EDITORIAL

Be vigilant for neonatal abstinence syndrome

AUTHOR
Dr Jez Thompson
MB ChB MSc MRCGP
GP Leeds and Clinical Director Lifeline Project, RCGP Regional Lead Substance Misuse

NEONATAL ABSTINENCE SYNDROME IS A SERIOUS CONDITION OF NEONATES THAT have been exposed to psychoactive drugs in utero. Exposure to opioid substances is responsible for the majority of cases, and while use of illicit opioids and opioid substitute treatments in opioid dependence are associated with a high incidence of the condition, concerns have been raised about increasing use of prescribed opioid analgesia during pregnancy.

While data show that the general use of opioid analgesics is increasing in a wide range of countries, specific data about use in pregnancy are available in Norway and the US where 6% and 14-22% of women respectively are reported to have filled at least one prescription for opioid analgesia while pregnant.

Published evidence on the risk of neonatal abstinence syndrome in non-maintenance opioid use is sparse, and up till now there have been no population-based studies on the risk of neonatal abstinence syndrome in infants born to mothers who have used prescription opioid analgesics during pregnancy.

Drawing data from a nationwide cohort of Medicaid-enrolled pregnant women, the authors of this study, published in the *BMJ,* set out to provide absolute and relative risk estimates for neonatal abstinence syndrome linked to duration and timing of prescription opioid use during pregnancy together with the presence or absence of additional risk factors.[1] The study included 290,605 women, from 46 US states, who had filled at least one prescription for an opioid analgesic during pregnancy, this represented 21% of pregnancies for which data were available.

Additional risk factors for neonatal abstinence syndrome were deemed to be: a documented history of opioid misuse or dependence; a history of alcohol misuse or non-opioid drug misuse; use of psychotropic medications in the third trimester; and smoking.

The majority of women, 194,001 (66.5%), had none of these four risk factors. There were 4,816 (1.7%) women with a documented history of opioid misuse or dependence, 28,553 (9.8%) with a history of alcohol or non-opioid drug misuse or dependence, 34,723 (11.9%) had filled at least one prescription for a non-opioid psychotropic medication during the three months before delivery and 28,512 (9.8%) had a history of smoking.

Of those women who used prescription opioids, the majority took them short-term, 256,494 (88.3%). Codeine, oxycodone, hydrocodone, and propoxyphene accounted for a majority of the prescribed opioids. The median duration of use among short-term users was five days with a median cumulative dose of 135 mg oral morphine equivalent. For long-term users the median duration of use and equivalent cumulative dose during the pregnancy were 55 days and 1,180 mg respectively.

'The incidence of neonatal abstinence syndrome was surprisingly high'

The study identified a total of 1,705 cases of neonatal abstinence syndrome for women who had filled an opioid prescription while pregnant, representing an absolute risk of 5.9 cases per 1,000 deliveries (95% CI: 5.6 to 6.2).

The risk was greater for long-term prescription opioid users. The risk of neonatal abstinence syndrome was relatively low in women with none of the other identified risk factors (4 cases and < 1 case per 1,000 for long- and short-term users respectively). The risk was highest for women with a documented history of opioid misuse or dependence (220 and 192 cases per 1,000 deliveries for long- and short-term users respectively).

Babies of women who used prescription opioids during the last trimester had a significantly higher incidence of neonatal abstinence syndrome compared with those who used them in the first two trimesters only.

Neonatal abstinence signs identified included respiratory symptoms (30.1%), feeding difficulties (17.1%), but only rarely seizures (2.7%). The duration of hospital stay for babies with neonatal abstinence syndrome was five days, compared with three days for babies without this condition.

The incidence of neonatal abstinence syndrome was surprisingly high in this large, population-based study. GPs must remain aware of both the general risk and the specific additional risk factors when giving advice or considering prescribing opioid analgesics during pregnancy.

REFERENCE
1 Desai RJ, Huybrechts KF, Hernandez-Diaz S et al. Exposure to prescription opioid analgesics in utero and risk of neonatal abstinence syndrome: population based cohort study. *BMJ* 2015;350:h2102

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