The transition from acute to chronic pain

Lamacraft G
Associate Professor of Anaesthesia and Head of Pain Control Unit, Universitas Hospital, Bloemfontein
Correspondence to: Prof Gillian Lamacraft, e-mail: lamacraftg@ufs.ac.za

Introduction

Why some patients develop chronic pain after an acutely painful event remains an enigma. For example, over 90% of the population will experience acute back pain at some time in their lives. In most cases this resolves but, in a few, it does not, even though these patinets have radiologic pathology similar to those in whom the pain does improve.

Similarly, there are few people who escape the hands of the surgeon. What is becoming increasingly apparent is that those who do experience the sharp end of the scalpel frequently experience persistent pain as a result of the damage caused by this instrument. The reasons for this chronic post-surgical pain are discussed in this presentation, as are possible preventative strategies.

Definition of chronic post-surgical pain (CPSP)

From Macrae and Davies:[1]

- Pain developed after a surgical procedure;
- Pain is of at least 2 months duration;
- Other causes for the pain should have been excluded (e.g. continuing malignancy or chronic infection);
- The possibility that the pain is continuing from a pre-existing problem must be explored and exclusion attempted.

Incidence

There are frequently wide variations in the incidence of chronic pain after specific operations. This is because studies that have been performed, which directly investigate the incidence of chronic pain after an operation, find a far higher incidence than those studies in which chronic pain incidence was only part of the study. Despite this, it is often startling to see how high the incidence of chronic post-surgical pain is, and there are suggestions that patients should be informed of this before consenting to surgery (Table I).

Table I: Procedure-specific incidence of chronic post-surgical pain[2]

Type of surgery	Incidence of chronic pain (%)
Amputation	30 - 85
Thoracotomy	5 - 67
Mastectomy	11 - 57
Inguinal hernia repair	0 - 63
Sternotomy	28 - 56
Cholecystectomy	3 - 56
Knee arthroplasty	19 - 43
Breast augmentation	13 - 38
Vasectomy	0 - 37
Radical prostatectomy	35
Gynaecological laparotomy	32
Iliac crest bone harvest site	30
Hip arthroplasty	28
Saphenectomy	27
Hysterectomy	25
Craniotomy	6 - 23
Rectal amputation	12 - 18
Caesarean section	12
Dental surgery	5 - 13

Aetiology

Pain is subjective, but may be caused by various factors. Exactly what causes CPSP remains unclear but it appears that it is related to both operative nerve damage, resulting in neuropathic pain, and that it is modified by psychosocial factors which may have been pre-existing or developed post-operatively as a consequence of the chronic pain experience.

Following surgery, neuropathic pain can be caused by damage to peripheral nerves or central nervous system (CNS) sensory transmission. Inflammatory pain due to persistence of the inflammatory response or chronic infection may also be a factor. It is important to differentiate neuropathic from non-neuropathic pain, in order to effectively design strategies to prevent and to treat these entities.

Neuropathic pain is diagnosed clinically, and there are no specific diagnostic tests for this condition. Rasmussen et al have proposed the following criteria for the diagnosis of neuropathic pain:[3]

- Pain in a neuroanatomically defined area, i.e, corresponding to a peripheral or central innervation territory;
- History of relevant disease or lesion in the nervous system, which is temporally related to development of pain;
- Partial or complete sensory loss in all or part of the painful area;
- Confirmation of a lesion or disease by a specific test, e.g. surgical evidence, imaging, clinical neurophysiology, biopsy.

Whilst studies based on self-reporting of symptoms by patients may not identify neuropathic pain, other studies which have used more refined investigative tools such as sensory threshold changes are more sensitive and more likely to elucidate neuropathic pain.[4,5]

The link between neuropathic pain and CPSP is complicated. Many patients in whom there are clear signs of peri-operative nerve damage (e.g. a numb area) do not experience CPSP.[6] When comparing cases where a sensory nerve was deliberately "sacrificed" during surgery with cases where efforts were made to preserve it, the incidence of CPSP appears to be similar.[7,8]

The mechanisms by which CPSP results from surgery have been suggested by Kehlet et al to be the following:[9]

