

Commentary

Women and the Experience of Pain and Opioid Use Disorder: A Literature-based Commentary

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ABSTRACT

It is generally understood that pain experience and opioid abuse have relied on male-dominated models. However, sex and gender play a role in both pain experience and opioid use disorder.

Using the previously validated Texas Tech University Health Sciences Center Sex and Gender Specific Health PubMed Advanced Search Tool, the authors used pertinent literature to develop this literature-based commentary on sex and gender differences in pain experience and opioid use disorder. Women report their experience of pain more frequently, have increased rates of diagnoses related to pain, have increased pain sensitivity, and have a variable response to pain and analgesia. This variable response is due to anatomic, physiologic, hormonal, psychological, and social factors that differ by sex and gender. Women have been found to be at greater risk for opioid abuse in all age groups. This may be due to the differences in pain experience, as well as sex and gender differences in prescribing patterns, cultural norms, and the increased likelihood to experience dependency and withdrawal. Approaches to the treatment of opioid use disorder are also subject to sex and gender differences—an area in need of further investigation. (*Clin Ther.* 2017;■:■■■-■■■) © 2017 Elsevier HS Journals, Inc. All rights reserved.

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care utilization has been discussed previously in the literature.¹ Of specific concern is that sex and gender are key variables in the current opioid epidemic for several reasons. In the context of the opioid epidemic and its effects on many populations, it is important to recognize those groups that are at higher risk for substance use disorder. It is also essential to understand the physiologic and psychological processes underlying these differences in risk, as well as the effectiveness of treatment modalities.

There are many differences between the sexes in diagnoses related to pain, pain perception, opioid disbursement, response to opioids, opioid use disorder, and psychosocial factors.² These differences occur in several areas. First, the experience of pain differs between the men and women. Women experience more pain-related diseases and have an increased sensitivity to the perception of pain.² Further, it is possible that expression of pain may be interpreted differently, depending on the gender of the provider.

Women are at greater risk than men for the misuse of prescription opioid medication and thus for the development of opioid use disorder, with a recent shift in the prevalence of opioid misuse and abuse toward the female population.³ Data from the National Health and Nutrition Examination Survey 1999–2012 indicate that women are more likely to be prescribed opioid analgesics (7.2% vs 6.3%).⁴ Although overall opioid overdose deaths are more prevalent among men, the percentage increase in

INTRODUCTION

The influence of sex and gender on the development and management of disease and on subsequent health

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overdose deaths among women has been more dramatic compared with men (5-fold increase for women vs 3.6-fold increase for males) between 1999 and 2010.⁵

Opioid use disorder treatments have focused largely on a “one size fits all” mentality that does not appropriately address these differences.

In this literature-based commentary, we explore what is known about women and both pain experience and opioid use disorder. Furthermore, we will discuss the importance of continued and increased awareness on the topic.

METHODS

Using the previously validated Texas Tech University Health Sciences Center Sex and Gender Specific Health PubMed Advanced Search Tool,⁶ we searched PubMed database from 2000 through 2016.

Search terms utilized were as follows:

((("opioid abuse") OR "opioid addiction") OR "opioid dependence")) AND ((sex based OR sex factors OR sex distribution OR sex characteristics OR sex dimorphism OR gender difference* OR gender based) AND (gender[ti] OR sex[ti] OR women[ti] OR female[ti]) AND (Humans[Mesh] AND English[lang])) and ("pain management") AND ((sex based OR sex factors OR sex distribution OR sex characteristics OR sex dimorphism OR gender difference* OR gender based) AND (gender [ti] OR sex[ti] OR women[ti] OR female[ti]) AND (Humans[Mesh] AND English[lang])).

Articles were also gathered by searching the article bibliographies and “related articles” sections using the search tool. The authors screened 200 titles and abstracts of the articles found using these processes for inclusion into this narrative literature-based commentary. Articles were included if the authors thought the content informed the commentary by specifically describing sex or gender differences in pain experience or opioid use disorder. Forty-eight articles were reviewed in depth and are included in this commentary. Given a broad topic affected by multiple factors, this commentary addresses the most relevant and recent articles as chosen by the authors.

COMMENTARY AND DISCUSSION

Response to Pain and the Pain Experience

The difference in pain experience between the genders is well-documented in the literature.^{2,7-10}

Women report more severe levels of pain, more frequent episodes of pain, more areas of pain on the body, and pain of longer duration than men.² Women have a higher prevalence of painful conditions, such as fibromyalgia, irritable bowel syndrome, and interstitial cystitis.¹¹ Other contributors to the increased prevalence of pain in women include a longer lifespan and increased risk of osteoporosis and joint inflammation.² Unfortunately, the side effects of the treatments for these conditions also differ between the genders. Women experience medication overuse headache much more often than men.¹² One potential psychosocial confounding factor to these pain reports is that men are less likely to report pain than women.^{9,13} The expression of pain can be perceived differently between the sexes by the prescriber.¹⁴ Male patients undergoing coronary artery bypass grafting receive opioids more often than female patients, and female patients receive sedatives more often, suggesting that female patients are more often perceived as anxious rather than in pain.¹⁴ It is important to reduce these disparities and be aware that there are gender differences in the assessment and treatment of pain.

Pain experience and perception are intrinsically different in men versus women. Estrogens and androgens play a role in the experience of pain, including both perception and modulation.^{2,7,8,15,16} Gonadal hormones and male and female biology differentially predispose individuals to pain and analgesic effects of drugs and stress.⁷ Variations in estrogen plasma levels in women during their menstrual cycle and those undergoing estrogen replacement correlate with recurrent pain.² The concentration of estrogen in the blood correlates with a fluctuation of number of opioid receptors in the tissue.² Estradiol increases the hyperalgesic response.² Male gonadal hormones have a nociceptive adaptive effect to pain. An inverse relationship exists between plasma testosterone and female patients with neck and shoulder pain.² Because females intrinsically have more estrogen, it can be inferred that fluctuations in opioid receptors are more drastic and pronounced in the female population. Further, given that males have intrinsically more testosterone, men may have increased endogenous nociceptive effect than women.

Bodnar and Kest¹⁶ found that testosterone replacement increases μ -opioid analgesia and estradiol replacement decreases μ -opioid analgesia.

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