Immediate and Long-Term Pain After Surgery in Humans (3-Dec-2002)

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The program of research that I am pursuing has 2 major objectives. The first is to assess, in a variety of clinical contexts, the contribution of peripheral injury to the development of pathological pain states in which the central nervous system plays a prominent role. The second is to design and systematically evaluate means of preventing the central neural sensitization that develops after injury and that often marks the transition from time-limited pain to chronic pathological pain.

Pre-emptive analgesia

The surgical arena provides a controlled setting in which the peripheral (primary/visceral afferent) and central (spinal) neural contributions of noxious intra-operative stimuli (e.g., incision) to subsequent pain can be teased apart and studied. The studies we are conducting are randomized, prospective, double-blind, placebo-controlled evaluations of the effects of pre-emptive analgesia [1,2] on psychosocial functioning, intra-operative stress, post-operative pain, and post-operative analgesic requirements.

A major focus of this work is on the clinical manifestation of noxious stimulus induced central neuroplasticity in contributing to acute post-operative pain [3,4]. The main objective of these studies is to determine whether postoperative pain and analgesic requirements after surgery are reduced by pre-operative administration of a variety of analgesic and local anaesthetic agents by different routes. Early work with human amputees [5] and rats using an animal model of phantom limb pain [6] suggested that regional anesthesia begun prior to surgery should reduce post-operative pain and analgesic consumption even after the clinical duration of action of the agents administered pre-operatively. We have tested this hypothesis in several randomized controlled studies and have found support for the sensitizing effects of surgery and their attenuation by a variety of analgesic and local anesthetic agents [7-12]. The results indicate that pre-emptive administration of opioids and/or local anesthetics reduce post-operative pain, hyperalgesia and/or morphine consumption beyond the clinical duration of action of the agents. These results support the idea that surgical incision induces a prolonged state of central neural sensitization (i.e., a somatosensory pain memory) that contributes to heightened pain after surgery.

Transition of Acute Pain to Chronic Pain

A second, related area of research is directed at elucidating the mechanisms responsible the transition of acute pain to pathological, chronic pain. We have approached this issue from 2 perspectives. One involves evaluating the role of pre-amputation pain in contributing to the central neuro-plastic changes that underlie phantom limb pain "memories" [5]. Although the literature suggests that somatosensory pain memories appear to be a common occurrence after amputation, there are no prospective data available on the incidence, duration, quality of sensation, and intensity of pre-amputation pains which persist as phantom limb pain after amputation. In this context, my colleagues (DiVadi and Brill) and I are currently evaluating the importance of deafferentation (i.e., loss of afferent input) and a variety of psychosocial factors by comparing prospectively, the incidence of persisting post-operative-pain among amputees with that of patients after other surgical operations in which pre-operative pain predominated.

A second approach to this problem involves following up patients after major surgery [13,14] or other invasive medical procedures [12,15] in an attempt to identify early predictors of subsequent pain. We followed-up 30 patients who had participated in a prospective, randomized study 1.5 years earlier, and classified them according to long-term pain status [14]. Fifty-two percent reported daily or weekly pain of moderate intensity, consistent with other reports of long-term post-thoracotomy pain incidence. Early post-operative pain was the only factor that significantly predicted long-term pain even though pain thresholds to pressure applied to a rib contralateral to the incision did not differ significantly between the groups. Thus, the differences in post-operative pain were not due to a generalized response bias to noxious stimulation, since contralateral pain thresholds to pressure were similar at times when post-operative pain intensity differed. This prospective
study was the first to provide clear evidence of a significant predictive relationship between the intensity and quality of acute post-operative pain and the development of chronic post-thoracotomy pain. Whether aggressively treating early post-operative pain will diminish the likelihood of long-term pain is not known, but it is a logical first step toward identifying factors responsible for the transition of acute, physiological pain to chronic, pathological pain. We are also looking at pain in patients with posttraumatic stress disorder to determine the extent to which these patients experience pains that may be linked to the original traumatic event. These pain “flashbacks” may not be unlike the pain memories reported by amputees and can cause continued suffering and pain years after the initial injury has healed [16].

Clinical Implications

Pain has been called the silent epidemic of our times [17]. It presents a challenge to the health care system and accounts for more than $90 billion annually in direct health care costs and even more when one includes indirect costs due to lost productivity and compensation. The cost of pain in terms of human suffering and misery is equally enormous. Prolonged pain impairs quality of life, demands constant attention, and drains the individual of vital energy. Life with pain often deteriorates into a single-minded and relentless search for relief. Despite these alarming statistics, we have been slow in addressing this tragedy.

Some of the most terrible pains develop as a direct consequence of surgical interventions designed to promote healing or save lives. It has been estimated that 80% of amputees continue to suffer with phantom limb pain up to 7 years after amputation. Chest surgery for lung cancer is followed by persistent pain and discomfort in 50% of patients years after the operation. These long term pain problems are iatrogenic. They are triggered by surgery in our efforts to help. Yet we know little about the factors that mark the transition of acute pain to chronic, pathological pain. When one considers that the vast majority of health care costs attributable to pain are generated by individuals with persisting symptoms, it behooves us to address the problem of persistent pain. The program of research I am pursuing has the potential to elucidate some of the factors responsible for the transition of acute, time-limited pain to chronic, pathological pain.

References


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