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Nerve Blocks in the Evaluation of Chronic Pain

A Plea for Caution in Their Use and Interpretation

In this issue of ANESTHESIOLOGY, Hogan and Abram[1] critically review the role of neural blockade for diagnosis and prognosis of chronic pain states. Of interest is that the classic textbook on pain, written by John Bonica and published in 1953, was entitled *The Management of Pain, With Special Emphasis on the Use of Analgesic Block in Diagnosis, Prognosis and Therapy.*[2] Bonica observed that analgesic blocks often resulted in dramatic and prolonged pain relief that "outlasted by hours and days" the duration of impulse blockade. Bonica lamented the lack of a scientific explanation for his clinical observations. In a subsequent monograph published in 1959, Bonica presented an objective assessment of the indications, effectiveness, advantages, disadvantages, complications, and limitations of nerve blocks as diagnostic and therapeutic tools in the management of chronic pain states.[3] Ironically, almost 4 decades later, the role of nerve blocks in the management of chronic pain is still under scrutiny. Nerve blocks for the diagnosis of chronic pain are not always performed on sound scientific grounds. Subsequent therapy based on the results of such nerve blocks may be misguided. Therefore, Hogan and Abram's caution in interpreting the diagnostic and prognostic value of nerve blocks in the management of chronic pain need reiteration.

Hogan and Abram draw attention to the scarcity of controlled studies that test the use of diagnostic nerve blocks. What are the possible explanations for the lack of more definitive studies? Unlike other disciplines within anesthesiology, the specialty of "pain medicine" is relatively new and evolving. Pain is a subjective sensation that is difficult to measure quantitatively. The prolonged distress and suffering in patients with chronic pain and the invasiveness of nerve blocks may preclude clinical researchers from justifying the inclusion of placebo controls in their studies. In addition, it is only recently that basic research in this field has led to important insights about the pathophysiology of chronic pain. This new information has necessitated a reevaluation of the scientific rationale for some of the commonly used diagnostic nerve blocks.

The mechanisms by which regional anesthetic techniques block acute pain resulting from surgery are now well understood. However, the use of neural blockade in the management of complex, chronic pain states continues to challenge clinicians and researchers. The surgical stimulus initiates impulses in nociceptors in the periphery, and conduction blockade interrupts these signals before they are perceived in the central nervous system. In contrast, the site of generation and the mechanism of maintenance of nociceptor drive is not always apparent in chronic pain states. For example, injury to a peripheral nerve can lead to spontaneous neural activity not only at the injury site but also at the dorsal root ganglion.[4] In addition, changes in spinal and supraspinal processing can occur such that previously innocuous afferent input from adjacent nerves produces pain.[5] Therefore, an anesthetic blockade of the injured nerve may not produce complete pain relief, and anesthetic blockade of an adjacent nerve may produce partial pain relief.

What are the potential risks of misinterpretation of the results of diagnostic nerve blocks? Anesthesiologists (and perhaps others) may perform diagnostic nerve blocks with the view that the risks are minimal and the patient is unlikely to be harmed by the test procedure. However, because the treatment and prognosis often depend on accurate diagnosis, the incorrect interpretation of the results of a nerve block may result in inappropriate therapy. For example, a recommendation of surgical treatment for a radiculopathy merely on the basis of a nerve root block can lead to a surgical procedure that fails to alleviate the pain. The possibility that patients with more distal pathologies may also experience similar pain relief with a nerve root block should be considered. Similarly, diagnosing sympathetically maintained pain based on the results of nonspecific sympathetic blocks, or a single diagnostic sympathetic ganglion block, can be detrimental to the overall management of the patient. The potential for false positive test results should be considered before subjecting the patient to multiple therapeutic sympathetic blocks. These concerns necessitate that the validity of diagnostic and prognostic nerve blocks be critically evaluated.

The scientific approach to making a clinical diagnosis

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has been compared to the investigative process used by Sherlock Holmes to solve his mysteries: observation, formulation of a hypothesis, testing, refutation, and reformulation of the hypothesis. Such a strategy requires proper collection of data, logical analysis of data, and the recognition of discordant data.[6] Flaws in data collection or logic can result in erroneous conclusions. As indicated in the review by Hogan and Abram, several factors, such as the improper use of pain measurement scales, observer errors, problems of placebo effects, and bias introduced by patient expectations, confound the interpretation of studies on the usefulness of neural blockade in the diagnosis of chronic pain.

