Balance in Opioid Prescription during Pregnancy

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IN this issue of ANESTHESIOLOGY, Bateman *et al.*[1] present an analysis of opioid prescription practices from a large U.S. private insurance database. The information derived from the database "InVision" for Data Mart is constructed from medical and prescription information from privately insured people in the United States. The authors identified a surprisingly high incidence of opioid prescription during pregnancy (14%) which was marked by considerable regional variation. The large majority of opioid prescriptions identified were for short courses of treatment with only 2.2% including two or more refills.

This work is important in that the absolute incidence of opioid prescription during pregnancy is much higher in this cohort compared with that identified in earlier U.S. cohorts[2,3] or Scandinavian cohorts.[4–6] Furthermore, the large regional variation suggests that a different balance is perceived between the value of treating the mother with a short course of opioid and potential risk to the fetus. To enhance the awareness of pain treatment among healthcare professionals, the American Pain Society promoted pain as the "fifth vital sign" in the latter half of the 1990s. The Veterans Health Administration (1999) and the Joint Commission on Accreditation of Healthcare Organizations (2000) subsequently adopted the "Pain as the fifth Vital Sign" initiative to establish standards for the routine screening, assessment, and documentation of a management plan for pain. In part, as a result of these campaigns designed to combat under treatment of chronic pain, U.S. opioid prescription has greatly increased over the periods covered by the above studies, even between the period considered by the National Birth Defects Prevention Study (1997 to 2005) and the current trial (2005 to 2011).[7]

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The potential impact of liberalization of opioid prescription on the fetus is certainly worthy of consideration and has been the subject of many studies. Since the rise of heroin use in the 1950s, the consequences of fetal opioid exposure have been documented for decades. Opioid use during pregnancy was associated with an excess of premature delivery, low–birth-weight infants, neonatal withdrawal, and birth defects.[8] However, the interpretation of these findings from small observational trials is complicated by the strong association of adverse social circumstances associated with illicit opioid use including comorbid disease and other drug use and poor maternal nutrition. Pregnant women who are prescribed a short course of opioids are less likely to be exposed to the above conditions.

The risk of short-term exposure to prescription opioids to the fetus under medical supervision is more difficult to assess and needs to be carefully examined in future studies. Most studies focus on exposure in early pregnancy during the period of organogenesis although pathology may occur through more subtle changes in neuronal structure or function. An early U.S. cohort from the Collaborative Perinatal Project documenting use of propoxyphene and codeine (1959 to 1965),[2] a study from a Swedish birth registry identifying use of dextropropoxyphene and codeine (1985 to 1989),[4] and a study based on the Norwegian Mother and Child Cohort that identified codeine (1967 to 2008)[5] did not find an association between opioid prescription and congenital malformation. In contrast, several case control studies, most notably the U.S. National Birth Defects Prevention Study (1997 to 2005),[3] have found

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associations between codeine and other opioid use and birth defects including atrial and ventricular septal defects, hypoplastic left heart syndrome, spina bifida, and gastroschisis in newborns. It is not clear whether differences in study design between the large cohort trials and case control trials might play a role in the difference in findings. However, the findings from recent case control trials should play a role in consideration of the best treatment for maternal pain and risk to the fetus. Maternal treatment with opioids in the third trimester, near the time of birth, is clearly a risk factor for neonatal abstinence syndrome and requires careful attention by the pediatricians caring for the newborn to avoid associated morbidity.[9]

Pain is very common in pregnancy as a result of weight gain, postural change, hormonally induced ligamentous relaxation, and pelvic floor dysfunction. Other studies have suggested that low back pain and pelvic pain are present in two thirds and one fifth of pregnancies, respectively, and are potentially improved by exercise and acupuncture.[10] Approximately 10% of the total prescriptions in the Bateman cohort were related to surgical procedures and approximately 1% was for women who were chronically using opioids before pregnancy. If opioids are considered obligatory for those patients, the remaining 89% of patients might consider alternative means for pain management. The majority of the indications for opioid treatment in the Bateman cohort were back pain (37%), abdominal pain, migraine, joint pain, and fibromyalgia, pain syndromes that are not particularly opioid responsive and are amenable to treatment with other drugs including nonsteroidal antiinflammatory drugs, physical and psychological therapy.

The use of nonsteroidal antiinflammatory drugs during pregnancy has been considered a risk factor for congenital malformation, but a recent study of more than 90,000 Norwegian mother–child pairs did not identify any increase in the risk for congenital malformation.[11] Nonsteroidal antiinflammatory drugs are used not only for pain but also for tocolysis later in pregnancy. Use of these drugs after 30 weeks of gestation is associated with 15-fold higher risk of premature closure of the ductus arteriosus before birth which can be complicated by persistent pulmonary hypertension.[12] The use of other drugs and treatments for pain management is not studied in this cohort; therefore, we do not know whether the opioids were prescribed after failure of other therapy.

The findings by Bateman *et al.* suggest that at least in some areas of the United States, the balance between inadequate pain management for the mother and risk to the fetus has shifted. Current studies continue to raise the specter of a small increased risk for birth defects when prescription opioids are used in early pregnancy. Opioids are not recommended as the first-line treatment of mild to moderate chronic pain even in the absence of the consideration of pregnancy. It may be perceived as easier for the practitioner and/or the patient to use opioids for the common pain conditions encountered in pregnancy rather than more time-intensive use of other therapies. The ratio between the relative risk and benefits of the available therapies for pain in pregnant women, such as nonsteroidal antiinflammatory drugs and opioids, needs further careful investigation. When long-term risk is added to the therapeutic equation, an emphasis on alternative therapy may be warranted and should be considered in prospective trials of pain management in pregnancy.

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Competing Interests

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