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Looking Beyond the Pain: Can Effective Labor Analgesia Prevent the Development of Postpartum Depression?

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Postpartum depression (PPD) affects 1 of 7 mothers.¹ PPD is debilitating, negatively impacts mother–infant attachment, and increases the risk for long-term psychological sequelae for her child.² In severe cases, PPD can result in maternal suicide, which is the leading cause of maternal deaths occurring in the first year after pregnancy.³ Given the approximately 4 million deliveries a year in the United States, PPD is a major public health challenge.

A neglected area of research is the relationship of pain during labor and delivery to PPD. It is well known that pain commonly cooccurs with depression, and emerging evidence suggests that an association exists among acute post-partum pain, chronic pain, and PPD.^{4,5} In 2014, Ding et al⁵ conducted a prospective observational study comparing the incidence of PPD between women who received epidural analgesia to those who did not. The use of epidural analgesia was associated with a reduced risk for PPD (odds ratio 0.3, 95% confidence interval [CI], 0.12–0.79). These results were promising; however, methodological issues such as the observational study design, potential misclassification bias, and uncontrolled confounding emphasized the need for additional investigations. Two

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articles published in this issue of *Anesthesia & Analgesia* seek to further our understanding of the relationship between labor analgesia and PPD.

The study by Orbach-Zinger et al⁶ evaluated the relationship between the intention to use epidural analgesia, the use of epidural analgesia, and PPD at 6 weeks. Due to logistical reasons (eg, lack of nurses or lack of labor rooms), a proportion of women who intend to use epidural analgesia were unable to receive it. The authors hypothesized those women, women who intended to use epidural analgesia but delivered without, would have the highest rates of PPD due to untreated labor pain and unmatched expectations during labor.

A total of 1497 women were enrolled in the study. On postpartum day 1, participants completed a survey that inquired about analgesic intent, whether or not epidural analgesia was used for labor, and satisfaction with analgesia. At 6 weeks postpartum, the Edinburgh Postnatal Depression Scale (EPDS) was administered. The primary outcome was the EPDS score at 6 weeks, with a score of 10 indicating a positive screen for PPD. The overall PPD rate was 6.6%; however, the PPD rate among women who intended to use epidural analgesia, but delivered without was not different than all other groups (risk difference [RD], 1.8%; 95% CI, -3% to 7%). A secondary analysis was conducted among the women who did not intend to use epidural analgesia. The relative risk of PPD was higher among those who ultimately received epidural analgesia than those who did not use epidural analgesia (RD, 7.2%; 95% CI, 2.3%–12.1%). An interaction analysis demonstrated a strong negative additive interaction between unmatched expectations (delivering with epidural analgesia when it was not intended, or delivering without epidural analgesia when it was intended) compared to matched expectations (delivering with epidural analgesia when intended, or delivering without epidural analgesia when not intended) (RD, -8.6%; 95% CI, -16.2% to -1.6%). In a multivariable logistic regression model, the interaction between intended and actual use of epidural analgesia decreased the adjusted odds of PPD (odds ratio, 0.92; 95% CI, 0.86–0.99). The authors acknowledge that unplanned epidural analgesia may be an indicator for physiologically difficult delivery.

Lim et al⁷ studied the relationship between the quality of intrapartum pain management and PPD. The authors hypothesized that PPD is associated with the pain experienced during labor. Data from 1882 women who labored over a 2-month time period were evaluated. Similar to the Orbach-Zinger et al's⁶ study, the authors used an EPDS score 10 as the primary outcome. Intrapartum numeric rating scores were extracted from the medical record, and percent improvement from baseline pain (PIP) was operationalized as the average change in pain per unit of time. For study inclusion, women must have received epidural analgesia for labor pain relief, had at least 2 pain scores recorded during labor (1 before the initiation of labor analgesia, and at least once afterward), and had PPD risk assessed using the EPDS at their 6-week post-partum visit. Of the original sample of 1882, a significant portion of women were excluded from the analyses due to lack of recorded EPDS scores or not having used epidural analgesia for labor (962 exclusions), or for incomplete pain data (179 exclusions), resulting in a final sample of 201 women (11% of the original sample). Using multivariable linear regression modeling to control for PIP, body mass index, baseline anxiety or depression, third or fourth degree lacerations, and baseline anemia, the authors found an association between greater improvements in pain and EPDS scores; however, only

6.6% of the variability in EPDS scores were explained by PIP. Twenty-five women had a positive EPDS screen, and worse labor analgesia remained significantly associated with positive EPDS screen (adjusted odds ratio 6.6; 95% CI, 1.9–22.4). While the effect of labor analgesia on EPDS scores was relatively small, these findings are significant because labor pain is treatable, and it is possible to improve intrapartum labor pain with effective epidural analgesia.

