HHS Public Access

Author manuscript

J Pediatr. Author manuscript; available in PMC 2021 February 01.

Published in final edited form as:

J Pediatr. 2020 February ; 217: 196–198. doi:10.1016/j.jpeds.2019.09.029.

Identifying Co-Exposure to Opiates and Gabapentin During Pregnancy

Sean Loudin, MD[1], **Jessica Haas, RN**[2], **Mary Payne, MD**[3], **Marianna Footo Linz, PhD**[4], **Dana Meaney-Delman, MD, MPH**[5], **Margaret A. Honein, PhD, MPH**[5], **Amy Saunders, MA**[6]

[1]Department of Pediatrics, Joan C. Edwards School of Medicine at Marshall University;

[2]NICU, Hoops Family Children's Hospital at Cabell Huntington Hospital;

[3]Department of Neurology, Joan C. Edwards School of Medicine at Marshall University;

[4]Department of Psychology, Marshall University, Huntington, WV;

[5]National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, GA;

[6]Marshall University Center of Excellence for Recovery, Huntington, WV

Abstract

Neonatal withdrawal can be difficult to treat in infants with co-exposure to opiates and gabapentin. Because maternal self-report can underestimate exposures, we evaluated the effect of universal toxicology screening for gabapentin. Identification of co-exposure to opiates and gabapentin increased after implementation of toxicology screening, with implications for improved neonatal care.

Gabapentin (Neurontin) was approved by the US Food and Drug Administration in 1993 and currently has indications for the treatment of neuropathic pain and epileptic disorders. It has recently been used in combination with medication assisted treatment for opioid use disorder (OUD) with some success.[1] However, misuse of gabapentin has been reported in 15%–22% of patients with OUD in a systematic review.[2] Gabapentin use among pregnant women with OUD is not well-studied, nor are the effects on the developing fetus or infant after birth. Neonatal withdrawal symptoms can occur in any infant exposed to opiates in utero, and symptoms may be harder to treat with co-exposure to gabapentin. Infants exposed to both opiates and gabapentin may be difficult to wean from opiate treatment and can exhibit unique symptoms, including general restlessness of the extremities and body, rapid eye movements, tongue thrusting, arching of the back, and exaggerated myoclonic jerks.[3]

Reprint requests: Amy Saunders, MA, Marshall University Center of Excellence for Recovery, 1 John Marshall Drive, Huntington, WV 25755. saunde22@marshall.edu.

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention. The authors declare no conflicts of interest.

Data Statement

Data sharing statement available at www.jpeds.com.

Maternal gabapentin use can be ascertained through self-report or through laboratory testing. Because appropriate and timely treatment of infant withdrawal requires accurately identifying in utero exposures, we sought to examine changes in the identification of co-exposure to opiates and gabapentin after the implementation of urine toxicology screening for gabapentin in a tertiary care center.

Methods

Universal maternal screening at delivery via urine toxicology for opiates and their metabolites, benzodiazepines, amphetamines, barbiturates, and tetrahydrocannabinol was initiated at Cabell Huntington Hospital (Huntington, West Virginia) in 2012. Toxicology screening was expanded to include gabapentin on September 16, 2017, because of maternal histories indicating an increasing number of infants with prenatal co-exposure to opiates and gabapentin, and clinical observation that some co-exposures to gabapentin were only ascertained after repeat maternal interviews for infants with atypical withdrawal symptoms. Among all liveborn infants delivered at Cabell Huntington hospital, we assessed the prevalence of prenatal opiate exposure and co-exposure to opiates and gabapentin after implementation of urine toxicology screening for gabapentin (9/16/2017 to 6/30/2018) compared with a time period when gabapentin exposure was only ascertained based on self-reported maternal history (1/1/2017 to 9/15/2017). During both time periods, clinicians screened patients for exposures based on self-report, but existing data did not allow for the examination of the relationship between veracity of self-report and toxicology analysis. This study was approved by the Institutional Review Board of Marshall University.

