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Modern Labor Analgesia

Although the experience of labor and delivery in America is quite different from that in Switzerland, Afghanistan, or sub-Saharan Africa, having a baby remains for most women the most emotionally and physically challenging, and at times dangerous, experience in their life. Childbirth, overwhelmingly a happy and desirable event, still carries a maternal death toll of 11 per 100,000 live births a year in the United States and claimed 2100 deaths per 100,000 live births in Sierra Leone in 2009.[1] In consequence, striking a balance between a quiet, private, intimate experience surrounded by the husband, family, and doula and a "medical" experience with midwives, nurses, obstetricians, and obstetric anesthesiologists is not simple to achieve and is undeniably sculpted by convention and culture, but also by the knowledge and resources allocated for women's health.

The International Association for the Study of Pain (IASP) declared 2007 to 2008 the Global Year against Pain in Women, with the slogan "real women, real pain."[2] Key points presented in the fact sheets published by IASP related to: (1) the importance of treating pain within the pregnant population and the substantial public health impact if pain is neglected, (2) the alarmingly high rate of acute or chronic pain after delivery, and (3) labor pain as a clinical model for studying acute pain.

Despite undeniable advances in our understanding of the physiology of labor pain that have resulted in the current safe and effective delivery of labor analgesia to the majority of women in the developed world, providing a "labor epidural" often remains a significant challenge in labor rooms in North America. During 9 months of pregnancy, which should provide ample time to seek information, women's expectations regarding the birthing process are remarkably diverse and are influenced by many factors. In no other field of medicine is the experience of a painful process described in such divergent ways: natural, beautiful, wonderful to the point of being exhilarating on the one hand, and overwhelmingly painful, horrible, distressing, and traumatic on the other.

For the subset of women who know from the start they want to deliver with minimal discomfort by means of an epidural, providing an ideal labor analgesic is nowadays quite simple to achieve effectively, and most women in high-resource countries do choose to take advantage of modern state-of-the art obstetrical anesthesia and labor analgesia techniques.[3] But interestingly, for women who are either undecided or think they prefer to remain unmedicated, the sense of disappointment and guilt when they ultimately "fail" and end up requesting an epidural often supersedes the benefits of pain relief, no matter how successful the analgesia.[4]

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Despite, and maybe even because of, living in the (mis)information era, the reality of labor pain comes as a shock to most women. The dominant source of information for women and their families has been shown to be nonmedical sources, by means of the media and the Internet.[5] Surprisingly (or not), the most frequently accessed and most popular websites are not authored by anesthesiologists, but rather by doulas and others who are not medical professionals. Consequently, the information is at best outdated, but more often it is biased, misleading, and totally erroneous.[6] As a result, in a recent survey we conducted in our institution, more than 50% of first-time mothers arrive in the labor room not wanting an epidural, yet more then 90% leave the hospital having required obstetric anesthesia care.[7]

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Factors associated with a woman's choice to deliver with an epidural vary tremendously worldwide.[8] Reasons women provide for not wanting an epidural typically include the "bad effects of epidurals," among which they include: (1) problems with the course of labor and delivery (prolonged labor and interference with the urge and ability to push, causing an increase in instrumental and Cesarean deliveries), (2) an increased risk of fetal distress (via maternal hypotension or direct effects of medication), (3) maternal risks and complications (back pain, infections, or neurological impairment, including spinal cord damage and paralysis), (4) an unnecessary medical intrusion in a natural physiological process (interference with "natural" childbirth), and finally (5) the negative effects on maternal bonding, breastfeeding, and even parenting.

