International Journal of Psychiatry Sciences
Online ISSN: 2664-925X, Print ISSN: 2664-9241
Received: 01-11-2019; Accepted: 02-12-2019; Published: 11-04-2019
www.psychiatryjournal.net
Volume 2; Issue 1; 2020; Page No. 01-03

Correlates of bowel dysfunction in opiate substitution patients

Aleksandra Nowicki[1], Marina Henein[2], Madeleine Moussa[3], Rana Elias[4], Zack Cernovsky[5]
[1, 3-5] Schulich School of Medicine and Dentistry, Western University, London, Ontario, Canada
[2] School of Medicine, National University of Ireland, Galway, Republic of Ireland, Europe
[3, 1] Psychiatric Clinic, London, Ontario, Canada

Abstract
Background: Chronic use of opioids is frequently associated with the syndrome of bowel dysfunction, most often with constipation. Little is known about the correlates of the syndrome.
Objective: We examined the relationship of bowel dysfunction in methadone patients to results of their urine screening tests.
Methodology: 51 patients (mean age 42.3 years, SD=11.5; 29 men, 22 women) of an urban psychiatric clinic participated. They were all undergoing the methadone maintenance therapy: their methadone dose ranged from 4 to 110 mg, with the average at 58.1 mg (SD=24.6). They completed a survey questionnaire about frequencies of 8 types of bowel dysfunction: constipation, nausea, emesis, abdominal pain, loss of appetite, heartburn, acid reflux, and intestinal bloating. For each of these 8 symptoms, the response categories were: never=0, only rarely=1, sometimes=2, often=3, very often=4, and always=5. At the time of this study in this particular clinic, all patients on higher doses of methadone were repeatedly encouraged to preventively use non-prescription remedies such as stool softeners to cope with their bowel dysfunction. All 51 patients were undergoing routine urine screening tests for benzodiazepines, cocaine, amphetamines, methamphetamines, fentanyl, oxycodone, and for opiates in general. The results of their 3 last urine screening tests were recorded.
We calculated the correlation matrix of relationships of these 7 urine tests to the 8 symptoms of bowel dysfunction. Given the large size of correlation matrix, the criterion of significance was set to $p<.01$, 2-tailed, in order to avoid spurious/weak correlations of negligible relevance for clinical hypotheses and predictions.
Results: When categories "very often" and "always" were pooled, these high frequencies of bowel dysfunction in our group of 51 patients were as follows: constipation (31.4%), nausea (7.8%), emesis (9.8%), abdominal pain (13.7%), loss of appetite (7.8%), heartburn (19.6%), acid reflux (15.7%), and abdominal bloating (13.7%).
No significant correlations ($p<.01$, 2-tailed) were found of outcomes of the patients' urine tests to any of the 8 types of bowel dysfunction. In this group of patients, their dose of methadone, their age, and gender were not significantly ($p<.01$, 2-tailed) correlated with signs of bowel dysfunction.
Discussion and Conclusions: Almost a half of our patients (45.1%) reported that they experience at least one of the 8 bowel dysfunction symptoms "very often" or "always." Constipation was by far the most frequent symptom.
Only 3.9% of patients indicated that they "never" experience any of the 8 bowel symptoms.

Keywords: opiate induced bowel dysfunction, narcotic bowel, methadone, addiction, opiates

1. Introduction
In their 2007 article in the journal of Clinical Gastroenterology and Hepatology, Grunkemeier, Cassara, Dalton, and Drossman [1] indicated that the syndrome of opiate induced bowel dysfunction "is under recognised and may be becoming more prevalent" in the current North-American epidemic of opioid use. They described this syndrome as "characterized by chronic or frequently recurring abdominal pain that worsens with continued or escalating dosages of narcotics."
In their 2012 article in the American Journal of Gastroenterology, Drossman and his co-authors [2] discussed the narcotic bowel syndrome (NBS) as "characterized by a paradoxical increase in abdominal pain associated with continued or escalating dosages of narcotics."
Panchal, Müller-Schweffe, and Wurzelmann [3] reviewed gastroenterological impact of opioid therapy in chronic pain patients and emphasized that constipation is "the most Common and debilitating symptom." They also listed other related common adverse effects such as a "decreased gastric emptying, abdominal cramping, spasm, bloating, delayed GI transit and the formation of hard dry stools." Panchal's team noted that the syndrome may, in extreme, "have a serious negative impact on the patient's quality of life (QOL) and the daily activities that patients feel able to perform." A recent study of the bowel dysfunction syndrome in an opiate substitution clinic by Sidhu's team [4] has focused on the following 8 symptoms: constipation, nausea, emesis, abdominal pain, loss of appetite, heartburn, acid reflux, and intestinal bloating.
The present study evaluates the correlations of these 8 symptoms of bowel dysfunction in patients of a methadone clinic to their methadone dose and to outcomes of their urine screening tests for concurrent abuse of benzodiazepines, cocaine, fentanyl, oxycodone, and of opiates in general.

2. Method

Fifty-one patients (29 men, 22 women) of an urban psychiatric clinic participated: they were all on a methadone maintenance program. Their age ranged from 25 to 66 years, with the average at 42.3 years (SD=11.5). Their methadone dose ranged from 4 to 110 mg, with the average at 58.1 mg (SD=24.6). All 51 patients signed the informed consent and completed a survey questionnaire about frequencies of 8 types of bowel dysfunction: constipation, nausea, emesis, abdominal pain, loss of appetite, heartburn, acid reflux, and intestinal bloating. For each of these 8 symptoms, the response categories were: never=0, only rarely=1, sometimes=2, often=3, very often=4, and always=5.

