Itopride increases the effectiveness of the management of opioid-induced constipation in palliative care patients: an observational non-interventional study

Tomasz Dzierżanowski1,2, Michael Kożłowski3

1Laboratory of Palliative Medicine, Department of Social Medicine and Public Health, Medical University of Warsaw, Warsaw, Poland
2Laboratory of Palliative Medicine, Chair of Oncology, Medical University of Lodz, Lodz, Poland
3Clinic of Pain Treatment and Palliative Care, Jagiellonian University Medical College, Cracow, Poland

Submitted: 28 March 2019
Accepted: 6 May 2019

Arch Med Sci
DOI: https://doi.org/10.5114/aoms.2019.85943
Copyright © 2019 Termedia & Banach

Abstract

Introduction: It is strongly recommended that laxatives be routinely prescribed for the prevention of opioid-induced constipation (OIC). The evidence supporting the effectiveness of prokinetics for this indication is sparse. This study aims to verify if itopride, added to preventive OIC therapy, increases the effectiveness of the prevention of opioid-induced constipation in adult palliative care patients.

Material and methods: In a questionnaire-based observational study, all patients received regular laxatives plus one of the following: oxycodone/naloxone (OXN); itopride (ITP); or oxycodone/naloxone + itopride (OXN+ITP). The primary measure was the decrease in the necessity of laxative use in a 0–4 scale assessed after seven days of treatment.

Results: Ninety-two patients met the inclusion criteria in the four groups: OXN (n = 12), ITP (11), OXN+ITP (9), and the control group (laxatives only if needed) (60). The necessity of laxatives decreased in groups where itopride was used, with a statistically significant difference versus control, oxycodone/naloxone (p = 0.009), or in combination. The OXN did not decrease laxative use (p = 0.22).

Conclusions: All interventions appeared similarly effective in the prevention of OIC. However, adding itopride, but not oxycodone/naloxone, resulted in a decrease in the necessity of laxative use in OIC patients, and it seems to be valuable in this often refractory condition. Randomised, controlled trials would be valuable to obtain good quality evidence without systematic bias.

Key words: palliative care, opioid-induced constipation, prokinetics, itopride.

Introduction

Opioid analgesics are the key element of pain management in cancer patients [1–3]. However, even a few days of opioid treatment may result in severe bowel dysfunction. Opioid-induced constipation (OIC) affects 42.4% of end-stage oncology patients and is one of the most frequent symptoms besides pain and cachexia in these patients [4]. OIC is defined in Rome IV Diagnostic Criteria as new or worsening symptoms of consti-
Bowel dysfunction results from both the central and peripheral action of opioids. The central mechanism consists of the activation of neurons in the spinal cord, leading to slower bowel passage and decreased secretions. However, OIC is mainly induced by activation of local μ-opioid receptors in the gut, which are present in the stomach, small intestine, and colon, mainly in the myenteric and submucosal plexus, and on immune cells of the lamina propria [25]. The influence of opioids ultimately sums up to three gastrointestinal effects: a decrease in secretion of fluids, depression of peristaltic contractions and promotion of non-propulsive motility patterns, and the spasm of all sphincters [26]. Dehydration of intestinal contents leads to the occurrence of faecal stones, which are difficult to defecate through the tensed anal sphincter. The gut is overloaded and extended by these hard stool masses [25, 26]. This explains why bulk laxatives are ineffective [13]. On the other hand, osmotic and stimulant laxatives are recommended in OIC. However, their effectiveness is poor because they do not address the opioid receptor-mediated mechanism of bowel dysfunction, so a substantial number of patients do not achieve adequate relief of symptoms [27].

Apart from this, long-term laxative use can be associated with damage to the muscular function of the bowel; nutritional deficits in terms of loss of water, vitamins, and minerals; and kidney stones or renal failure, in addition to modifying the effects of other medicines [28].

So, an alternative or supplemental method could be adding prokinetics, which might increase the effectiveness of laxatives or opioid antagonists. However, the clinical evidence for this effect is sparse, except for the 5-HT4 receptor agonist prucalopride [29]. Metoclopramide does not act on the gut, and thus should not be considered in constipation.

Itopride is a dopamine D2 antagonist with acetylcholinesterase inhibitory actions. It has a stimulatory action on colonic peristalsis, propelling colonic luminal contents, different from that of cisapride and mosapride, and therefore it may be a useful drug for the treatment of functional constipation [30]. Polish guidelines suggest using prokinetics, such as itopride, for the treatment of constipation [14]. Therefore, some palliative care specialists use it off-label, not only for dyspepsia but also for the management of constipation.