Results

There were 1762 liveborn infants delivered in approximately 9 months before universal maternal urine toxicology screening for gabapentin, compared with 1753 liveborn infants delivered in about 9 months after implementation of gabapentin toxicology screening (Table I). There was no significant change in the proportion of infants with prenatal opiate exposure, but the identification of any opiate exposure decreased slightly during the time period after compared with before implementation of gabapentin toxicology screening (7.13% vs 8.91%; prevalence ratio, 0.78; 95% CI, 0.61–1.00). One mother was identified with gabapentin only exposure before universal screening was implemented, and 4 were identified after implementation of screening. There was an increase in the identification of co-exposure to both opiates and gabapentin after implementation of toxicology screening for gabapentin (1.94% vs 1.14%; prevalence ratio, 1.72; 95% CI, 0.99–3.01) that was of borderline statistical significance.

There were 54 infants identified with withdrawal symptoms and co-exposure to opiates and gabapentin; 20 infants were identified with co-exposure based on self-report before universal screening was implemented, and 34 infants were identified with co-exposure after universal screening was implemented (Table II). The average length of hospital stay for infants with co-exposure to gabapentin and opioids was shorter after implementation of universal toxicology screening than before (47.9 days vs 57.6 days). Before universal toxicology screening, the infants with co-exposure who were treated with gabapentin therapy started

this treatment on average at 20.4 days of life, with a range of 3–48 days. After implementation of universal screening, the infants with co-exposure who were treated with gabapentin were started on gabapentin therapy sooner, on average at 14.5 days of life, with a range of 1–34 days.

Discussion

Maternal self-report might underestimate some in utero exposures, such as substance use. The observed increase in identification of co-exposure to opiates and gabapentin after the implementation of urine toxicology screening could reflect better identification of gabapentin exposure, an increase in the combined use of opiates and gabapentin among pregnant women, or both. However, there are limitations to both self-reported data and laboratory testing. Self-reported data might be limited by maternal apprehension about reporting some exposures, particularly if the medication was not prescribed by a healthcare provider. A lack of maternal awareness of tainted substances used may also influence the accuracy of self-report. The sensitivity and specificity of laboratory testing varies considerably between systems, which can result in false-positive or false-negative results; results of laboratory testing will be influenced by timing of exposure relative to testing, the sample tested, and other medications being administered that might impact test results.[4,5] Therefore, universal toxicology screening through laboratory testing should be considered as an addition to continued dialogue and rapport between the clinician and the patient about substance exposure. This strategy might also promote a more trusting, transparent relationship that could promote better adherence to treatment after discharge.

In this hospital setting, 1.94% of infants were identified with prenatal co-exposure to opiates and gabapentin during the time period after the implementation of universal toxicology screening, and identifying these exposures helped to inform optimal infant care for neonates experiencing withdrawal, particularly those exhibiting atypical symptoms. This was an increase over the level of co-exposure identified based on self-report (1.14%), and there was no increase in exposure to any opiate during this time period that would suggest a change in the prevalence of neonatal abstinence syndrome in this population. We acknowledge that this is an estimate for one institution, with a somewhat unique catchment area population in terms of socioeconomic status and education, and there could be higher or lower co-exposure in other settings. An analysis of 2000–2010 Medicaid prescription data for pregnant women with at least 1 outpatient prescription filled for an opioid medication showed that only 0.3% also filled a prescription for gabapentin, but the prevalence of co-exposure from illicit sources or for those with OUD is unknown.[6] Implementation of universal gabapentin toxicology screening at other institutions with high prevalence of OUD among pregnant women or other approaches to increase detection of co-exposure may improve pediatric care of affected infants.

Identifying co-exposures may assist in selecting the optimal infant therapy in a timely manner. The identification of co-exposures through universal screening in this health-care facility led to more rapid initiation of infant gabapentin therapy (average of 14.5 days vs 20.4 days) for those infants treated with gabapentin and shorter average lengths of stay (47.9 days vs 57.6 days). The charge for laboratory testing increased only modestly with the

addition of screening for gabapentin; in contrast, the potential cost savings by reducing the average length of stay in either the neonatal intensive care unit or neonatal therapeutic unit was much larger.

