Prevalence, severity and impact of opioid-induced gastrointestinal side effects in the EU: results of a patient survey

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Introduction

- Opioids are considered the gold standard for treating moderate-to-severe pain; however, therapy can be complicated by opioid-induced gastrointestinal (GI) side effects such as constipation (straining, hard/lumpy stools and incomplete evacuation) and other GI symptoms (abdominal pain/discomfort, bloating and decreased appetite).[1,2]
- The morbidity associated with these GI side effects can be significant, potentially resulting in treatment non-compliance or discontinuation of therapy.[3]
- Despite these known effects, few data are available regarding the prevalence, frequency and severity of opioid-induced GI side effects, as well as their impact on quality of life (QOL) and activities of daily living (ADLs).

Objective

- To assess, via a patient survey, the prevalence, frequency and severity of opioid-induced GI side effects and their impact on QOL and ADLs in patients receiving opioid therapy for chronic pain and taking laxatives.

Methods

Study population

- Patients from France, Germany, Spain, Italy and the UK, who were receiving opioids and taking laxatives, and who had participated in a previous survey (the National Health and Wellness Survey[4] in 2005) were invited to complete a follow-up questionnaire. The Patient Reports of Opioid-related Bothersome Effects (PROBE) questionnaire was administered via the internet in January 2006.

Data analysis

- Subsequent data analysis included only responses from patients reporting use of their main opioid on ≥2 days/week and answering "Yes" to the following questions:
  - "Do you currently suffer from long-term or persistent pain?"
  - "Do you generally take laxatives during the same period that you use an opioid?"
- Responses from patients taking >4 opioids at the time, or data from survey respondents who did not have a main opioid identified, were excluded from subsequent data analysis.
- Only response data from patients receiving oral opioids, (i.e. no opioid patch therapy) and taking laxatives were included in data analyses.
- Patients meeting the inclusion criteria outlined above were asked to select from a comprehensive list, symptoms or side effects they had experienced while using their current opioid(s) to treat their pain condition, and indicate the frequency and severity with which they occurred. (GI symptoms reported as side effects were classified as opioid-induced GI side effects, and are referred to as such in the remainder of this poster.)
- Patients rated the impact of GI side effects on QOL and ADLs using a 5-point scale, with 0=no impact and 4=greatest impact. Examples of normal ADLs included going to work or school, going on holiday or planning trips out with family and friends, shopping, walking, driving, etc.

Results

Study population

- A total of 502 patients completed the survey.
- Of these patients, 427 met eligibility criteria, with 361 reporting use of only oral opioids and laxatives.
- The majority of the 361 patients were female (65%) and reported current use of ≥2 opioids (55%), with ≥1 opioid taken on a daily basis (56%); 66% of these patients reported having used ≥1 of their current opioids for >1 year (Table 1).

Table 1. Patient demographics and characteristics of opioid use

	Patients taking oral opioids and laxatives (n=361)
Gender, n (%)	
Male	126 (35)
Female	235 (65)
Median age, years	45
No. of opioids currently used per patient, n (%)	
1	161 (45)
2	177 (49)
3	23 (6)
Highest frequency of opioid use for any current opioid, n (%)	
2–3 Days/week	86 (24)
4–6 Days/week	73 (20)
Daily	202 (56)
Longest duration of opioid use for any current opioid, n (%)	
<1 Month	26 (7)
1–12 Months	95 (26)
1–5 Years	127 (35)
>5 Years	113 (31)