This study aimed to verify whether itopride is effective in the management of opioid-induced constipation in adult palliative care patients in the clinical setting.

The primary outcomes were:

• the mean change in the necessity of laxative use in a 0–4 scale assessed after seven days...
of treatment; a negative number means a decrease,
• the mean number of bowel movements,
• the mean intensity of bowel symptoms,
• the frequency [%] of constipation, defined as at least one of the following:
  – the last defecation > 2 days,
  – the number of days with defecation < 4,
  – any subjective bowel symptom with intensity > 2 in a 0–4 scale (as below in p. 4 c–h).
The secondary outcomes were:
• the frequency (%) of the patients with bowel movements only after enema (or manual stool evacuation) after seven days of treatment,
• adverse effects.

Material and methods
This open observational study was performed in adult palliative care patients with constipation, who were receiving strong opioids and had not been treated with itopride before the observation. All patients received regular laxatives, and additionally oxycodone/naloxone (OXN group), or itopride (ITP group), or oxycodone/naloxone + itopride (OXN+ITP group). The control group (CTRL) used only laxatives, if necessary.

The inclusion criteria were: legible and complete documentation, age ≥ 18 years, home hospice or in-patient hospice or palliative care outpatient clinic, at least two visits performed in 7–8 day intervals (day 0 and day 7), strong opioids used seven days before day 0 until day 7, no itopride used up to day 0.

Structured questionnaire
The palliative care practitioners used a questionnaire to report data collected in their medical documentation. The questionnaire included the following items:
1. Date.
2. Place (home, ambulatory, hospital palliative care ward, in-patient hospice).
3. ECOG performance status, assessed by a physician.
4. Bowel symptoms in the last seven days, assessed by the patient:
   a. the last defecation [days],
   b. the number of days with bowel movements [days],
   c. the difficulty of defecation in a 0–4 scale, where 0 – no difficulty (“normal defecation”), 1 – mild (“rather normal”), 2 – moderate, 3 – significant/often, 4 – extreme difficulty/always,
   d. too few stools in a 0–4 scale, where 0 – normal stools, 1 – from time to time (mild intensity), 2 – quite often (moderate intensity), 3 – very often, 4 – always,
   e. stools too hard in a 0–4 scale (see above),
   f. the feeling of incomplete bowel movement in a 0–4 scale, where 0 – no symptom, 1 – mild intensity/sometimes, 2 – moderate intensity/quite often, 3 – significant intensity/very often, 4 – extreme intensity/always,
   g. straining or squeezing to try to pass bowel movements, in a 0–4 scale (see above),
   h. the necessity of use of laxatives in a 0–4 scale, where 0 – no laxatives used, 1 – from time to time (occasionally), 2 – often used, 3 – bowel movements only after the use of regular laxatives, 4 – bowel movements only after enema or manual stool evacuation.
5. The daily doses of opioids, recalculated to the oral morphine equivalent (Table I).
6. Itopride used 50 mg t.i.d. (yes/no).
7. Adverse effects.

All the practitioners had participated in a specialisation course on symptom control before data collection. They were aware of the Polish guidelines on prevention and treatment of constipation in palliative care patients. The aim of laxative treatment, according to these guidelines, was to assure bowel movements in the patients taking opioids at least three times a week (preferably every second day) [14].

Source of data
The data were collected in 2018 by 16 palliative care practitioners in 10 (home, inpatient, and ambulatory) palliative care centres for adult patients

Table I. Equianalgesic doses of opioids (based on Caraceni et al. 2012 [2])

<table>
<thead>
<tr>
<th>Opioids</th>
<th>Relative analgesic ratio to oral morphine</th>
<th>The strength of the recommendation for use</th>
<th>The equivalent of 60 mg oral morphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral oxycodone</td>
<td>1.5 : 1</td>
<td>Strong</td>
<td>40 mg</td>
</tr>
<tr>
<td>Transdermal buprenorphine</td>
<td>75 : 1</td>
<td>Weak</td>
<td>35 μg/h</td>
</tr>
<tr>
<td>Transdermal fentanyl</td>
<td>100 : 1</td>
<td>Strong</td>
<td>25 μg/h</td>
</tr>
<tr>
<td>Oral tapentadol</td>
<td>1 : 3.3</td>
<td>NA</td>
<td>200 mg</td>
</tr>
<tr>
<td>Parenteral morphine</td>
<td>3 : 1</td>
<td>Weak</td>
<td>20 mg</td>
</tr>
</tbody>
</table>
in Poland. The study received approval of the bio-
etical committee.

The size of subgroups was one of the outcomes
and not to be estimated using statistical methods.
We assumed that a minimum of 100 question-
naires collected should be satisfactory to verify
the prescribing behaviours regarding the prevent-
on of constipation.

