Accidental unsupervised ingestions of Nucynta® ER in children less than six years-old: Frequency and risk of severe outcomes

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Introduction

- Nucynta® ER is an extended release (ER) formulation of tapentadol, a Schedule II opioid analgesic used for the treatment of moderate to severe pain.
- Nucynta ER has crush-resistant properties intended to deter abuse via unintended routes of administration. However, Nucynta does not have official abuse deterrent labeling.
- The crush-resistant properties of Nucynta ER may reduce the severity of outcomes among pediatric accidental unsupervised ingestions as it may prevent children from unintentionally bypassing the extended release properties by chewing then ingesting the tablet.
- Rates of single substance accidental unsupervised ingestions and rates of severe adverse events (SAEs) among these exposures are calculated for Nucynta ER and compared to other ER opioids and immediate release (IR) opioids. Rates are calculated per gram of drug dispensed.

Methods

- Data from the Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS®) System Poison Center Program were used. As of 2015, The RADAR System Poison Center Program includes 50 centers and covers over 90% of the US population (Figure 1).
- Unintentional general exposures were assessed in children less than 6 years involving either Nucynta ER, other ER opioids or IR opioids from July 2011 through March 2016.
- ER opioids include ER oxycodone, ER oxymorphone, ER hydrocodone, ER hydromorphone, and ER morphine.
- IR opioids include IR oxycodone, IR oxymorphone, IR hydrocodone, IR hydromorphone, and IR morphine.
- SAEs are defined as exposures resulting in death, a major medical outcome, or admission to a heath care facility.
- Analyses were restricted to single substance cases with known medical outcomes to control for potential confounding effects of multi-substance exposures.
- Grams dispensed data were obtained from IMS Government Solutions.
- Cumulative rates of exposures and SAEs per gram of drug dispensed were compared using Poisson regression analysis.

The RADARS® System is part of Denver Health and Hospital Authority, a division of the state of Colorado. It is supported by subscriptions from pharmaceutical manufacturers.

Figure 1. Poison center coverage map

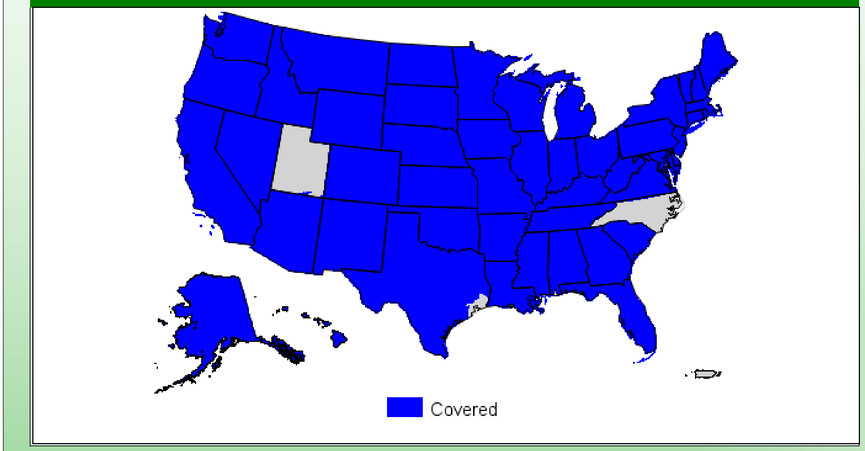

Table 1. Total exposures and SAEs

Drug Group	Single Substance Accidental Unsupervised Ingestion Exposures	SAE, n (%)
Nucynta ER	22	5 (22.7)
ER opioids	867	351 (40.5)
IR opioids	6409	288 (4.5)

Table 2. Rate of exposures per 10 million grams of drug dispensed

Drug Group	Rate	Rate Ratio (95% CI)	p-value
Nucynta ER	0.023	---	---
ER opioids	0.055	2.37 (1.55, 3.62)	**<0.001**
IR opioids	0.131	5.65 (3.72, 8.58)	**<0.001**

Table 3. Rate of SAEs per 10 million grams of drug dispensed

Drug Group	Rate	Rate Ratio (95% CI)	p-value
Nucynta ER	0.005	---	---
ER opioids	0.022	4.22 (1.75, 10.20)	**0.001**
IR opioids	0.006	1.12 (0.46, 2.70)	0.807

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Results

- There were 22 accidental unsupervised ingestions involving Nucynta ER compared to 867 involving an ER opioid other than Nucynta ER and 6,409 involving an IR opioid.
- Five (22.7%) Nucynta ER exposures resulted in an SAE. In contrast, there were 351 (40.5) other ER opioid exposures and 288 (4.5%) IR opioid exposures that resulted in an SAE.
- The relative risk (adjusted for grams dispensed) of an exposure to other ER opioids and IR opioids was significantly higher than Nucynta ER (RR=2.37; p-value<0.001; RR=5.65; p-value<0.001, respectively).
- The relative risk of SAEs per gram of drug dispensed was significantly higher for other ER opioids than for Nucynta ER (RR=4.22; p-value=0.001) but no difference was noted between IR opioids and Nucynta ER (RR=1.12; p-value=0.807).

Conclusions

- The risk of accidental unsupervised ingestions of other ER opioids is over 2 times higher and for IR opioids is almost 6 times higher than Nucynta ER (adjusting per gram of drug dispensed).
- There is also a 4 times greater risk of SAEs per gram of opioid dispensed for other ER opioids than for Nucynta ER.
- These results suggest that the safety profile of Nucynta ER may be more similar to an IR rather than other ER formulations.
- These risks should be considered when prescribing pain medication to patients with children or grandchildren in the home.

Limitations

- Poison Center data are self-reported and may reflect a bias towards more severe medical outcomes.
- Poison Center data may underestimate the number of drug exposures in the population.
- The number of Nucynta ER cases was small, so statistical power is low.