in the use and abuse of branded and generic extended release oxycodone and fentanyl products in the United States

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Abstract

Background: A great deal of previous work on the pharmacoeconomics of alcohol, tobacco and illicit drug abuse indicates that as cost decreases, abuse increases and vice versa. The application of these cost principles to the abuse of prescribed medications is largely unknown. In this paper we assessed whether the introduction of generic products in the U.S. increased the therapeutic use and illicit abuse of extended release oxycodone products and the fentanyl patch.
Methods: As an index of therapeutic use, we purchased prescription data for each of the ZIP codes in which we had corresponding abuse data. To gather information about prescription drug abuse, we elicited cases with quarterly questionnaires completed by a key informant network.
Results: The introduction of generic extended release (ER) oxycodone and fentanyl patch did not significantly change the total prescriptions written for these products, but markedly altered the composition of sales: branded sales dropped precipitously over a very short time and this was compensated for by a corresponding increase in sales of generics. Surprisingly, the introduction of generic products did not increase the abuse of ER oxycodone or fentanyl products; the branded version was the drug of choice for at least 2 years.
Conclusions: Our data suggest that drug costs alone do not increase the overall likelihood that a prescription opioid analgesic will be used therapeutically or abused. However, while generics are rapidly endorsed by insurance companies as a prescribed entity, abuse of the branded versions of ER oxycodone and fentanyl remains predominant for some time.

Keywords: Opioids; Oxycodone; Fentanyl; Generics; Prescription drug abuse; Pharmacoeconomics

1. Introduction

A great deal of previous work from the United States, Canada, Europe and Asia on the pharmacoeconomics of drug abuse indicates that as cost decreases, abuse increases and vice versa (Plamper et al., 2006; Hyland et al., 2005; Zhang et al., 2006; Caulkins, 2001; Hyatt and Rhodes, 1995; Petry, 2001; Sloan et al., 1994). These data were derived mostly from the use of tobacco and alcohol and the applicability of these models to prescribed drugs with abuse potential has never been assessed to our knowledge, with the exception of a single study we carried out with the non-scheduled opioid analgesic tramadol. We documented that the introduction of generic tramadol, which was far cheaper (<50%) than the branded product – Ultram (Ortho-McNeil Pharmaceutical) – had no discernable effect on its therapeutic use or rates of abuse (Cicero et al., 2005a). Since tramadol products (immediate release [IR] and extended release [ER] preparations and tramadol-acetaminophen containing products) were non-scheduled opioid drugs and their use was already extensive, it is possible that their market share may have already been so high that cheaper versions would not have had a measurable effect. Furthermore, tramadol products have very low rates of abuse, and command a very small street price—less than US$ 1–2 per tablet (Cicero et al., 2005a), such that price probably did not inhibit or encourage its use. Thus, we felt that our results with tramadol did not conclusively invalidate the intuitive assumption that cheaper generic drugs would lead to more use and abuse.

Unlike tramadol, oxycodone and fentanyl products, which have very high abuse rates and command very high prices in the illicit market (Cicero et al., 2005c), would seem to be perfect prescription opioid analgesics to more definitively

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assess the hypothesis that decreased costs will drive up both the use and abuse of opioid analgesics. Most importantly, we had an unprecedented opportunity to track total persons prescribed oxycodone and fentanyl products and the corresponding rates of abuse, both before and after the introduction of generics.

The concept that lowering the price of prescription drugs with abuse liability will increase their therapeutic use has never been tested, but there is a significant world-wide literature on the influence of price on the use of prescribed medications. For example, it has been shown across the world (e.g. Europe, North America and Japan) that price limits the therapeutic use of 15 different non-opioid classes of therapeutic agents to a very significant extent (Monnet et al., 2005; Huskamp et al., 2005; Paterson et al., 2006; Walker and Willey, 2004; Taira et al., 2003; Smith, 1993; Wadland et al., 2005; Campo et al., 2005; DeWitt et al., 2006; Federman et al., 2001; Goldman et al., 2004). All of these studies showed dramatic increases (up to 30%) in the use of prescribed drugs when prices dropped. Based on our previous experience with tramadol in which we found no such trend (Cicero et al., 2005a), it can be hypothesized that the use of analgesics may be price insensitive. However, this represents an N of only one with an unusual drug that is not scheduled, and, as a result, is prescribed more readily by physicians than scheduled drugs (Cicero et al., 1999, 2005a; Adams et al., 2006). In the current studies we were able to examine in much greater detail the intuitively obvious hypothesis that price will influence both the use and abuse of opioid analgesics, much as it does for other prescription, therapeutically useful drugs.