Table 2. Prevalence and bothersomeness ranking of opioid-induced GI side effects

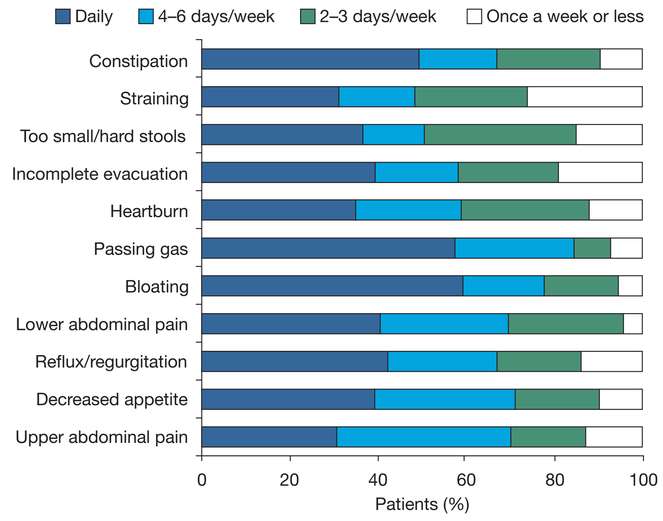
GI side effect	Prevalence, n (% of patients) (n=361)	Bothersomeness rank[a]
Constipation	222 (61)	1
Straining	148 (41)	2
Too small/hard stools	134 (37)	4
Incomplete evacuation	115 (32)	6
Heartburn	110 (30)	3
Passing gas	103 (29)	5
Bloating	97 (27)	7
Lower abdominal discomfort	76 (21)	8
Reflux/regurgitation	63 (17)	9
Decreased appetite	62 (17)	10
Upper abdominal pain	54 (15)	11

[a]Bothersomeness ranking was determined based on the relative number of patients reporting each GI side effect as bothersome

Prevalence, bothersomeness, frequency and severity

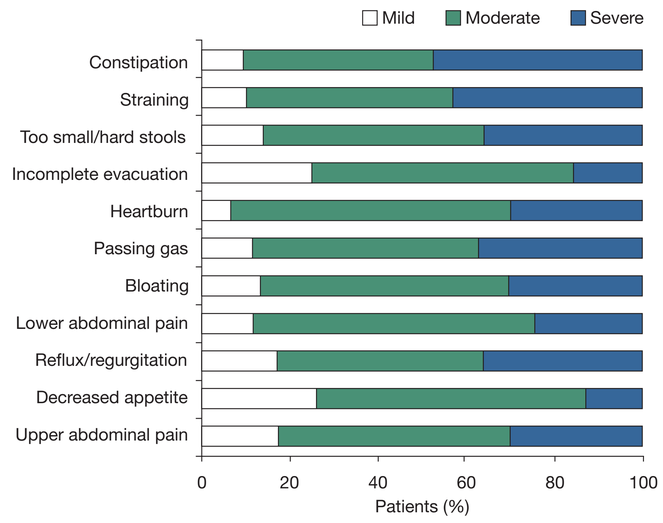
- Constipation and associated symptoms of straining, small/hard stools and incomplete evacuation were the most frequently reported GI side effects, despite the use of laxatives in this population (Table 2).
- Constipation, straining and heartburn were the most bothersome GI side effects associated with opioid use (Table 2).
- Opioid-induced GI side effects were experienced by ≥48% of patients on 4 or more days of the week, with up to 67% of patients experiencing the most prevalent side effects of constipation, straining, too small/hard stools, incomplete evacuation and heartburn on ≥4 days/week (Figure 1), and approximately 60% of patients experiencing bloating and gas on a daily basis.
- The majority of patients (75–94%) reported experiencing moderate-to-severe opioid-induced GI side effects (Figure 2); 75–94% of patients experienced moderate-to-severe constipation, straining, too small/hard stools, incomplete evacuation and heartburn (Figure 2).

Figure 1. Opioid-induced GI side effect frequency



Note: constipation (n=199); straining (n=102); too small/hard stools (n=73); incomplete evacuation (n=57); heartburn (n=80); passing gas (n=70); bloating (n=53); lower abdominal pain (n=45); reflux/regurgitation (n=36); decreased appetite (n=31); upper abdominal pain (n=30)

Figure 2. Opioid-induced GI side effect severity

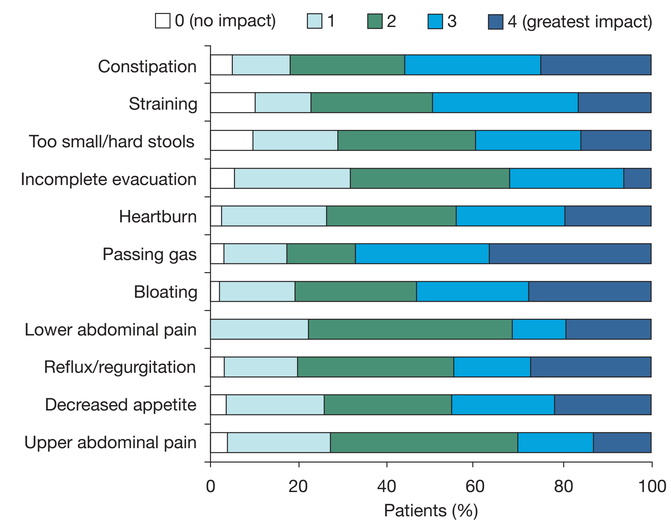


Note: constipation (n=199); straining (n=102); too small/hard stools (n=73); incomplete evacuation (n=57); heartburn (n=80); passing gas (n=70); bloating (n=53); lower abdominal pain (n=45); reflux/regurgitation (n=36); decreased appetite (n=31); upper abdominal pain (n=30)

