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Clinical Importance of Pain Sensitization in Gynecology

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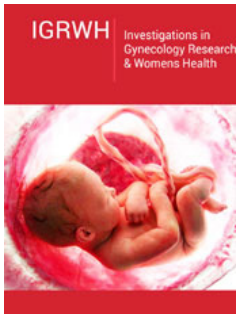

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Introduction

Peripheral and central sensitizations are conditions of the nervous system that are characterized by increased tone and responsiveness, a lower threshold for the experience of pain and a tendency for pain to persist long after the original stimulus has ended [1]. The mechanism of the development of chronicity is under intense investigation involving a variety of important biochemical and sensitization processes. From a clinical perspective however, the situation can be summed up that pain per se, if not kept under control, may initiate the processes causing the transition from acute to chronic pain.

Basic Investigations

Investigations into the origins of central sensitization in particular, have focused on the role of continuous peripheral drive from the nociceptors (defined as neurons that are activated by noxious stimulation). It has been shown these nociceptors can become sensitized after being injured and develop a lower threshold for activation. Further, the persistence of afferent stimulation and neuronal firing continuously activate the dorsal horn nuclei of the spinal cord and thereby cause central sensitization by e. g. long-term potentiation and neuronal phenotype reorganization. Thus, the central nervous system has the capacity to modify the pain experience such that it can be more or less dependent of the peripheral state, but generally chronic pain patients have some degree of sensitization [2]. There is a disconnection in the relationship of stimulus to response [2] as seen in many chronic conditions where there is a disconnect between pain intensity and size of injure e.g. degree of joint damage in osteoarthritis, size of ulcer, degree of nerve damage and extend of endometriosis [3].

Clinical Investigations

Clinical experience with centralized sensitization has been shown to be present in many clinical conditions such osteoarthritis, rheumatoid arthritis, headache, chronic opioid administration, neuropathic pain and visceral/gynecological pain syndromes [4]. In relation to pelvic pain in women, the known risk factors for non-cyclic pelvic pain are associated with numerous general gynecological and obstetrical factors, including heavy menstrual bleeding, endometriosis, anxiety and depression [5]. Central sensitization can be associated with inflammatory conditions such as endometriosis and interstitial cystitis and can be demonstrated at the bedside by the documentation of allodynia, hyperalgesia and temporal summation of pain from the abdominal wall [6,7].

In a quantitative sensory testing study abdominal allodynia was present in 62.1% women chronic pelvic pain. Allodynia is significantly associated with pain from a visceral origin [8]. Women with allodynia had a significantly greater rate of severe dysmenorrhea and significantly greater duration of severe dysmenorrhea [9]. Temporal summation, present in women with allodynia means that repetitive testing will increase the experience of pain and is a characteristic of central sensitization [10]. Recently a set of clinically applicable bed-side sensory tests was developed for quantitative assessment of hyperalgesia and allodynia over

the abdominal wall in patients with chronic pain and discovered the dynamics of such cutaneous stimulation where repeated stimulation of the hyperalgesic area caused a dramatic increase in the extent of the allodynic area [11]. The figure below shows the extension of the allodynic area by dermatome after repeated tactile stimulations of the hyperalgesic area (Figure 1).

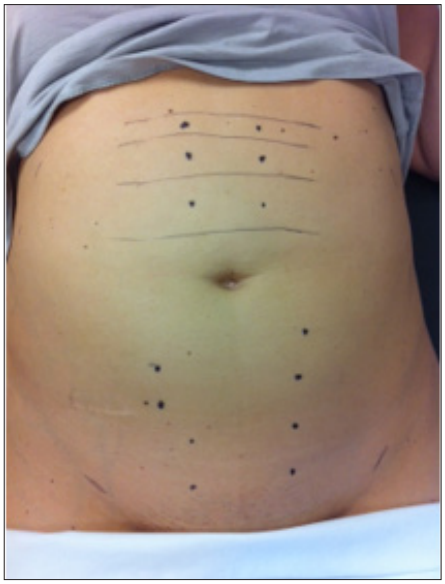

Figure 1: Demonstration of cutaneous allodynia in a woman with severe chronic pelvic pain from embolization of the uterine arteries for post-partum hemorrhage.