Considering possible co-exposures for infants with a complicated postnatal course and atypical symptoms may assist providers in determining the best treatment for each infant.[3] Long-term developmental and behavioral effects of gabapentin exposure to the developing brain are unknown. Longitudinal surveillance data are needed to understand the full impact of prenatal opioid exposure and to determine differential outcomes associated with polysub stance combinations such as opiate and gabapentin co-exposure.[7]

Abbreviations:

OUD	Opioid use disorder

References

1. Toce MS, Chai PR, Burns MM, Boyer EW. Pharmacologic treatment of opioid use disorder: a review of pharmacotherapy, adjuncts, and toxicity. J Med Toxicol 2018;14:306–22. [PubMed: 30377951]
2. Smith RV, Havens JR, Walsh SL. Gabapentin misuse, abuse and diversion: a systematic review. Addiction 2016;111:1160–74. [PubMed: 27265421]
3. Loudin S, Murray S, Prunty L, Davies T, Evans J, Werthammer J. An atypical withdrawal syndrome in neonates prenatally exposed to gabapentin and opioids. J Pediatr 2017;181:286–8. [PubMed: 27889067]
4. Ondersma SJ, Chang G, Blake-Lamb T, Gilstad-Hayden K, Orav J, Beatty JR, et al. Accuracy of five self-report screening instruments for substance use in pregnancy. Addiction 2019;114:1683–93. [PubMed: 31216102]
5. Jarvis M, Williams J, Hurford M, Lindsay D, Lincoln P, Giles L, et al. Appropriate use of drug testing in clinical addiction medicine. J Addict Med 2017;11:163–73. [PubMed: 28557958]
6. Huybrechts KF, Bateman BT, Desai RJ, Hernandez-Diaz S, Rough K, Mogun H, et al. Risk of neonatal drug withdrawal after intrauterine co-exposure to opioids and psychotropic medications: cohort study. BMJ 2017;358:j3326. [PubMed: 28768628]
7. Honein MA, Boyle C, Redfield RR. Public health surveillance of prenatal opioid exposure in mothers and infants. Pediatrics 2019;143(3): e20183801. [PubMed: 30655335]

Table I.

Opiate and gabapentin exposure among pregnancies resulting in 1 or more liveborn infants at Cabell Huntington Hospital [*]

Variables	Before toxicology screening [†]	After implementation of universal toxicology screening	Prevalence ratio (95% CI)
Total number of pregnancies delivering ≥1 live birth	1762	1753	–
Any opiates (with or without gabapentin)	157	125	–
Opiates + gabapentin	20	34	–
Opiates only	137	91	–
Gabapentin exposure only	1	4	–
Deliveries screening positive for any opiates	8.91%	7.13%	0.78(0.61–1.00)
Co-exposure to opiates and gabapentin	1.14%	1.94%	1.72(0.99–3.01)

[*] Comparing deliveries before toxicology screening for gabapentin (January 1 to September 15, 2017) with deliveries after the implementation of universal toxicology screening for gabapentin (September 16, 2017 to June 30, 2018).

[†] Gabapentin exposure based on maternal self-report.

Table II.

Clinical course and outcomes

Variables	Infants with co-exposure identified before toxicology screening for gabapentin (n = 20) (1/1/2017–9/5/2017)	Infants with co-exposure identified after implementation of universal toxicology screening for gabapentin (n = 34) (9/16/2017–6/30/2018)
Length of hospital stay (days)		
Mean	57.6	47.9
Median	57.5	45.5
Range	22–106	17–94
Infant treated with gabapentin		
Yes	16	18
No	4	16
Day of life when gabapentin started for those treated with gabapentin		
Mean	20.4	14.5
Median	19.5	17.5
Range	3–48	1–34

OUD Opioid use disorder