- Surgical nerve injury results in the production of local and systemic inflammatory mediators by denervated Schwann cells and infiltrating macrophages. These potentiate the transmission of pain by lowering the excitability threshold.
- As nerves heal, the cut ends may develop into neuromata. These may exhibit ectopic spontaneous excitability which, in sensory neurones, will result in pain.
- Intense noxious peripheral stimuli (and inflammatory mediators released from damaged tissue) act centrally. Activation of intracellular kinases leads to alterations in pre-existing proteins in dorsal horn neurons. After several hours, altered gene transcription can be seen, which enhances the action of excitatory transmitters and reduces the action of inhibitory transmitters.
- Death by apoptosis results in loss of inhibitory interneuron. In addition, microglial activation amplifies sensory flow.
- Brainstem and cortical changes occur. Marked changes in functional topography occur in the cortex, and cortical grey matter may be lost. Alterations in the connections between the spinal cord and brain result in an increase in descending facilitatory influences and a reduction in inhibitory stimuli.

Risk factors for CPSP

- Surgery: Both major and minor procedures are associated with CPSP (see Table I). The incidence and severity of CPSP has not been shown to be related to the extent of the surgery.

- Age: Older patients tend to have a lower incidence of CPSP than younger adults. For breast cancer surgery, this may be because younger patients tend to have larger and more aggressive tumours.[10] Conversely, children seem to experience less CPSP than adults.[11] This phenomenon has been attributed to immaturity of the child's nervous system and/or enhanced neuronal plasticity.[12]

- Gender: Women have a higher incidence of CPSP.[13]

- Genetic susceptibility: There is a hereditary component to both the generation and experience of pain. Genetic polymorphisms of catecholamine-O-methyltransferase have been linked to an increased risk of chronic pain.[14]

- Pre-operative pain: A number of studies have linked the duration and intensity of pre-operative pain to CPSP. For mastectomy and amputation, experiencing pain for more than a month before surgery is predictive of CPSP.[15] Even experiencing pre-operative pain that is not related to the surgical site increases the risk of CPSP.[16]

- Psychological problems; pre-operative anxiety is associated with acute postoperative pain, as is catastrophising.[17,18] It remains debatable whether anxiety and depression predispose to CPSP, or are a result of the pain.[19] However, as there is a link between acute postoperative pain and CPSP, it is likely that there is a relationship between pre-operative anxiety and/or depression and CPSP.

- A multitude of other factors may play a role in CPSP. For example, whether cancer patients have radiotherapy or chemotherapy may be relevant. Social issues such as work, physical activity and social environment also affect a person's response to pain.

Prevention of CPSP

It is become increasingly apparent that, in order to prevent CPSP, one must prohibit noxious inputs from reaching the CNS for the entire peri-operative period. Failing that, one has to prevent the CNS changes that result from painful stimuli starting. If, at any time during the peri-operative period, there is an episode of "breakthrough" pain, then irreversible CNS changes may be triggered and CPSP may result.

This explains why pre-emptive regional anaesthesia does not consistently reduce CPSP, whereas preventative regional anaesthesia may do. Here the difference is that, in the former, the block is given before surgical incision but not continued whereas, in the latter, the block is given before incision but continued well into the postoperative period.

Pre-emptive antineuropathic pain medication similarly shows no effect on CPSP, whereas preventative antineuropathic pain medication may be beneficial.[20,21]

Multimodal analgesic techniques are being increasingly used to provide maximal analgesia with minimal side-effects with the aim of reducing CPSP.[22] Whilst, in theory, these can be highly effective,

more often than not the problem remains of ensuring that the patient actually receives the analgesic medication prescribed and at the correct time. All too frequently the patent only receives analgesia when pain has returned. Nursing staff must be educated to administer analgesia regularly in order to prevent pain. Surgeons need to understand the importance of maintaining epidural infusions well into the postoperative period and not to discontinue them prematurely.

Conclusion

Over the last ten years, there has been a substantial increase in the understanding of the problem of CPSP amongst anaesthesiologists. This information needs to be more widely disseminated to other healthcare professionals. Patients should be given information regarding the likelihood of CPSP so that they can make more informed decisions regarding whether to undergo certain operations and, if they do proceed with surgery and develop CPSP, understand why it has occurred and not attribute undeserved blame to the surgeon. The patient would also then be more likely to have his or her pain acknowledged and receive appropriate treatment.

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