Predicting Postoperative Pain Based on Preoperative Pain Perception

Are We Doing Better Than the Weatherman?

WE are nearing the end of the Decade of Pain Control and Research (2000–2010). The bill passed by the U.S. Congress and signed by President Clinton dedicated this decade to improving professional training in pain care, educating patients about pain management, providing access to pain treatment, and expanding pain research. Significant progress during this period include advances in our knowledge of the pain signaling pathways and the plasticity of the peripheral and central nervous systems leading to chronic pain, the acceptance of pain as the "fifth vital sign," and the development of standards for pain evaluation and care by the Joint Commission on Accreditation of Health Care Organizations.

Surgery is the most common and predictable source of pain. Although considerable advances have been made in the management of perioperative pain, a significant proportion of patients still suffer from inadequate pain control. A better understanding of the predictors of postsurgical pain will help in identifying the subset of patients who are likely to require additional care to optimize their perioperative pain management. In this issue of ANESTHESIOLOGY, Werner *et al.*[1] critically review the literature on the predictive factors for postoperative pain based on preoperative quantitative testing of a patient's basal pain perception. They conclude that quantitative testing of pain perception may predict nearly half of the variance in postoperative pain experience. This finding highlights the individual differences in pain perception and response to tissue injury. However, from a clinician's perspective, we are still only as good as the weatherman in predicting an individual's postoperative pain experience.

Preoperative pain represents a consistent risk factor for development of persistent postoperative pain for a series of surgical conditions, such as limb amputation, breast surgery, hysterectomy, thoracotomy, and hernia repair.[2] The challenge in predicting the patients who will experience the most postoperative pain or who require the most treatment is that the risk factors for perioperative pain include not only quantitative sensory measures but also psychosocial and genetic factors. The complexity of the sensory and emotional aspects of pain, particularly in pathologic cases, makes it highly un-

likely that one single measure, be it psychosocial or biomechanical, could predict all aspects of acute or more persistent postoperative pain.

The report by Werner *et al.* suggests that despite the complexity of pain perception, preoperative quantitative sensory testing (QST) may be a clinically relevant predictor of postoperative pain. Their article reported that preoperative QST may also predict up to 54% of the variance in acute postoperative pain across individual patients. In addition, one of the studies included in the Werner's report noted that higher preoperative heat hyperalgesia predicted higher postoperative consumption of morphine, using patient-controlled analgesia.[3] These findings that QST and heat hyperalgesia can be predictive of postoperative pain are consistent with the existing literature in other areas of pain research. QST of patients with chronic pain has provided valuable mechanistic insights.[4,5] QST has been used for prediction or early identification of neuropathies to classify the sensory abnormalities in peripheral and central neuropathic pain states,[6] as a tool in more accurately diagnosing fibromyalgia,[7] and in illuminating patient characteristics that are associated with treatment outcomes. Regarding heat hyperalgesia, our study of postherpetic neuralgia demonstrated that higher heat pain threshold at an unaffected site and baseline pain intensity best predicted the response to opioid analgesia.[8]

To find the 15 studies analyzed in their report, Werner *et al.* used the Medical Subject Headings terms "postoperative pain," "predictive value of tests," and "pain measurement." A systematic search is not better than the weakest link in the chain, and it is not clear if apparent (possible) missing studies are not included because the Medical Subject Headings search did not pick them up or because the authors' quality assessment excluded them. For example, a study that examined the predictive value of preoperative pressure–pain thresholds in the limb and the subsequent development of stump and phantom pains seems to have eluded their search strategy.[9] The data in this article were consistent with the findings in the articles by Werner *et al.*: a weak but significant

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inverse relationship between preamputation mechanical sensitivity and early stump and phantom pains was observed.

The observed relationship among preoperative sensory testing, postoperative pain, and analgesic needs raises some important questions. What factors influence individual differences in response to noxious stimuli? Could the response to noxious stimuli provide insights into individual endogenous pain control mechanisms and response to exogenous opioids? And perhaps more directly applicable to clinical practice: if we know someone is more likely to experience postoperative pain, is it possible to modify their pre- and perioperative pain regimen to prevent postoperative pain? Would, for instance, pretreatment with an antihyperalgesic agent before surgery in the group of patients most at risk for postoperative pains improve their outcomes?

Research has already started to answer some of these questions. Several studies show that individual differences in pain sensitivity reflect a combination of genetic and environmental factors that contribute to central and peripheral modulation of pain signaling.[10] Human genetic studies suggest that single nucleotide polymorphisms of specific genes, such as the μ-opioid receptor gene and the catechol-O-methyltransferase gene, are associated with differences in basal pain sensitivity, with altered pain-induced μ-opioid receptor binding in the central nervous system, response to opioid analgesics, and rates of chronic pain.[11–15] Recent studies also indicate that carriers of the guanosine triphosphate cyclohydrolase-1 haplotype exhibit a reduced hyperalgesia in experimental pain models.[16] Additional large-scale studies are needed to determine whether the baseline QST may help in providing insights on polymorphisms of genes that may play a role in pain perception and analgesic response.

We are still relatively ignorant of the various potential risk factors for development of persistent pain states. Surgical procedures seem to represent ideal "models" for studying these risk factors, because the pain-inducing stimulus can be controlled in a standard fashion before, during, and after the operation. The present study by Werner *et al.* suggests that certain specific preoperative experimental pain stimuli have a different predictive value across different surgical procedures. A similar approach has been taken by the Procedure Specific Postoperative Pain Management (PROSPECT)* group that consists of a series of experts analyzing existing evidence and provides recommendations for postoperative pain for different surgical procedures. Additional and larger studies are needed to examine this in more detail for specific surgical procedures. Hopefully, analysis of these multiple preoperative parameters[17] will allow us to determine the most significant risk factors to minimize persistent postoperative pain for each specific surgical procedure and perhaps even allow us to develop protocols for preventative management in high-risk patients.

* http://www.postoppain.org. Accessed March 1, 2010.

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