The levels of allodynia are demonstrated to start above the umbilicus but rise by dermatome with each subsequent pass of the cotton-tipped applicator. The dots indicate tender areas associated with the anterior cutaneous nerves as they perforate the abdominal wall fascia [11]. Hyperalgesia to distention of the uterine cervix in women with dysmenorrhea has been shown to be associated with central sensitization [12]. Pain from the female reproductive organs manifest as referred pain areas according to the so called Head Zones and the size of those referred pain areas in patients with chronic visceral/gynecological pain reflect the degree of central amplification/sensitization of pain [13].

In addition, there modality specific sensory changes are found in the referred pain area of patients with e.g. dysmenorrhea [14]. A recent interrogation of this database studied prior pelvic surgery (caesarian section, hysterectomies, oophorectomies laparoscopies) in 40 women presenting with chronic pelvic pain [9]. The overall rate of allodynia was 52%. Those testing negative for allodynia reported 24 total pelvic procedures in 19 women or 1.31 per woman while those testing positive for allodynia reported 34 procedures in 11 women or 3.1 procedures per woman. Most of the difference was due to the frequency of allodynia in laparoscopies (4 of 17 women with allodynia with no previous laparoscopy vs 8 of 16 women with allodynia with at least one previous laparoscopy). Although this difference may be due to underlying disease mechanisms, it is possible the procedure itself may contribute to increased sensitization.

Hyperalgesic Priming

The term hyperalgesic priming designates the process whereby a prior pain stimulus may evoke the full sensitization when additional pain is applied [3]. This may be the phenomenon experienced when women undergo surgery e.g. hysterectomies in patients with high degree of pre-operative pain and evolve into a chronic pain state postoperatively [15,16]. Clinical pain conditions by their nature raise the significant likelihood that repetitive nociceptive activation reach the central nervous system and provoke the central sensitization [17]. Experimental pain models have demonstrated similar changes where peripheral nociceptive barrage is provoked by the application of algogenic substances such as capsaicin (chilli) [18]. From an evolutionary perspective, the recent remarkable secular increase in lifetime exposure to repetitive menstrual pain may have led to a maladaptive susceptibility to pain chronicity [19]. Repeated pelvic surgeries and orthopedic revision surgeries are common and may yet play a role in the development of increased sensitization [20-22].

A comparative survey explored the frequency of lifetime surgical intervention among volunteers without chronic pain and women attending a chronic pain clinic. The study (REB 16-1866 University of Calgary Research Ethics Board) compared a one-time questionnaire of age, parity, menstrual pain, oral contraceptive use and lifetime surgical exposure between 21 volunteer women with no chronic pelvic pain and 21 women attending a chronic pain

clinic. The study identified no difference in age, parity or menstrual pain. Women at the pain clinic had a significantly greater use of oral contraceptives and a much greater prior surgical exposure. Volunteers reported two laparoscopies in two women for a total surgical exposure rate of 2/21 *100=9.5%, those attending the pain clinic identified 58 procedures among 16 of 21 women=76%. Among the 16 women who had surgery, there was an average of 3.6 procedures for each woman. Although this is a preliminary study, it raises the possibility of unintended iatrogenic contribution to the development of chronic pelvic pain through the processes of hyperalgesic priming and central sensitization. Further analysis of this problem is warranted.

Conclusion

The clinical manifestations of central pain facilitation is an important factor for many patients with gynecological disorders such as chronic pelvic pain (e.g. endometriosis, interstitial cystitis, pelvic inflammatory disease), vulvodynia, and dysmenorrhea, in many patients after surgery e.g. hysterectomies, for endometriosis, cesarian section, and gynecological patients undergoing repeated surgeries. The neuroplasticity of the central nervous system and exacerbation of sensitization by repeated surgeries for painful conditions should be critically evaluated.

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