Sex Differences in Overlapping Chronic Non-cancer Pain Conditions in a Tertiary Pain Clinic

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Abstract

Sex differences have been reported repeatedly in pain and response to opioid analgesia with women representing the majority of chronic non-cancer pain (CNCP) patients as well as a growing population of opioid users and misusers. However, none of these reports has investigated sex differences in the prevalence of overlapping multiple pain conditions (MPC), especially among patients under opioid therapy. Two hundred eighty-three charts were reviewed of patients attending a tertiary pain clinic with multiple sub-practices in a large Canadian city over a one-year period. 201 patients suffering from CNCP and under opioid therapy were selected. A significant sex difference was found in the number of patients, while no statistically significant sex difference was found in type of opioids prescribed. Moreover, significant sex differences were found in the prevalence and types of overlapping CNCP conditions as well as in the pattern of opioid misuse. With respect to overlapping pain conditions, Chronic pelvic pain (CPP) was the most common pain condition to co-occur in women, while in men, fibromyalgia was the most common. Taken together, all of these suggest that sex differences are significant in patients with overlapping CNCP conditions, and taking them into consideration might provide more comprehensive pain management.

Keywords: Chronic non-cancer pain (CNCP); CNCP conditions; Opioid treatments

Introduction

Chronic non-cancer pain (CNCP) is one of the most common reasons for seeking health care with one in five Canadians suffering from CNCP [1]. Moreover, CNCP accounts for up to 78% of visits to emergency care facilities, and usually leads to both a severe decline in the quality of life and a startling rise in the incidence of disability [2]. Successful treatments are few and far between with one of the most potent analgesics, opioid medications, associated consistently with concerns about problematic opioid use (POU) (i.e. misuse, abuse or addiction) [3-6].

Sex differences in both the incidence and types of chronic pain conditions have gained increasing attention as an area of research with the potential to lead to a better understanding the differences in CNCP patients’ response to treatments [7-9]. Clinical pain studies have reported repeatedly that women represent the majority of patients suffering from CNCP conditions like Fibromyalgia, Chronic Headaches; Temporomandibular disorder (TMD) Pain; and Chronic Pelvic Pain (CPP) [2,7,10]. All of the CNCP conditions are often treated with opioids and, as with pain, the available human studies have reported a significantly greater analgesic effect in women in comparison to men [11-15]. Moreover, recent studies report that women now represent the majority of chronic non-cancer (CNCP) patients as well as a growing population of opioid users and misusers.

Based on these findings, sex differences would seem especially pertinent in understanding both the reasons and treatments for CNCP. However, work in this area consists of studies investigating of only one CNCP condition at a time [19]. This approach leaves a serious gap in understanding both the reasons and treatments for CNCP. Consequently, we decided to review charts of CNCP patients under opioid medication in order to determine whether there are sex differences in the prevalence of overlapping MPC and if so, the constellation of types of condition between women and men under opioid therapy.

Methods

After obtaining approval from the Research Ethics Boards of both the University of Toronto and Mount Sinai Hospital, a chart review was conducted of all patients under opioid treatment referred to three different practices at the Wasser Pain Management Centre, a tertiary pain clinic in Toronto, ON from July 1, 2012 until July 31, 2013. Two hundred eighty-three charts were reviewed in total; 82 patients were excluded because they were ineligible (10 patients had cancer and 72 CNCP patients were not using opioids 56 (87%) of which were women), leaving 201 patients with CNCP under opioid treatment. If patients could be cross-referred to more than one practice, they were counted only once.

Data collected included: sex, age, pain condition or conditions, type of treatment, duration of pain condition, responses to the long form McGill Pain Questionnaire (Pain Rating Index, PRI) [26], Pain Intensity Scale scores [27], Pain Catastrophizing Scale scores [28], history of surgery or trauma, types of pain medication, Hamilton Anxiety Scale (HAS) [29], Beck Depression Inventory (BDI) [30], history of drug abuse, and whether or not a patient was diagnosed with POU.
Statistical analysis

Data were analyzed using SPSS (SPSS 15.0.1, 2006, Chicago - Illinois, Software Inc.). Means and standard deviations were calculated for the above patient characteristics in the form of continuous numerical variables. In order to study sex differences between nominal variables, a comparison between female and male patients with CNCP was made using a Student t-test and Pearson Chi-square test for non-parametric data. P-values of <0.05 were considered significant.