2. Methods

2.1. Patients using prescribed opioids

To calculate the therapeutic use of opioid analgesics, we purchased data from Verispan Inc. (Yardley, Pennsylvania) for each of the 3-digit ZIP codes for each quarter in which we had abuse data and calculated the average number of persons who filled a prescription, dubbed Unique Recipients of Dispensed Drugs (URDDs). This data base does not count the same patient more than once during each quarterly reporting period and, hence, the term URDDs best describes the denominator. We purchased URDDs for all oxycodone products including the branded version from the 4th quarter of 2003 through the 3rd quarter of 2006. In the case of the fentanyl patch, a breakdown of branded and generic forms was available for only the last two calendar quarters—the 2nd and 3rd quarters of 2006.

2.2. Key informant questionnaires

To gather information about prescription drug abuse we employed a key informant network consisting of 351 drug abuse experts, mainly treatment specialists, located in 217 of the nation's 973 three-digit ZIP codes. This informant network, which has been fully described in earlier reports (Cicero et al., 2005a; Cicero and Inciardi, 2005b), has previously been shown to be sufficiently sensitive to identify abuse of generic versions of branded drugs as they become available. The validity, reliability and limitations of the key informant network as a source of cases of abuse has been discussed in-depth elsewhere (Cicero et al., 1999, 2005a; Cicero and Inciardi, 2005b). A quarterly questionnaire asked whether the informant had direct, first hand knowledge and evidence of abuse or dependence which satisfied DSM-IV criteria (American Psychiatric Association, 1994) for ER oxycodone products and that the informant could distinguish with certainty whether the branded or generic drugs were utilized.

2.3. Cases of abuse

To standardize our results, we expressed rates of abuse as cases/100,000 population in the reporting ZIP codes for each quarter. This corrected for both differences in the number of ZIP codes and large population differences between ZIP codes.

2.4. Patient/subject confidentiality

The protocol was approved by the Washington University Institutional Review Board (IRB).

3. Results

3.1. Patient exposure

Fig. 1 shows the average number of URDDs for hydrocodone, ER oxycodone [branded OxyContin® and all generics], and the fentanyl patch (branded Duragesic and the generic products) during the 3-year period from quarter 4, 2003 through the end of quarter 3, 2006 in the ZIP codes reporting each quarter. The use of hydrocodone and fentanyl increased slowly but steadily over the 3 years we studied it, as was true for most opioid drugs over this time period (Cicero et al., 2007), but ER oxycodone use remained relatively flat. The introduction of generic ER oxycodone and fentanyl products did not significantly change the total use of these products.

3.2. Branded versus generic sales compositions

As shown in Fig. 2, the composition of the prescriptions filled for ER oxycodone (panel A) changed dramatically over this period; sales for branded oxycodone products dropped slightly with the introduction of a single dosage form from one company and then decreased precipitously in the last quarter of 2005 through quarter 3 of 2006 corresponding to the introduction of a large number of generics. As a mirror image, sales for generics rose in direct proportion to the loss of branded sales such

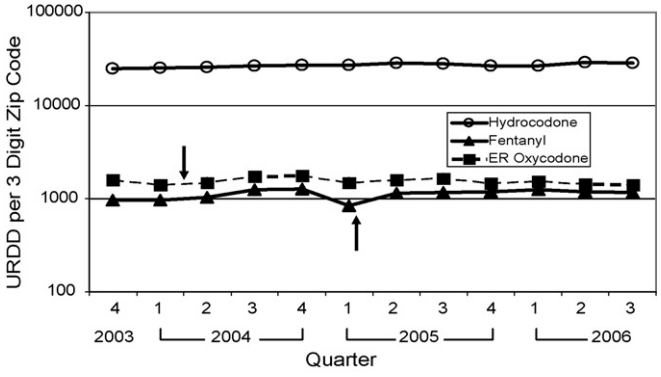

Fig. 1. The average number of Unique Recipients of Dispensed Drug (URDDs) for all ER oxycodone (OxyContin® and all generic extended release forms), the fentanyl patch (parent compound – Duragesic and all generic versions) and all hydrocodone products. The arrow indicates the introduction of generic formulations of oxycodone in 2004 and fentanyl in 2005.