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Editorial

Endometriosis-Related Pain, the Forgotten

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Endometriosis is an estrogen dependent disease defined by growths of uterine tissue at ectopic places. More than 15% of women of reproductive age suffer from this disease and up to 50% of women suffer from vaginal hyperalgesia and pelvic pain [1]. Evidence from both human and animal studies suggest that abnormal immune, vascular and neural activities in the ectopic endometrium contribute to inflammatory signs and symptoms associated with endometriosis [2]. Nevertheless, mechanisms are poorly understood because most investigators and clinicians agree that the growths do not predict pain symptoms. Standard treatments often fail to provide long-term relief. Pain can be diminished by removing peritoneal implants, nodules and ovarian cysts. Another strategy is to induce lesion suppression by eliminating ovulation and menstruation through hormonal manipulation with progestins, oral contraceptive and gonadotropin-releasing hormone agonists [3]. The main problem is that medical therapy is symptomatic and surgery is associated with high recurrence rates. In spite of it is known that nerve fibers are present in ovarian endometrioses in higher density than normal ovarian cortex from women with ovarian endometriosis [4,5], the research of novel treatments has only focused on the antiangiogenic strategy [6,7], but the relation between antiangiogenic treatments and vaginal hyperalgesia has been totally forgotten. This fact is really surprising due to the percentage of women that develop chronic pelvic pain, vaginal hyperalgesia (dyspareunia), dysmenorrhea (excessive menstrual pain), dyspareunia (vaginal hyperalgesia), and dyschezia (pain with defecation), which can co-occur with a range of other painful conditions [8]. Symptoms can range from moderate to severe [2] and could have a high impact in the life of such patients, leading to serious problems like depression [9]. Nevertheless, it seems that the study of pain in endometriosis is starting to be seriously considered. One of the reoccurring problems is the fact that the study of pain is really difficult and is it is also hard to establish an animal model of endometriosis which allows for the study of pain. In this regard, the group of Dr. Berkley and Dr. Dmitrieva has developed a rat model of vaginal hyperalgesia [10,11] which allows the study of novel drugs in the hyperalgesia related to endometriosis. In such model, endometriosis is surgically-induced. To achieve this, fragments of uterus from the same rat are sewn around the mesenteric arteries. Similar to women, animals develop cysts in the abdomen [12] and these cysts attract their own nerve and blood supply [5,11]. Importantly, like in women, the establishment of the cysts causes the animals, both vaginal hyperalgesia [13] and vaginally-referred abdominal muscle hyperalgesia. In previous studies, vaginal hyperalgesia in rats has been assessed either with a behavioral test [13] or with a technique that measures abdominal muscle electrical activity in response to vaginal distention. This later measured, which refers to abdominal muscle response to noxious stimuli, which is called visceromotor response (VMR). These techniques have been successfully used to reveal estrous differences in pelvic nociception and the effects of drugs and surgical manipulations [13,14]. Nevertheless, these techniques are labor-intensive and cumbersome to use for drug testing. Due to these limitations Dmitrieva and col developed a new technique that combined VMR with vaginal distention and telemetric methodology [2]. validating its applicability in two experimental settings. This model consists in the implantation of a telemetric probe (Data Sciences International, DSI, MN, USA), which allows the study of the vaginal hyperalgesia in awaken rats. So, this model is suitable to study the effects of new drugs in endometriosis-related vaginal hyperalgesia. Unfortunately, it is not widely known. In my opinion we should focus on this model and more groups should work with it to improve it. Endometriosis-related pain is a fact, a fact that an important number of women suffer from every day. We have the tools to make the difference, why should not we try?

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