Impact on QOL and ADLs

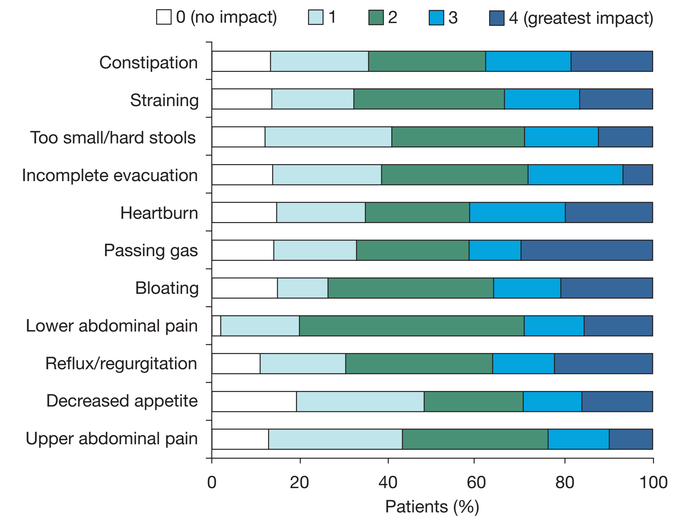
- The majority of patients (68–83%) reported that GI side effects had a moderate-to-great negative impact (i.e. score of 2–4, where 0=no impact and 4=greatest impact) on overall QOL or overall well-being (Figure 3); over 80% of patients who reported experiencing constipation, bloating, reflux or gas also reported that these side effects had a moderate-to-great negative impact on QOL (Figure 3).
- Similarly, the majority of patients (52–80%) reported that GI side effects had a moderate-to-great negative impact (i.e. score of 2–4) on ADLs (Figure 4). A moderate-to-great impact on ADLs was most commonly reported by patients experiencing lower abdominal pain, bloating and reflux.

Figure 3. Impact of opioid-induced GI side effects on QOL



Note: constipation (n=199); straining (n=102); too small/hard stools (n=73); incomplete evacuation (n=57); heartburn (n=80); passing gas (n=70); bloating (n=53); lower abdominal pain (n=45); reflux/regurgitation (n=36); decreased appetite (n=31); upper abdominal pain (n=30)

Figure 4. Impact of opioid-induced GI side effects on ADLs



Note: constipation (n=199); straining (n=102); too small/hard stools (n=73); incomplete evacuation (n=57); heartburn (n=80); passing gas (n=70); bloating (n=53); lower abdominal pain (n=45); reflux/regurgitation (n=36); decreased appetite (n=31); upper abdominal pain (n=30)

Conclusions

- The PROBE survey is one of the first patient surveys to investigate the prevalence, frequency and severity of opioid-induced GI side effects and their impact on patients' lives.
- The survey results reflect a high prevalence of opioid-induced GI side effects of moderate-to-severe intensity, which occur frequently in individuals taking oral opioids for chronic pain, despite laxative use. These side effects include constipation and associated symptoms, in addition to other symptoms linked with the upper GI tract, e.g. heartburn.
- Of all the opioid-induced GI side effects, constipation, straining and heartburn were considered to be the most bothersome.
- Importantly, these results also indicate the substantial negative impact opioid-induced GI side effects such as constipation, bloating and reflux can have on patient QOL and daily activities.
- New targeted therapies to improve the management of these troubling opioid-induced GI side effects are clearly required.

References

1. Kurz A and Sessler DI. Drugs. 2003;63:649–671.
2. Pappagallo M. Am J Surg. 2001;182(Suppl 5A):11S–18S.
3. Thorpe DM. Curr Pain Headache Rep. 2001;5:237–240.
4. Consumer Health Sciences National Health and Wellness Survey. http://www.nhwsurvey.com

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