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Editorial comment

Assessment of persistent pelvic pain after hysterectomy: Neuropathic or nociceptive?

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In this issue of the *Scandinavian Journal of Pain*, Satu Pokkinen and coworkers report from a small prospective observational study of patients examined median 30 months after laparoscopic and vaginal hysterectomy for benign conditions in two hospitals in Tampere, Finland [1]. The authors included patients who previously had participated in a questionnaire study, where as many as 26% of the responders (59 out of 227) reported pelvic pain 6 months after surgery [2]. Those reporting pain were further invited to participate in this clinical follow-up study. However, only 16 patients were willing to be included.

The reported post-operative clinical assessment included a gynaecological examination and a sensory examination performed by two different physicians. The gynaecological examination included inspection of the vulva and vagina, as well as a bimanual palpation of the pelvic area. The sensory examination of the lower abdomen/groin and the vulvar/perineal area was then performed by an anaesthesiologist specialised in pain medicine. A cotton stick was first used for assessing dysfunction in the low-threshold mechanoreceptor system (touch). Furthermore, the nociceptors/thermoreceptor system were tested using a special thermal roller instrument, as well as a pin prick with a wooden tooth pick. In each case, the patient was asked to compare from one site to another and rate the change on a numerical rating scale (NRS). The results were drawn on an illustrative sketch.

Of the sixteen patients tested, 10 still reported pain in the questionnaire given before the examination. Eight patients had sensory changes (mostly hyperestesia) corresponding to the iliohypogastric, the genitofemoral or the ilioinguinal nerves verified by the different sensory tests performed, and equally distributed after vaginal and laparoscopic hysterectomy. A conclusion of probable neuropathic pain was drawn from five of these patients. Not surprisingly, the women in this cohort scored lower on health related quality of life scores than the average women in Finland.

1. Chronic pelvic pain and post-hysterectomy pain

Pain is subjective, and the IASP taxonomy working group has defined chronic pelvic pain (CPP) as chronic or persistent pain *perceived* in structures related to the pelvis [3]. Studies from the UK show a yearly prevalence of CPP in general practice of 4% for women aged 15–73 years, this means, as common as back pain and asthma [4].

Chronic, or persistent, post-surgical pain is originally defined as pain of at least two months duration, developed after a surgical procedure, and other causes of the pain and the possibility of a continuum of the pain from the preoperative period should have been excluded [5]. Studies have shown different prevalence of post-surgical pain depending on the procedure performed, with the highest prevalence of pain after amputations, thoracotomies and breast surgery [6]. In gynaecological surgery, hysterectomy is one of the major procedures performed [7], and Denmark, Sweden and Finland have their own hysterectomy-registers [8–10]. However, only a few studies have systematically studied post-hysterectomy pain, reported in 5–32% [11]. Norwegian population data from the Tromsø study have found a self-reporting rate of 14–17% after surgery on the urinary tract and reproductive organs [12]. One would believe that the introduction of minimal invasive surgery could spare nerves and decrease the prevalence of post-hysterectomy pain, although this has not been found so far [11].

According to its definition, the phenomenon of post-surgical pain says nothing about the nature of the pain causing it: nociceptive or neuropathic or a combination of the two [13]. In addition, the pain could be a continuum of the two, starting as nociceptive, caused by tissue injury, an inflammatory response or visceral pain towards neuropathic pain initiated by a primary lesion in the peripheral or central nervous system, see Fig. 1 [14].

2. Neuropathic versus nociceptive pain and peripheral and central sensitisation

Neuropathic pain is rather strictly defined by the IASP as pain caused by a lesion or disease of the somatosensory nervous system [15]. This kind of pain is usually accompanied by sensory abnormalities like hyperesthesia, which includes both

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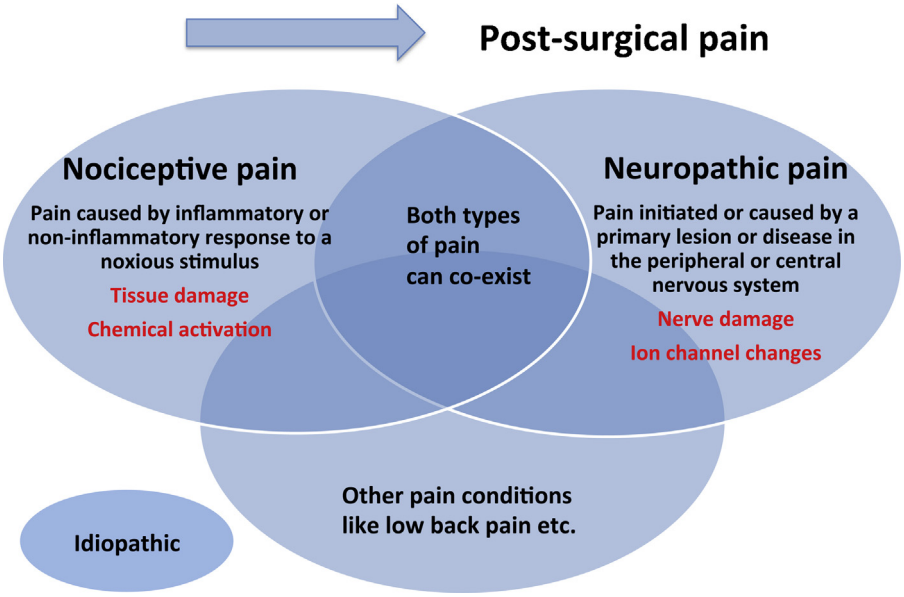

Fig. 1. Post-surgical pain could be nociceptive or neuropathic or a combination of the two. (Kindly provided permission from Tony Dickenson to modify his figure [14].)

the phenomenon of hyperalgesia and allodynia [16], as well as hypoesthesia.