Results

Patient characteristics

A total of 283 charts comprising a mix of women and men were reviewed. Women were disproportionately represented in this pain clinic, 185 (68%) patients were women, while 88 (32%) were men.

Each chart was examined for the types of treatments patients were given. Therapies varied both in type and in modalities. On average, patients had been prescribed six different kinds of treatment, ranging from antidepressant medications (Cymbalta; duloxetine, serotonin-norepinephrine reuptake inhibitor (SNRI), Elavil, amitriptyline, tricyclic antidepressants), and anticonvulsants (Lyrica; pregabalin, gabapentin, carbamazepine; anticonvulsant and mood stabilizer) to nerve blocks, local steroid injections, Botox injections, physiotherapy, massage, acupuncture, psychotherapy, mindfulness, chiropractor, and aggressive treatment such as opioids.

During this year, 201 patients were under opioid treatment and 88 were not. Oxycodone was the most prescribed opioid for both female and male patients, followed by morphine, methadone and fentanyl. While, no statistically significant difference was found between men and women in type of opioids prescribed, a significant sex difference was found in the number of CNCP patients under opioid treatment (n=201), (women: n=129 (64%); men: n=72 (36%) (χ²=32.677, df=1, p<0.01)). Moreover, out of the total of 201 patients under opioid treatment, of the 79 suffering from POU, 56% were women and 44% were men. Interestingly, although no significant sex difference was found in the percentage of patients with POU (χ²=0.074, df =1, p=0.44), men were significantly more likely to have a history of drug abuse compared to women: 44% of men and only 19 % of women (χ²=14.035, df=1, p<0.01) (Figure 1).

Women were significantly more likely than men to have a history of surgery (women, n=42, men n=21 χ² =37.977, df=1, p<0.01). In fact, 66% of those women had surgery in the abdominopelvic area. However, no sex differences were found on the PRI, Pain Intensity Scale scores, or Pain Catastrophizing Scale scores. Similarly, no sex differences were found either on the BDI or the HAS.

In spite of the sex differences found in some of the characteristics, there was no difference in the type of information gathered from women or men in the charts in that the charts contained no information about number of births, menstrual cycle irregularities, or any menstrual cycle link with pain severity (Table 1).

Prevalence and Types of MPC

A total of 119 (59%) patients presented with MPC with a statistically significant sex difference: of 129 women, 100 (78%) reported MPC, while of 72 men, only 19 (26%) did so (χ² =50.017, df=1, p<0.0100) (Figure 1).

There were, also, sex differences in the constellation of pain conditions comprising the MPC. In women, CPP was the most common co-occurring condition (56%) followed by fibromyalgia (49%), LBP (33%), chronic headaches (29%) and TMD (16%). In contrast, in men, fibromyalgia was the most common co-occurring CNCP (68%) followed by chronic headaches (53%), TMD (47%), LBP (42%), and CPP (5%). The sex difference in the most common overlapping condition was significant (χ²=16.470, df =1, p<0.01) (Table 2). Notably, in women, endometriosis and/or irritable bowel syndrome (IBS) together were the most common reasons for co-occurring CPP in women with 36 out of 56 (64%) having one or both of these conditions.

Note that the full percentages do not all add up to 100% as the CNCP conditions are overlapping

Moreover, 38% of the women suffering from MPC had POU while 53% of the men had POU. In women with POU, CPP was also the most common co-occurring condition (58%), while fibromyalgia and chronic headaches were equally the most represented co-occurring conditions in men with POU (50%) (Figure 1).

Relationship of chronic pain to reproductive years

The mean age of female patients at their initial visit was 42(SD ±13) and male patients was 45(SD ±15). While there was no sex difference in the mean age between patients, when the range of ages were divided into groups: those who were 18-48 (as a proxy for women's reproductive years) and 49-71 (as a proxy for women in menopause), we found that women in their reproductive years (18-49) represented 90% (n=95) of the women with MPC, 75% (n=33) of women with POU and 79% (n=53) of women with co-occurring CPP. For men who had MPC, POU, or co-occurring CPP, there was no difference between the two age groups.

