Commentary

Is There Support for Abuse-Deterrent and Tamper-Resistant Opioid Formulations?

Recent attention has been given to the development of abuse-deterrent and tamper-resistant opioid formulations in light of concern over the epidemic misuse of opioids prescribed for the treatment of chronic pain.\(^6,7\) Statistics provided by the Centers for Disease Control and Prevention have demonstrated a 4-fold increase in opioid-related overdose deaths over the past decade in response to the increased availability of prescription opioid analgesics.\(^2\) The Food and Drug Administration (FDA) has specifically targeted the abuse of extended-release (ER) and long-acting (LA) opioid formulas by issuing a call for Risk Evaluation and Mitigation Strategies (REMS) designed to reduce opioid abuse and misuse.\(^4\) Ever since the original Oxycontin (OC) was approved by the FDA in 1995 and subsequently found to have a high potential for abuse, multiple pharmaceutical companies have been targeting the development of controlled-release opioid products that are resistant to abuse by physical (chewing, crushing, grinding) or chemical (extracting) manipulation. However, despite the introduction of many reformulated opioid products, there has been reluctance by the FDA to approve a change in the labeling of these oral opioid products because of lack of epidemiological evidence that they do what they were intended to do and fear that these products will contribute to further abuse.

In this issue, Butler et al\(^1\) present a very timely paper on abuse rates and routes of administration of the original OC compared with reformulated Oxycontin (ORF). The new ORF was designed to be hard to crush and turn into a stringy gooey substance when dissolved in water. The abuse-deterrent design was expected to lower the street value of this drug because it would make it difficult to extract the oxycodone in order for it to be chewed, snorted, or injected, and hence reduce its overall likeability. In this study, the authors were able to collect data from over 140,000 individuals from 357 substance abuse treatment centers around the U.S. using an electronic version of the Addiction Severity Index (known as ASI-MV). Unique data were compared from a year before and a year and a half after the date that Purdue Pharma stopped shipping OC and began substituting ORF (August 5, 2010).

Among the sample of opioid abusers surveyed in this study, most were male, Caucasian, and below the age of 35. The investigators examined outcome measures of the ORF compared with the original OC and found a significant reduction in 8 of the outcome measures. Overall, the ORF was shown to be abused 41% less often compared with OC, with the most dramatic reduction (66%) noted in the nonoral abuse (ie, injection, snorting, smoking) of the drug. Less striking was the 17% reduction in oral abuse between the 2 formulas. No reduction in abuse was noted in comparative products of ER morphine and oxymorphone over the same period of time.

These results could be seen as very encouraging for the manufacturers of abuse-deterrent opioids. Initial evidence suggests that ORF works as it was intended by deterring tampering relative to the original formulation. The authors are careful to identify the limitations of this study. Although the self-report data were obtained from a very large population of high-risk opioid abusers, the possibility for selection bias exists. We also know that abusers can be inventive in finding ways to misuse a substance (which a quick search of online comments on the Internet will confirm) and trends may change over time. A bit troubling is a recent report indicating that replacement with alternative opioid medications and abuse of heroin is
on the rise as a possible direct response to the change in the Oxycontin formulation.\textsuperscript{3}

While this paper does not highlight the fact that individuals will always be able to take multiple doses of an opioid to achieve euphoria, whether reformulated or not, and that the additional costs of reformulated drugs represent a major concern among providers and carriers, the authors need to be congratulated for their efforts in presenting these important comparative data. There is continued need for studies to help assess and identify those individuals who would be at greater risk for misuse of opioids. We also know that behavioral interventions designed to improve compliance with opioids among chronic pain patients can be moderately effective.\textsuperscript{5} As other opioid formulations are introduced into the market, future epidemiological studies will be needed to document evidence of efficacy in reducing nonmedical use of the drugs. As yet, more evidence is needed that abuse-deterrent and tamper-resistant formulations should be favored over traditional opioids in the treatment of pain. However, the results of this important study indicate that there is certainly hope for the future.

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References