While these data are promising, the fundamental question of “does effective epidural analgesia, that matches a priori expectations, alter PPD outcomes?” remains largely unanswered by these studies for several reasons. The data-sets did not include important variables which could affect the depression outcome such as insurance status and level of education.¹ In addition to sociodemographic variables, additional patient-level contributors, such as the role of adverse life events, environmental factors, and a family history of depression, need to be included to fully understand the relationship between pain and depression.^{8,9} A history of depression and anxiety does not define the depressive symptom level at term pregnancy, and no measure of depressive symptoms was obtained before epidural analgesia in either study. Neither study included an assessment of the pain experience at 6 weeks postpartum. While most consider the pain of labor to be a transient event, for many women, persistent pain after delivery will negatively impact their quality of life.¹⁰ This information is critical to understanding the evolution of new onset psychiatric disorders, which peak across the first 3 months after birth.¹¹

The Lim et al⁷ study was retrospective, and had significant missing data. Fifty-one percent of eligible women were not eligible for study inclusion due to missing EPDS data or nonuse of epidural analgesia. An additional 38% of the total sample was excluded for missing pain data, which reduces our ability to create robust models and determine the relationship between intrapartum pain and subsequent depression. Furthermore, while the authors stated that it is expected that pain scores be recorded every 1 to 3 hours during labor, the median number of pain scores recorded among the final sample was only 3, despite the median duration of labor being 8 hours. When pain scores were imputed using a worst-case scenario, that is, assuming all missing pain data resulted in the lowest possible improvements in pain, there was no association between labor analgesia and PPD.

Future research must include the relationships between each of the postulated factors that contribute to the development of PPD to develop appropriate and targeted interventions. For example, Lim et al⁷ considered antenatal depression or anxiety to represent a potential confounder between the relationship of intrapartum pain and PPD. Another interpretation, which is supported by Orbach-Zinger et al's⁶ data, could be that intrapartum pain is a mediator or effect modifier of the known association between antenatal and PPD. While the percent improvement in pain is an interesting variable to assess the adequacy of epidural analgesia, the woman's experience of pain control after labor is likely to contribute more to the evolution of depression, as supported by the finding that perineal lacerations had the greatest association with higher EPDS scores.⁷ If future studies verify that intrapartum pain or unmet analgesic expectations are indeed associated with PPD, systems for counseling these women and close follow-up could be created.

Despite these limitations, these studies have important messages for perinatal providers. The most important is the urgent need for better documentation and evaluation of local data. It is unlikely that pain was not assessed intrapartum in Lim et al's⁷ study. It is more likely that pain was assessed and never recorded in the medical record. Similarly, postpartum EPDS scores were only recorded on 55% of the women who had a vaginal delivery in that study.⁷ Universal PPD screening is recommended by multiple national organizations, including the American College of Obstetricians and Gynecologists,¹² the American College of Nurse-Midwives,¹³ and the US Preventive Services Task Force.¹⁴ Earlier this year, the Council on Patient Safety in Women's Healthcare developed a consensus bundle on maternal mental health, with recommendations on how to implement PPD screening—intended for use in every clinical care setting and with every woman.¹⁵ Given the public health importance of perinatal depression, a multidisciplinary team should be convened to review and implement the Council's bundle recommendations and ensure all women receive education and screening on PPD.

While high-quality prospective studies are needed to understand the complex interplay between intrapartum pain and PPD, anesthesiologists could have a multigenerational public health impact by working collaboratively with obstetricians and perinatal psychiatrists to ensure that hospitals prioritize screening and treatment for PPD.

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