Statistical analysis

Kruskal-Wallis and Mann-Whitney U tests were
applied for the statistical analysis of non-paramet-
ric data. Frequency analysis was performed using
the chi-square and Fisher’s exact tests appropri-
ately. P-values less than 0.05 were considered sta-
tistically significant. The data were analysed using
Statistica 13 (StatSoft).

Results

The studied population

The data of 130 patients were collected. Nine-
ty-two patients met the inclusion criteria (female
54.3%) and were analysed in four groups: OXN+ITP
(N = 9), ITP (N = 11), OXN (N = 12), and CTRL (N =
61). The study flow is presented in Figure 1.

The groups did not differ in terms of sex, age,
diagnosis, and oral morphine equivalent of strong
opioids on day 0 and day 7. The opioids used were
as follows: morphine (oral or parenteral), oxyco-
done, fentanyl, buprenorphine, and tapentadol.
The demographic details are presented in Table II.

The symptoms of constipation

The aim of the laxative prevention or treatment
was to achieve at least three bowel movements
a week and an acceptable intensity of abdomi-
nal symptoms, and this aim was achieved in all
groups. There were no statistical differences found
for the mean values among the groups in terms
of particular symptoms of constipation (Table III).
Eighty-two patients (89%) had diagnosed con-
stitution, with insignificant differences among
groups. However, the anti-constipation strategy
appeared successful, on average, in all four groups.

Overall, manual stool evacuation was per-
formed in four patients receiving laxatives only,
and not in other groups. Enemas were used in 16
patients, and 14 of them were in the control group.

The reduction of laxative use

Although there were no statistical differences
among groups regarding bowel symptoms or the
frequency of bowel movements, the necessity of
laxatives decreased in groups in which itopride
was used (Kruskal-Wallis ANOVA p = 0.0027). In
the ITP group, the necessity to use laxatives de-
creased by 0.64 (–0.64; 95% CI: –1.6–1.8) and
in the OXN+ITP group by 0.67 (–0.67; 95% CI:
–1.5–1.7) in the 0–4 scale. These values might
seem insignificant, but they were statistically dif-
ferent (Mann-Whitney U test) from oxycodone/
naloxone (ITP vs. OXN p = 0.009, OXN+ITP vs. OXN
p = 0.017) and the control group (ITP vs. CTRL
p = 0.010, OXN+ITP vs. CTRL p = 0.025). There
was no decrease in laxative use in patients tak-
ing oxycodone/naloxone vs. the control group
(p = 0.22) (Figure 2).

Adverse effects

This study was a retrospective analysis of the
structured history of patients, and none of the
130 patients reported any side effects. This does
not mean that there were no adverse effects of
treatment, but rather that they were typical and
of mild or moderate intensity, so it was not neces-
Itopride increases the effectiveness of the management of opioid-induced constipation in palliative care patients: an observational non-interventional study

Itopride increases the effectiveness of the management of opioid-induced constipation in palliative care patients:
an observational non-interventional study

sary to report them in routine documentation. No patient stopped using itopride between day 0 and
day 7. Although the cases in which itopride was
used on day 0 were excluded from the analysis,
none of the patients stopped itopride use in the
next seven days. Thus, it can be inferred that the
medicine was well tolerated.

The history after day 7 was not analysed.

Discussion

This was a non-interventional study, with all
limitations that non-randomised clinical trials
bear. However, its advantage is a gross effect in
the real environment, when using itopride as an
element of laxative prevention and treatment.
This is probably the first clinical report aiming di-
rectly at the use of itopride in OIC.

Physicians did not participate in the analysis
and were only asked to provide structured data
without specific study goals, to limit possible bias.
They delivered the questionnaires regardless of
their laxative therapy pattern and use of proki-
netics. It also explains the over-representation of
a control group, because most patients received
regular laxatives, and a minority were treated with
oxycodone/naloxone or itopride.

The number of collected cases was sufficient to
achieve statistically justified conclusions.

There were no statistical differences between
studied groups in terms of age, sex, primary diag-
nosis, performance status (ECOG), opioids used,
or the intensity of symptoms of constipation
among the groups.