While some of the above problems were caused by obstetric *anesthesia* as provided 20 years ago, modern obstetric *analgesia* has overcome these challenges and avoids these unwanted effects.[9,10] Unfortunately, these advances have not been sufficiently well disseminated to the larger audience that includes women, their families, doulas, midwives, family doctors, obstetricians, and even anesthesiologists. The American College of Obstetrics and Gynecology (ACOG) delivered the following statement in 2002:[11] "Labor results in severe pain for many women. There is no other circumstance in which it is considered acceptable for a person to experience untreated severe pain, amenable to safe intervention, while under a physician's care. In the absence of a medical contraindication, maternal request is a sufficient medical indication for pain relief during labor." Nevertheless, the priority and importance of labor analgesia somehow continue to be questioned. The fact that women can safely be offered an early epidural, with very low doses of medication, and that they are able to control the amount of medication they receive, is still often ignored. It may seem quite incredible to the IASP readership that neither ACOG, the Society of Obstetric Anesthesia and Perinatology (SOAP), the American Society of Anesthesiology (ASA), or IASP have succeeded in making labor pain a model of acute pain, and in establishing its obvious relief with an epidural as the undisputed standard of care for all parturients seeking pain relief.

Labor Pain

Characteristics of Labor Pain

The neuroanatomy of uterocervical nociception in labor has been described as follows. The pain of first-stage labor is conducted by thin afferent, *visceral* sympathetic fibers, entering the spinal cord at thoracic and lumbar roots (T10–L1), while second-stage labor pain is conducted via thicker *somatic* nerve fibers entering the spinal cord at sacral roots S2–4.[12] It has long been noted that labor pain, particularly in first-time mothers, is one of the most severe types of pain that a woman will endure in her entire life.[13] Challenges that are specific to management of obstetric pain relate to the fact that effective analgesia needs to be balanced with the need for women to be able to actively push and deliver their baby. Adequate sacral analgesia frequently requires more concentrated local anesthetic solutions than first-stage pain, due to the thicker nerve roots that need to be blocked, just when obstetricians and women worry that women may lose the "urge to push" and may develop a motor block that may preclude spontaneous vaginal delivery. Obstetric anesthesiologists understand nowadays that optimal labor pain relief requires an effective sensory block (i.e., selective analgesia) with the *least* amount of local anesthetics with opioids, while at the same time affording sacral analgesia.

In recent years there has been interest in evaluating pregnancy-induced changes in pain perception and analgesia. Pregnancy-induced analgesia has been suggested as a "coping mechanism" to allow women to tolerate and survive the intense pain endured during childbirth. Pregnancy-induced analgesia may have interesting implications for the understanding of pain modulation at the time of labor and delivery, in particular with regard to why some women are able to tolerate this intense pain while others

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are not. The proposed mechanism for this phenomenon is based on animal studies that have demonstrated activation of the opioid system at the spinal level in response to the pregnant state.[14] Several investigators have been testing pain modulation with quantitative sensory tests during pregnancy[15] and around the time of delivery[16,17] to see whether pregnancy-induced analgesia can be evaluated and to predict women's tolerance to labor pain or postcesarean pain. Research suggests that fear of labor may affect evoked pain tolerance during pregnancy as well as in the postpartum period,[18] adding a new dimension to the already complex concept of testing women's response to evoked pain to predict pain outcomes during labor and delivery. Further directions for

research may include testing the hypothesis that women with increased pain thresholds and enhanced endogenous pain inhibition before or during labor would have lower labor analgesic requirements. Confirmation of this hypothesis may translate into clinically relevant outcomes such as neuraxial analgesia requests at a later stage in labor, reduced analgesic requirements for effective labor or post-cesarean analgesia, and perhaps better long-term postpartum outcomes.[19]

Effects of Labor Pain on the Mother

Maternal physiological responses to labor pain may affect maternal and fetal wellbeing and influence the progress of labor.[12,20] The sympathetic nervous system response to pain results in a marked increase in circulating catecholamines, such as norepinephrine and epinephrine. This maternal catecholaminergic surge results in increased maternal cardiac output, systemic vascular resistance, and oxygen consumption. For women with preexisting cardiac or respiratory compromise, such increases may be difficult to sustain. Increases in cardiac output and vascular resistance may increase maternal blood pressure. Pain, stress, and anxiety cause release of stress hormones such as cortisol as well as beta-endorphins. Effective analgesia attenuates or eliminates these responses.