Researchers in the field of laboratory medicine have emphasized, for decades, that clinicians making decisions based on data obtained from a diagnostic test must be familiar with the limitations and applications of the data — that is, the accuracy and precision of the data.[7] Accuracy refers to the closeness between the measured and true values for the chemical analyzed, whereas precision is synonymous with reproducibility. Similar concepts of sensitivity and specificity are important in interpreting the results of nerve blocks when used for diagnosis or prognosis of clinical pain states. Although the ideal test would have a specificity and sensitivity of 100%, no clinical diagnostic test meets these criteria. Hogan and Abram provide a comprehensive discussion of the different issues — neurophysiologic, local anesthetic, psychosocial, and anatomic — that influence the sensitivity and specificity of nerve blocks for chronic pain.

The sensitivity of diagnostic nerve blocks can possibly be enhanced by improvements in techniques during the performance of certain blocks, such as the use of fluoroscopy or computed tomography guidance. However, the specificity of the blocks are more difficult to control, because it is influenced by several factors. Two primary factors that result in decreased specificity of diagnostic nerve blocks are placebo effects and expectation bias, both of which lead to false-positive responses. The placebo effect was used by physicians well into the latter part of the last century as a therapeutic tool.[8] More recently, however, placebo effects are considered a problem to be avoided rather than a helpful aspect of clinical care.[9] As stated by Wall,[9] the placebo effect is often perceived by researchers as a "tiresome and expensive artifact" that interferes with the demonstration of the "true effect" of a manipulation or therapy.

There are considerable misconceptions among practitioners about the nature of the placebo response. In reviewing the importance of placebo effects in pain treatment and research, Turner and coworkers[10] showed that placebos can closely mimic active medications in their time-effect curves, peak, cumulative, and carryover effects. Apart from their effect on subjective sensations such as pain, placebo responses may be associated with objective changes in physiologic parameters. For example, in angina pectoris, placebo effects reduced not only nitroglycerin usage, but also improved the electrocardiogram and increased exercise tolerance.[11] Note that a placebo response does not imply a psychosomatic illness. The placebo response results from a complex interaction of patient expectations, provider expectations, effects on endogenous analgesic mechanisms, and psychophysiologic states such as stress, anxiety, and relaxation.[9] The possibility of a placebo response demands that the results of nerve blocks be interpreted with caution.

Anxiety, expectation, and learning play important roles in the placebo response.[12,13] The three essential components of a placebo effect are: (1) positive beliefs and expectations of benefit on the part of the patient; (2) positive beliefs and expectations on the part of the physician or health care professional; and (3) a good relationship between the two parties.[14] Positive expectations of the physician and patient can lead to positive outcomes, negative expectations may negatively influence the outcome of the diagnostic tests. Standardization of the instructions to the patient before a diagnostic test may help minimize the influence of expectation bias.

How can the specificity of diagnostic nerve blocks be improved? Specificity of diagnostic nerve blocks can be improved greatly if selective agents are developed that act differentially on the nerve fibers of interest. Basic research into the membrane receptors involved in neuropathic pain has already pointed to some possibilities. For example, development of specific sodium channel blockers may be useful in the diagnosis of neuropathic pain where the ectopic neural activity is thought to be due to an accumulation of sodium channels.[15] In addition, N-type voltage-sensitive calcium channel blockers have been found to reduce the behavioral signs of neuropathic pain in animal models.[16] Similarly, the development of more selective adrenergic antagonists may prove to be useful in the diagnosis of sympathetically maintained pain.

Diagnostic nerve blocks have the potential to guide therapy if their sensitivity can be improved. The pain practitioner has very little information at his disposal

to help identify which diagnostic nerve block will predict success of subsequent therapy with specific pharmacologic agents or interventional strategies. The specialty of pain medicine can benefit from the experience of researchers in the fields of cardiology and oncology. Studies on the negative and positive predictive values of intravenous lidocaine infusion on the efficacy and tolerance of subsequent therapy with oral mexiletine for ventricular arrhythmias have helped establish the prognostic value of the lidocaine test in arrhythmias.[17,18] Preliminary studies to determine the prognostic value of infusion tests are now being conducted in the pain field.[19] In a series of well-controlled experiments, Lord and coworkers validated the use of placebo-controlled diagnostic blocks of the cervical zygapophysial joints after whiplash injury.* In randomized, double-blind, placebo-controlled trials, these workers also demonstrated the efficacy of radiofrequency neurotomy of the lower cervical medial branches in these patients. Similar, carefully conducted studies to document the diagnostic and prognostic value of other procedures used in chronic pain are required.

Until recently, the use of diagnostic blocks in the management of chronic pain states has been an art. Attempts are currently being made to develop more specific and sensitive diagnostic tests for certain pain syndromes that are based on pathophysiologic mechanisms.[20–22] For "pain medicine" to evolve from an art to a science, clinicians and researchers in this field should constantly question the validity and scientific basis of the prevailing clinical practices. Newer diagnostic tests should be developed based on improved understanding of the pathophysiologic mechanisms involved and be validated with carefully conducted clinical trials.

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