In this particular clinic, at the time of the present study, all patients on higher doses of methadone were frequently reminded and encouraged to preventively use non-prescription remedies such as stool softeners to cope with bowel dysfunction.

They were all undergoing routine urine screening tests for benzodiazepines, cocaine, amphetamines, methamphetamines, fentanyl, oxycodone, and also for opiates in general. The results of their 3 last urine tests were recorded.

We calculated the correlation matrix of relationships of these various urine tests to the 8 symptoms of bowel dysfunction. Given the large size of Pearson correlation matrix, we adopted $p<.01$, 2-tailed, as the criterion of significance to avoid spurious/weak correlations of negligible relevance for clinical predictions and hypotheses.

We also evaluated correlational relationships of age and gender to signs of bowel dysfunction.

3. Results

Frequencies of the 8 types of bowel dysfunction are listed in Table 1. To facilitate perusals of the tabular data, the categories "never," "only rarely," and "sometimes" were pooled into one column and similarly the categories "very often" and "always" are also pooled together in one column as the other extreme.

Table 1: Frequencies of 8 symptoms of bowel dysfunction (N=51)

	Never, only rarely, or sometimes	**Very often or always**
constipation	57.4%	31.4%
nausea	84.4%	7.8%
emesis (vomiting)	88.9%	9.8%
abdominal pain	80.0%	13.7%
loss of appetite	75.6%	7.8%
heartburn	73.3%	19.6%
acid reflux	80.0%	15.7%
problem intestinal gas	68.9%	13.7%

As shown in Table 1, constipation was reported as the most frequent problem. The rates of reported constipation in this sample of 51 methadone maintenance patients were as follows: never in 11.1%, only rarely in 17.8%, sometimes in 28.9%, often in 15.6%, very often in 8.9%, and always in 17.8%.

Almost a half (45.1%) of the 51 patients reported experiencing at least one of the 8 bowel dysfunction symptoms "very often" or "always."

At least 3 of the 8 symptoms with the frequency of "very often" or "always" were reported by 11.8% of the patients.

Only 2 patients (i.e., 3.9% of this sample) indicated "never" for all 8 bowel symptoms.

Only 29.4% of the 51 patients reported that they experience any of these 8 bowel symptoms only "sometimes" or even less often, i.e., "never" or "only rarely."

In this sample of 51 patients, the dose of methadone was not significantly ($p<.01$, 2-tailed) correlated with any of the 8 symptoms of bowel dysfunction.

Age and gender were also unrelated to scores on these 8 symptoms ($p>.01$, 2-tailed).

The 8 items in the left column of Table 1, scored from 0 ("never") to 5 ("always"), could be considered as a measuring scale of the extent of opiate induced bowel dysfunction. The Cronbach alpha coefficient of internal consistency calculated for this scale was. 80, i.e., satisfactory. It is noteworthy that the Cronbach coefficient calculated for this measuring scale of bowel dysfunction syndrome in a recent study of 68 opiate substitution patients by Sidhu's team [4] was very similar. 86, i.e., also satisfactory.

In our study, the total score calculated as an algebraic sum of these 8 types of bowel dysfunction ranged from 0 to 32 points, with the average at 13.0 (SD=7.6).

This total score was not significantly correlated with age, gender, and with the dose of methadone. The total score of bowel dysfunction was also not significantly correlated with a total score obtained by adding the outcomes of all 7 urine screening tests, i.e., those for cocaine, benzodiazepines, amphetamines, methamphetamines, fentanyl, oxycodone, and for opiates in general.

4. Discussion

The data in our Table 1 are similar to frequencies reported recently in a study by Sidhu's team [4] on patients in the same city (London, Ontario, Canada): the opiate induced bowel dysfunction is frequent and interferes with the quality of the patients' lives. Almost a half (45.1%) of our 51 patients indicated that they very often or always suffer from at least one of the 8 symptoms of bowel dysfunction.

In the study on Sidhu's patients, higher methadone dose was associated significantly with more frequent bowel dysfunction. In contrast, in the present study, this statistical relationship was perhaps eliminated by very frequently reminding and encouraging the patients who were on higher doses of methadone to use preventive measures such as stool softener and thus no significant correlations of signs of bowel dysfunction to methadone dose were found.

The same as in other investigations such as by Panchal's group [3] or by Sidhu's team [4], our study indicates that constipation is the most common symptom associated with prolonged opioid use.

It would be of interest in future studies to collect longitudinal rather than only cross-sectional data, to map the changes or trends in the bowel dysfunction symptoms over time, for example, from the start of methadone treatment to some later point in time such as one year. Similarly, it is of clinical interest to evaluate how the symptom profile of the bowel dysfunction syndrome changes with the use of stool softeners and related preventive substances.

5. Conclusions

As in most other studies of bowel dysfunction in opiate users [4, 5], the most frequently reported symptom by our patients was constipation. It appears from our data, that encouraging and very frequently reminding patients who are

on higher dose of methadone to preventively use stool softeners might perhaps somewhat reduce the intensity or frequency of the bowel dysfunction in that particular subgroup of methadone patients. Further medical research on the use of stool softener in this population group and on its relationship to symptoms of bowel dysfunction is needed. The 8 item measuring scale for assessing the bowel dysfunction syndrome as used in the present study seems to be a useful tool in this field of research.

6. Acknowledgement
The authors thank Abe Cernovsky, B.A., for his editorial assistance on the manuscript.

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