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Besides these acute maternal hemodynamic and metabolic responses to labor pain, intense labor pain has been associated with postpartum posttraumatic stress,[21] postpartum depression, and persistent pain.[22] Epidural analgesia has been shown to reduce the risk of immediate postpartum depression.[23]

Persistent pain after vaginal and cesarean delivery has been a recent field of investigation for obstetric anesthesiologists.[22,24] The incidence of chronic pain after cesarean delivery seems to be in the order of 5–10%,[25,26] and even though persisting pain is often described as mild, a high proportion of women may require more targeted pain management to prevent long-term adverse effects.[27,28] A large and increasingly growing proportion of women undergo repeated cesarean delivery, which may constitute a unique surgical model that may allow researchers to test women's residual hypersensitization from the previous surgery and identify those at risk for subsequent chronic pain. Indeed, scar hyperalgesia was found in 40% of women scheduled for a repeated cesarean delivery, and the extent of that hyperalgesia correlated with acute postsurgical pain and the presence of wound hyperalgesia.[29] Therefore, further research to identify valid models to predict chronic pain are needed, to allow targeted interventions to women who are most likely to need more tailored antihyperalgesic therapies.

Effects of Maternal Pain on the Neonate

It has been clearly established that labor induces a massive catecholamine surge in the fetus, particularly in the second stage of labor, which helps preserve adequate blood flow to the brain, heart, and adrenal glands and ensures postnatal adaptive circulatory changes and surfactant release. While this fetal stress response is initially favorable to the fetus, unmodified "natural" labor causes maternal changes that may be deleterious. Maternal hyperventilation in response to pain has long been known to have adverse fetal effects. It causes (1) respiratory alkalosis and a left shift in the oxygen dissociation curve (potentially disadvantageous to placental transfer of oxygen); (2) a compensatory metabolic acidosis, which becomes progressively more severe with progression of labor and is also conveyed to the fetus; (3) episodes of hypoventilation, causing hemoglobin desaturation between contractions; and (4) uterine vasoconstriction.[30] Despite this body of evidence, women still believe that natural childbirth with its "unmodified" labor is harmless to the baby,

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and that any pharmacological form of analgesia must have adverse effects, contending that epidural analgesia, the most invasive form of pain relief in labor, being the most damaging to the fetus.

In fact, systemic opioids, in addition to producing less effective analgesia than neuraxial techniques, also have a less advantageous profile for the newborn. A mix of 50% nitrous oxide and 50% oxygen (Entonox), very popular in the United Kingdom, is not only more effective than systemic opioids, it is also less likely to depress the newborn. Expectant mothers should be reassured that, although epidural analgesia may be associated with some short-term maternal side effects, its effects on the baby, when compared with systemic analgesia, are more consistently beneficial in terms not only of Apgar scores but also of acid-base status, and it is less likely than systemic opioids to impair breastfeeding.[31]

Advances in Modern Obstetric Analgesia

Timing of Epidural Labor Analgesia

One of the most important recent advances directly influencing clinical practice has been the unequivocal demonstration in 2005[32] that provision of neuraxial analgesia *early in labor* has

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distinct advantages for maternal analgesia and satisfaction, with no negative impact on mode of delivery. In other words, the risk for a cesarean delivery is *not* influenced by early combined

spinal epidural (CSE) or epidural analgesia. These findings create a real paradigm shift for care providers and allow women to benefit from early neuraxial analgesia.[33] The idea that there is "no need to wait for a cervical dilatation of at least 4 cm" has received full media coverage, and this information should be disseminated widely.

Ultra-Low-Dose Neuraxial Analgesia

Modern, state-of-the-art, low dose neuraxial analgesia is typically provided through a combination of two relatively recent techniques: (1) initiation of labor analgesia with a CSE[34] and (2) maintenance of labor analgesia with a low-dose infusion of local anesthetics with opioids via a patient-controlled epidural analgesia (PCEA) device.[35]

Patient-controlled epidural analgesia is at the forefront of today's service of labor analgesia

Recognition of the major advantages of CSE over epidurals has contributed to the widespread use of this technique for obstetric analgesia and anesthesia in the new millennium.[36] Besides its most observable advantage of a rapid and spectacular onset of effective analgesia provided by remarkably low doses of local anesthetics, opioids, or a mixture of both, CSE appears to afford better analgesia throughout the course of labor, thus reducing the request for additional doses for recurrent breakthrough pain. Why CSE analgesia should be associated with fewer requests for additional analgesia remains unclear. There is evidence that epidural infusions are more effective in the presence of a small dural puncture. Several mechanisms may be at play, including the effect of epidural injections on spinal analgesia level, the effect of dural puncture on passage of epidural medication to the cerebrospinal fluid, or an intrinsic superior efficacy of spinal versus epidural analgesia. An important (perhaps persuasive) factor in favor of the CSE technique is that most studies have reported higher maternal satisfaction scores with CSE in comparison to epidurals for labor or cesarean deliveries.