Hypoesthesia is a symptom of nerve damage while hyperesthesia could also be due to sensitisation [13]. The phenomenon of peripheral and central sensitisation rather complicates the diagnosis of the type of pain. Nociceptive pain is initiated by tissue damage from harmful mechanical, thermal or chemical stimuli (Fig. 1) [14]. Sensitisation of the peripheral nervous systems occur when there is continuous stimulation of the nerve endings or accelerated nervous firing due to inflammation or continuous release of pain-inducing chemicals from the surroundings. On the other hand, visceral pain is characterised by a more diffuse sense of localisation and the phenomenon of "referred pain" [13,17,18]. The latter is due to the spinal segmental overlap with somatosensory innervation from skin/musculature. From viscera, a wind-up process from repeated neural firing (temporal summation of pain) could be responsible for peripheral visceral sensitisation [19].

Furthermore, the increased activity in the peripheral nerve and dorsal root ganglions could induce central sensitisation due to a state of increased excitability of neurons at several levels of the CNS. This phenomenon, together with decreased inhibitory inputs, results in an amplification of signalling that elicit a state of pain hypersensitivity [16].

3. Pain assessment and clinical quantitative sensory testing (QST)

Regarding post-hysterectomy pain, a thorough history of pain should be undertaken before any surgery. Preferably, validated questionnaires should be used before and after the operation, for diagnosing the prevalence, the severity (reported with the help of NRS/VAS scale), and the quality of the pain (in neuropathic typically described as burning, lancination, electrical). Symptoms of sensory disturbances (hypoesthesia, hyperesthesia, or both) in the pelvis or lower extremities should be recorded. The area of the body where pain is reported should undergo a clinical sensory examination (testing for loss or gain of sensory function in a neuroanatomical area) in order to differentiate between pre- and postoperative pain and to classify the pain as "probable" or "possible" neuropathic (to classify the pain as "definite" neuropathic necessitates e.g., skin biopsy, MRI or neurographic diagnostic tools) [20].

A standardised quantitative sensory testing (QST), evaluate pain thresholds ("the minimum intensity of the stimulus that is perceived as painful"), perceived pain intensity (NRS/VAS) and pain tolerance ("the maximum stimulus intensity tolerated") to a variety of sensory stimuli [13], usually from cold/warm testing devices and/or mechanical testing devices (calibrated vonFrey filaments, vibrameter, brush and calibrated pins or algometer/palpometer, the latter testing sensitivity to blunt pressure and could be applied both abdominally or vaginally) [21]. In addition, the phenomenon of temporal summation (wind-up) could be tested by pin-prick stimulation repeatedly applied with a standardised frequency and time to the area of the body to be tested [21]. To our knowledge, only the two Nordic studies have reported similar sensory testing in the abdominal or vaginal/vulvar area after hysterectomy [1,21]. Even if the test tools used by Pokkinen and coworkers probably not qualify to be named a proper QST, the authors present valuable non-standardised sensory data which could be used by the clinicians in practice. It means that the Finnish study adds to our knowledge regarding the assessment of persistent pelvic pain after such surgery. However, available preoperative QST-like data would have helped in the assessment of the phenomenon.

4. Conclusion and implications

Diagnosing a neuropathic component of post-hysterectomy pain could be helpful for the patient, thereby guiding the physician in the medical treatment of the phenomenon. Pharmacological agents, such as gabapentin, pregabalin, amitriptylin and venlafaxine could be tried in addition to topical lidocaine or capsaicin. In addition, nerve growth factor and similar agents could prove helpful in the future. Even if nerve dysfunction seems to be prominent in post-surgical pain, coexistent other pain conditions are prevalent and must be treated appropriately, for example in interdisciplinary teams. As already stated visceral and central sensitisation could complicate the picture of post-surgical pain. Promising animal experimental data also suggest that new pharmacological oral agents like ultramicronised palmitoylethanolamide (PEA) could influence at the level of mast cells and prove useful for managing visceral hyperalgesia, and that PEA alone or in combination with classic anti-inflammatory/analgesic treatments could be offered patients [22].

All surgical procedures have complications and should be kept under strict surveillance. The best way of gathering such information is through National and Multi-National health registers. We call for such a Nordic register. We gladly welcome the development of alternative treatment options to hysterectomy for heavy bleeding and uterine fibroids (hormonal intra uterine contraceptive, minimal invasive trans-cervical surgical procedures, uterine artery embolisation and pharmacological agents like progesterone receptor modulators) making hysterectomy superfluous.

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