

Differences in the severity of medical outcomes of exposures reported to poison centers involving XTAMPZA® ER and other opioid analgesics

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INTRODUCTION

Opioids are a frequently used treatment for acute and chronic pain in the United States. Misuse of these medications is also common and places the individual at significant risk of overdose and death. The development of abuse deterrent formulations (ADFs) is one approach to reduce the harms of prescription opioid misuse. In a guidance to pharmaceutical manufacturers, the Food and Drug Administration outlined four categories for evaluating the effectiveness of ADFs with the fourth category being demonstrated reduced abuse, misuse, and related adverse outcomes such as overdose and death in the post-approval, real-world setting. XTAMPZA® ER (Collegium Pharmaceutical, Stoughton, MA) is an oxycodone analgesic with properties intended to discourage tampering. XTAMPZA ER was granted abuse-deterrent labeling with respect to oral, nasal and intravenous routes of administration based on premarket studies. Post-marketing studies of XTAMPZA ER are consistent with the aim of reduced abuse and tampering. However, it is unclear whether these changes correspond with meaningful reductions in adverse outcomes associated with misuse and abuse such as overdose and death. Poison centers can assess medical outcomes such as overdose and death related to misuse of pharmaceuticals. We assessed whether XTAMPZA ER corresponded to less severe outcomes among intentional exposures (e.g. abuse, misuse, or suspected suicidal).

To test whether the severity of outcomes for exposures involving XTAMPZA ER were less severe than exposures involving other opioids.

METHODS

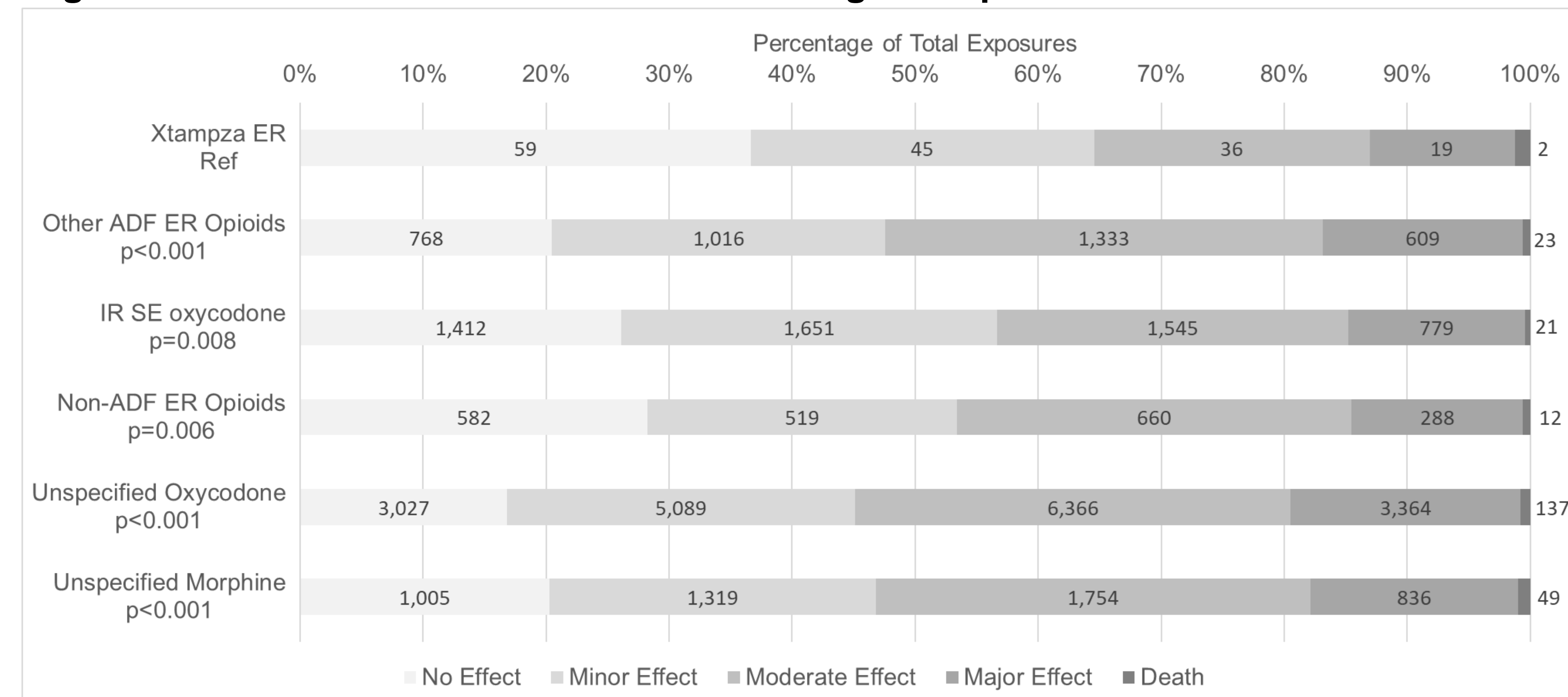
Data collected between 1st quarter 2016 through 4th quarter 2021 from the Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS®) System Poison Center Program were used. Data from cases involving: XTAMPZA ER and comparators: 1) immediate-release (IR) single-entity (SE) oxycodone 2) other ADF extended-release (ER) opioids (including OxyContin®, Hysingla®, and generics), 3) non-ADF ER opioids 4) unspecified oxycodone, and 5) unspecified morphine were analyzed. Analyses were among exposures followed to a known outcome and to instances where the route of administration was known to involve ingestion, inhalation, or injection. Multinomial logistic regression was used to compare the proportion of XTAMPZA ER exposures that were either abuse/misuse/unknown or suspected suicidal to other opioids. To compare severity of medical outcome between drug groups we used nonparametric Kruskal-Wallis test. If there was a statistically significant difference between drug groups based on the Kruskal-Wallis test, we conducted the Dunn test to compare differences between XTAMPZA ER to each comparator. Multiple comparisons were adjusted for using the false discovery rate.