The effect of ambulation on labor is controversial, but early studies have shown that ambulation is as valuable as oxytocin augmentation in managing dysfunctional labor. The purported advantages of walking throughout labor include the influence of gravity in helping the descent of the fetal head. However, if this phenomenon exists, walking should be encouraged in advanced stages of labor, when fetal head descent is expected to happen. Data accumulated from all these studies are not in favor of ambulation during labor, and the general belief is that the only benefit lies in the fact that mothers generally have a positive view of walking.[37]

PCEA is at the forefront of today's service of labor analgesia.[35] Initial studies have attempted to establish the advantages of different infusion regimens (no background infusion and self-administration of boluses for breakthrough pain).[38] Some recent studies have evaluated the concept that intermittent boluses provide better analgesia than the same amount of local anesthetics delivered continuously, as the spread of the solution will be improved when the solution is given all at once.[39] Other studies have incorporated high-tech algorithm-based computer-integrated PCEA, with the idea that it may allow better targeted dosing as labor pain increases with more advanced cervical dilation.[40] Overall, input into the amount of medication being used lends a sense of control and greater satisfaction to the experience of labor and delivery.

Spinal Microcatheters

Unfortunately, because spinal microcatheters (27–29 gauge) were associated with a cluster of cauda equina syndrome in the United States in the early 1990s, they were banned by the U.S. Food and Drug Administration (FDA). Several years later, the FDA authorized a large multicenter study with the challenging goal of investigating the safety of continuous intrathecal labor analgesia with microcatheters. The recently published results of this trial were able to refute the purported association of this technique with neurological injury.[41] However, larger studies to evaluate the safety of continuous spinal analgesia are still required before this technique can be routinely utilized to provide labor analgesia. The use of microcatheters has potential clinical implications, as it enables easily titratable use of intrathecal analgesia in women with complex cardiac or pulmonary diseases, or in women with previous spinal surgery (laminectomy, fusion, or Harrington rods) that might have altered the integrity of the epidural space.[42]

Ultrasound-Guided Epidural Placement

Although some experts have advocated the routine use of lumbar spine ultrasound scanning to improve the ease of performing epidurals as well as adding to patient safety and comfort,[43] this recent technique has not been incorporated in day-to-day clinical practice. Its current use in academic centers has been limited to training purposes and to facilitate the placement of neuraxial procedures, especially in patients with challenging anatomy. Limiting it from widespread use, particularly in obstetric anesthesia, is the fact that it is labor intensive.[44]

Conclusions

Recent investigations have given us a wide range of technologies and techniques with which to provide analgesia during labor. We have honed our skills and adjusted doses in an effort to have as little impact as possible on the "natural childbirth" process and limit our effects on the parturient's physical and psychological condition. But it is the recent demonstration that early administration of neuraxial analgesia clearly does not increase the risk for operative delivery that has had the greatest effect on our practice. No longer must a woman undergo pain that she does not wish to endure in early labor because she has not reached an arbitrary degree of cervical dilatation.

Providing updated and accessible information to women and their partners on the real advances in our field is an important task, and ensuring knowledge transfer to obstetricians and other medical partners along with effective ongoing education for obstetric anesthesia providers remains a true challenge. We have achieved

safe and effective labor analgesia over the last decade and believe it is close to being optimal. Although minute refinements may prove useful in the future, it is unlikely that novel pharmacological compounds, the application of pharmacogenomics, or computerized algorithm-based infusions will provide substantial improvements over the current safe and effective practice of early, tailored, low-dose neuraxial labor analgesia.

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