Sex Differences in Pain

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Overview

Women and men experience pain differently as a result of both biologic and physiologic differences as well as psychosocial influences on the perception and expression of pain. Sex differences in the treatment of pain have been suggested by studies that indicate women are less likely to receive adequate treatment for pain compared with men. These issues will be further explored using two patient vignettes of women presenting to the Emergency Department (ED) with painful conditions followed by a discussion of the pertinent literature.

Patient 1

HPI

PL is a 48 year-old Hispanic woman with a recent diagnosis of breast cancer who presented to the hospital with severe right-sided breast pain. She was one month post-op from a lumpectomy and axillary node dissection. PL described constant sharp pain around the surgical site of her right breast with radiation to the right axilla and to the back. She also reported thick white-colored discharge from the surgical wound. She had been seen by her primary care physician who had prescribed her hydrocodone/acetaminophen, but the patient reported that the medication made her feel dizzy and nauseous, therefore she had not been taking it. PL denied fevers, chills, and shortness of breath.

Pertinent Exam Findings

On exam, PL was tearful and anxious with her family at her bedside. She had a healing incision in the location of the right areola. The entire right breast was hypersensitive to touch with maximal tenderness just superior to the right nipple. There was no surrounding erythema, a small amount of serous drainage, and no appreciated fluctuance or induration.

ED Course

PL was treated with intravenous morphine (4 mg each) that did not improve her pain. This was then followed by two doses of hydromorphone (1 mg each) which ultimately had good effect and significantly improved her pain. Her labs were unremarkable, and she had an ultrasound of her breast showing no fluid collection concerning for an abscess. Her home pain medication regimen was changed to oxycodone/acetaminophen, and social work was consulted for support services surrounding her recent diagnosis of breast cancer. She was discharged with follow-up appointments with both the social worker and her oncology physician.

Patient 2

HPI

CC is a 54 year-old female who presented to the ED with severe right-sided shoulder pain after opening a heavy door at the local grocery store. Of note, one week earlier, CC had tripped and

fallen onto her outstretched arms, sustaining an anterior should dislocation. She had been seen in the ED, reduced, and discharged home; now she was concerned that her dislocation had recurred. She denied numbness of the affected upper extremity but described a mild sensation of “pins and needles” in the right hand.

Pertinent Exam Findings

CC’s exam was consistent with an anterior shoulder dislocation: she had a clear right-sided deformity with anterior fullness over the lateral chest wall. She had normal, full upper extremity pulses and normal sensation.

ED Course

Over the course of her ED stay, CC received 4 mg of intravenous morphine once, 1 mg of intravenous hydromorphone once, and 5 mg of intravenous valium. It required two attempts to reduce her shoulder dislocation using two doses of propofol (40 mg doses or approximately 0.5 mg/kg) for moderate sedation. CC was still having mild discomfort at the time of discharge for which she received two hydrocodone/acetaminophen tabs.

Discussion

Each of these women presented with severe pain and required multiple doses of different types of analgesics to achieve even partial analgesia. Did gender play a role in these cases?

Women and men have been shown to have differences in sensitivity to painful stimuli as well as differences in their responses to treatment of pain with the majority of studies showing that women are more sensitive to pain and require more pain medication.[1,2] Gender differences in pain are due to a variety of factors including differential hormonal effects, differences in the inhibition of pain signals, and psychosocial effects related to gender.[1,2,3] Hormonal effects are thought to play a role in gender differences in pain for several reasons. First, there are multiple pain-related conditions that have similar incidence between genders in childhood but then become more prevalent in women after menarche.[1,4] Other evidence for hormonal effects on gender differences in pain come from literature showing higher levels of chronic pain in patients on hormone replacement therapy.[1] Proposed mechanisms of hormonal effects on pain include an inflammatory effect of estrogen on peripheral tissues, different distributions and characteristics of opioid receptors in the central nervous system, and hormonal effects on both dopamine and serotonin levels.[1,2]

Both animal and human studies have investigated gender differences in the response to pain medications, particularly opioids. While the majority of rodent studies suggest that females have a smaller response to opioids, some human studies suggest that women have a greater response to opioid analgesics and some suggest the opposite.[2,3,5,6,7] Other studies have suggested that women and men benefit differently from different types of opioids. Specifically women may experience more pain relief from medications like butorphanol that work on kappa receptors compared to morphine, which works primarily on the mu receptor.[8] The authors of one extensive literature review suggest that when opioids are administered by providers, women use higher doses than men but that when opioids are administered by patient-controlled analgesia

(PCA) devices, women use lower doses.[1] They speculate that this could be a result of genderroles with men being less likely to request pain medication from a provider and women feeling more pain relief when they are in control of the amount of pan medication they receive.[1] Finally, data suggests that women experience more side effects of opioid medications compared to men, specifically nausea and vomiting.[5,9]

Psychosocial constructs including cultural and societal gender roles may also affect the way women and men tolerate and report pain. Multiple studies have shown that masculine and feminine gender roles affect pain thresholds, pain tolerance, and patients' willingness to report pain.[10,11,12] Specifically, a higher sense of masculinity has been associated with higher levels of pain tolerance and less willingness to report pain to providers.[1,12] Interestingly, studies that have attempted to emphasize gender roles by pairing male subjects with female providers found that having providers of the opposite sex seemed to increase pain tolerance of men.[1,10]

Finally, female gender has been shown to be a risk factor for both oligoanalgesia and increased delays to analgesic administration.[13,14,15] In one large prospective study of ED patients with abdominal pain, women were between 13% and 25% less likely to get opioids for pain and waited an average of 15 minutes longer for their pain medications, even after adjusting for other confounders including age, race, pain score and triage level.[16] Not all data is consistent with this finding, however. A study of ED patients complaining of headache, neck pain, and back pain showed that provider's perception of the patient's pain level was the strongest predictor of analgesic administration and that patient gender was not a significant predictor.[17] Interestingly, though, this particular study surveyed ED physicians and found that women were perceived to have higher levels of pain compared to men.[17] Another large study of hospitalized patients in Canada showed that women were more likely than men to be treated for their pain.[18] Provider gender may also be important as illustrated by a study of pain management decisions using case vignettes of patients with kidney stones and back pain. In this study, the authors found interactions between provider gender and patient race and between provider gender and patient gender in regards to hypothetical pain management decisions.[19]

Conclusions

In summary, data suggests that women may experience more pain and/or higher sensitivity to painful stimuli compared to men. Studies regarding sex differences in response to analgesic medications, including opioids, are conflicting and will require further investigation. There is evidence that social and cultural gender roles affect pain tolerance by patients and medication administration by clinicians. Going forward, more research should be devoted to sex and gender differences in pain with the aim of understanding how to effectively treat pain while considering gender. Until then, however, as providers we must be cognizant of gender when treating, pain, and in particular, how our biases may affect therapy. Providers should understand that a patient's pain is a result of complex interactions of biologic, physiologic, and psychosocial influences, all of which may be closely related to sex and gender.

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