RESULTS

Table: Routes of Administration Among Intentional Exposures

	XTAMPZA ER	Other ADF ER Opioids	IR SE oxycodone	Non-ADF ER Opioids	Unspecified Oxycodone	Unspecified Morphine
Ingestion Use Only	63 (100.00%)	2,484 (91.90%)	3,042 (91.68%)	1,123 (97.99%)	12,978 (92.95%)	3,215 (94.92%)
Inhalation or Injection Use	0 (0.00%)	219 (8.10%)	276 (8.32%)	23 (2.01%)	985 (7.05%)	172 (5.08%)

Figure: Distribution of Medical Outcome Among All Exposures with Dunn Test for Rank Order



The rank order for XTAMPZA ER medical outcomes was significantly lower than other drug groups, indicating that, on average, a case involving XTAMPZA ER is likely to be a less severe outcome.

From 2016 through 2021 there were 161 exposures involving XTAMPZA ER that were followed to a known outcome. Of these, 16 (9.9%) were intentional misuse/abuse/unknown exposures, and 47 (29.2%) were suspected suicidal exposures. The percentage of XTAMPZA ER exposures that were either abuse/misuse/unknown or suspected suicidal were statistically significantly less than for other drug groups.

Among all exposures, there was a statistically significant difference in the distribution of medical outcomes among all comparators ($\chi^2=350.80$, $df=5$, $p<0.001$). Differences in medical outcomes compared to individual comparators were significant for all comparators (Figure).

Among intentional exposures, there was a statistically significant difference in the distribution among all comparators ($\chi^2=15.2$, $df=5$, $p=0.010$), but XTAMPZA ER values were not statistically significantly different from any individual comparator based on the Dunn test.

CONCLUSIONS

Both the lower number of intentional exposures and lack of manipulation may explain the lower severity of medical outcomes for XTAMPZA ER across all exposures. Among intentional exposures involving XTAMPZA ER, no differences relative to other opioids were observed. For all drug groups, most intentional exposures involved multiple substances or the intent was self-harm. Overall, these findings are consistent with reduced abuse related outcomes in the post marketing setting. However, additional efforts are needed to reduce the burden of prescription opioid misuse, including effective identification and treatment of mental health conditions, increased naloxone access, and treatment for polysubstance use disorders.

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