Title: Medical Outcomes Associated with Unintended Routes of Prescription Opioid Abuse

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Abstract:

Purpose: Public health risks associated with injection drug abuse are well-documented and include increased risk of drug dependence, overdose, and infectious disease (e.g. HIV and Hepatitis C). For an oral (tablet or capsule) formulation of a drug, unintended routes include all non-oral routes of administration such as inhalation and injection. The severity of the immediate clinical outcomes associated with prescription opioid abuse via unintended routes has not been well studied. Poison centers receive large numbers of calls addressing the acute health effects of prescription opioids. We hypothesized that death and major medical outcomes would occur more frequently among prescription opioid abuse exposures reported to poison centers via unintended routes compared to oral ingestion.

Methods: Data from the Researched Abuse, Diversion, and Addiction-Related Surveillance (RADARS®) System Poison Center Program from 2006 through 2014 were limited to adult (>12 years) intentional abuse cases (an exposed individual) involving any oral prescription opioid product containing hydrocodone, hydromorphone, morphine, oxycodone, oxymorphone, or tapentadol and for which the case was followed to a known medical outcome. Analyses were focused on cases classified as Intentional Abuse (“an exposure resulting from the intentional, improper, or incorrect use of a substance where the patient was likely attempting to gain a high, euphoric effect or some other psychotropic effect, including recreational use of a substance for any effect”) (National Poison Data System Manual, version 3.1, 2014). The severity of outcome was based upon standardized definitions of death-direct, major effect, moderate effect, minor effect, no effect, and unrelated effect. Percent of subjects with a death or major outcome were compared between exposures via oral ingestion (includes swallowing intact and crushed or chewed then swallowed) and those involving unintended routes (inhalation [includes snorting and smoking], injection, and other/multiple). Cases with unknown routes were excluded. Abuse exposures where multiple routes were reported were considered unintended route cases if any unintended route was reported. Relative risks were calculated for having an outcome of death or major effect (life-threatening or significant disability) given that the exposure involved an unintended route.
**Results:** There were a total of 25,432 intentional abuse exposures to prescription opioids identified. Of these, 17,837 intentional abuse exposures met the inclusion criteria of a known medical outcome during the period of interest. Of these, 2,321 (13.0%) involved unintended routes, 11,093 (62.2%) reported oral ingestion only, and 4,423 (24.8%) had unknown routes. Among all unintended route cases, 11.7% resulted in death or major medical outcomes compared to 7.2% of oral ingestion exposures. The relative risk was 1.63 (95%CI: 1.43, 1.86), suggesting that exposures involving an unintended route were 63% more likely to be associated with death or major medical outcomes than exposures with a route of oral ingestion. When data were examined by specific route of administration, 802 (4.5%) involved inhalation, 693 (3.9%) involved injection, and 826 (4.6%) involved other/multiple routes. Death or major medical outcomes occurred in 12.5% of inhalation cases, 13.4% of injection cases, and 9.4% of other/multiple cases. The relative risks for inhalation, injection, and other/multiple routes were 1.76 (95%CI: 1.45, 2.13), 1.87 (95%CI: 1.53, 2.29), and 1.32 (95%CI: 1.05, 1.64), respectively, suggesting that exposures involving these routes were more likely associated with death or major medical outcomes than exposures with a route of oral ingestion.

**Conclusions:** Based upon RADARS Poison Center data, unintended routes are associated with more severe medical outcomes than abuse via oral ingestion. The proportion of cases resulting in death or major medical outcomes was highest for injection followed by inhalation, other/multiple routes, and oral ingestion. These data suggest acute safety risks associated with unintended routes of prescription opioid abuse, in addition to the known long-term public health concerns. Additional interventions are warranted to curb the increasing prescription opioid abuse via unintended routes and, in turn, mitigating both the immediate and long-term associated risks.

**Keywords:** prescription drug abuse, route of abuse, opioid abuse, medical outcomes