Discussion

This retrospective chart review is the first chart review of CNCP patients that includes a comparison by sex in the prevalence of
8(±6)
23(±13)
30(42%)
*Statistically significant sex difference, SD: Standard Deviation.
Table 1: Patient characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Women n=129</th>
<th>Men n=72</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPC</td>
<td>n=100</td>
<td>n=19</td>
</tr>
<tr>
<td>CPP</td>
<td>56(56)</td>
<td>1(5)</td>
</tr>
<tr>
<td>TMD</td>
<td>18(16)</td>
<td>9(47)</td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td>49(49)</td>
<td>13(68)</td>
</tr>
<tr>
<td>LBP</td>
<td>33(33)</td>
<td>8(42)</td>
</tr>
<tr>
<td>Chronic Headaches</td>
<td>29(29)</td>
<td>10(53)</td>
</tr>
</tbody>
</table>

MPC: Multiple Pain Conditions, CPP: Chronic Pelvic Pain, TMD: Temporomandibular Joint Disorder, LBP: Low Back Pain
Table 2: Frequencies of individual pain conditions in patients with MPC.

With respect to the constellation of MPC, at least in this clinic, CPP was the most commonly co-occurring pain syndrome in women. Interestingly, when we studied the type of co-occurring CPP, 64% of those women had CPP due to endometriosis and/ or IBS, which have been repeatedly reported in many studies as estrogen-sensitive conditions [33-36]. This chart review also revealed that the most of the women with MPC and CPP were in their reproductive years and approximately 66% of the women with MPC and CPP had a history of abdomino-pelvic surgery, including hysterectomy, oophorectomy and laparoscopy.

It is currently believed that peripheral sensitization due to endometriosis significantly influences pain processing via the connection between the central nervous system and the sensitized inputs from ectopic endometrial growths [37,38]. These endometrial growths can actually influence neuronal activity by modulating both the inhibitory and excitatory mechanisms that in turn modulate pain signals transferred to central pain areas [37,39]. Hence, while the charts could not report directly on the relation of the women's CNCP condition and their menstrual and reproductive status, nor their levels of ovarian hormones, the fact that CPP co-occurs with other CNCP conditions such as fibromyalgia, chronic migraines, TMD and LBP, suggests that estrogen might as well modulate other co-occurring conditions. The effects of hormonal variation might be important to follow up in these types of patients.

Additionally, the literature confirms that hormonal treatment specifically is of benefit for CPP associated with endometriosis [19,25], thus suggesting the necessity of evaluation for the presence of co-occurring CPP condition especially among women with MPC and CPP within their reproductive years and the potential benefit of hormonal therapy for managing their pain [37,39-43]. Moreover, it is also known that opioid efficacy waxes and wanes with the cyclic variations in reproductive hormones, and since those women were on opioid treatment, it would be useful to better understand how the ovarian cycle, pain, and opioid efficacy interact to modulate CNCP in order to achieve more successful treatment in those women.

Strengths and Weaknesses of the Study

An important strength of this study is that it is the first chart review of a Tertiary Pain Clinic to look at the intersection of sex differences, multiple chronic pain conditions, and opioid treatment. Our findings suggest that more such studies should be done in order to obtain more generalizable knowledge and to verify the treatment recommendations below.

A weakness of this study is that there were so few men, as compared with women, being treated by this pain clinic in the year studied. This may be due to the particular focus of this pain clinic as well as to the already identified disproportionate burden of chronic pain for women. Never the less, with even a small sample of men it is possible to gain a

psychotropic treatments which again, may abolish sex differences. It may also be the case that once a person has a chronic pain condition the condition, itself, equalizes the likelihood of depression. This is an area that would benefit from further study.

This study also corroborated overwhelming that CNCP conditions rarely occur as single condition but rather as MPC with overlapping symptoms spanning different pain conditions. In the clinic we studied, these overlapping conditions included chronic headaches, TMD, fibromyalgia and CPP. Interestingly, overall, CNCP patients were disproportionately women who were also disproportionally affected by MPC when compared to men.

Consistent with other studies, women were disproportionately represented in this clinic in general, and disproportionately represented in the opioid treatment group. Nevertheless, no sex differences were found in pain, depression, anxiety and catastrophizing scales. This is interesting since women are believed to have higher pain, depression, anxiety and catastrophizing scores in general [9]. One explanation for this lack of sex difference might be that the chronicity of the pain conditions, especially in women, masks sex differences in the scales. Another is perhaps because both men and women were under

References