Following the aforementioned recommendations,
every patient receiving opioid analgesics
should also receive constipation prophylaxis
through the use of laxatives or by using opioids
in combination with antagonists (e.g. oxycodone/
naloxone) [2, 3]. The Polish guidelines suggest
that adding prokinetics may increase the effect-
iveness of laxative therapy, but there was no
direct clinical evidence for that [14]. According to
these guidelines, verified in a medium-sized co-

Table II. The studied population

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Total</th>
<th>OXN</th>
<th>ITP</th>
<th>OXN+ITP</th>
<th>CTRL</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>92</td>
<td>12</td>
<td>11</td>
<td>9</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>Sex (%):</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>54.3</td>
<td>66.7</td>
<td>58.3</td>
<td>44.4</td>
<td>53.3</td>
<td>0.7916</td>
</tr>
<tr>
<td>Male</td>
<td>42.4</td>
<td>33.3</td>
<td>41.7</td>
<td>55.6</td>
<td>41.7</td>
<td></td>
</tr>
<tr>
<td>NA</td>
<td>3.3</td>
<td></td>
<td></td>
<td></td>
<td>5.0</td>
<td></td>
</tr>
<tr>
<td>Age [years]:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>67.4</td>
<td>68.5</td>
<td>72.5</td>
<td>70.6</td>
<td>67.2</td>
<td>0.4166</td>
</tr>
<tr>
<td>Range</td>
<td>29–91</td>
<td>54–87</td>
<td>43–85</td>
<td>50–91</td>
<td>29–88</td>
<td></td>
</tr>
<tr>
<td>95% CI</td>
<td>57.4–80.9</td>
<td>60.4–87.0</td>
<td>63.6–85.0</td>
<td>62.6–91.0</td>
<td>57.6–81.1</td>
<td></td>
</tr>
<tr>
<td>NA</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Primary diagnosis:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>7</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Other GI cancer</td>
<td>12</td>
<td>1</td>
<td>11</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-GI cancer</td>
<td>70</td>
<td>11</td>
<td>10</td>
<td>7</td>
<td>42</td>
<td>NS</td>
</tr>
<tr>
<td>Non-cancer</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NA</td>
<td>2</td>
<td>1</td>
<td></td>
<td>1</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>ECOG</td>
<td>2.65</td>
<td>1.9</td>
<td>3.0</td>
<td>2.1</td>
<td>2.8</td>
<td>NS</td>
</tr>
<tr>
<td>Mean opioid dose [OME mg]:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 0</td>
<td>134.7</td>
<td>134.4</td>
<td>106.8</td>
<td>130.9</td>
<td>140.9</td>
<td>0.4729</td>
</tr>
<tr>
<td>95% CI</td>
<td>26.2–258.1</td>
<td>45.1–286.1</td>
<td>0–259.6</td>
<td>38.4–308.1</td>
<td>26.9–280</td>
<td></td>
</tr>
<tr>
<td>Day 7</td>
<td>164.7</td>
<td>139.4</td>
<td>182.9</td>
<td>192.3</td>
<td>162.0</td>
<td>0.2855</td>
</tr>
<tr>
<td>95% CI</td>
<td>57.5–287.4</td>
<td>42.2–304.6</td>
<td>68.7–358.8</td>
<td>129.8–312.1</td>
<td>48.6–300.3</td>
<td></td>
</tr>
</tbody>
</table>

OXN – oxycodone/naloxone group, ITP – itopride group, OXN+ITP – oxycodone/naloxone + itopride group, CTRL – control group.
hort study [7], the prevention of OIC should be provided with an intensiveness that ensures bowel movements at least three times per week and good subjective control of bowel symptoms. This goal was achieved in all studied groups, which did not differ from each other in terms of the intensity of symptoms of constipation. In other words, all four strategies appeared equally effective in the prevention of OIC: (1) itopride added to laxatives, (2) oxycodone/naloxone used with laxatives, (3) oxycodone/naloxone and itopride added to laxatives, or (4) regular laxatives only. It was achieved by intensifying laxative use if necessary.

Table III. The intensity of symptoms of constipation

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Scale</th>
<th>Total</th>
<th>OXN</th>
<th>ITP</th>
<th>OXN+ITP</th>
<th>CTRL</th>
</tr>
</thead>
<tbody>
<tr>
<td>The last defecation:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td></td>
<td>91</td>
<td>12</td>
<td>11</td>
<td>9</td>
<td>59</td>
</tr>
<tr>
<td>Mean Days</td>
<td></td>
<td>1.6</td>
<td>1.5</td>
<td>1.5</td>
<td>1.1</td>
<td>1.7</td>
</tr>
<tr>
<td>95% CI</td>
<td></td>
<td>0.2–3.2</td>
<td>0.3–3.5</td>
<td>0–4.0</td>
<td>0–4.0</td>
<td>0.3–3.4</td>
</tr>
<tr>
<td>The number of days with bowel movements:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td></td>
<td>92</td>
<td>12</td>
<td>11</td>
<td>9</td>
<td>60</td>
</tr>
<tr>
<td>Mean Days</td>
<td></td>
<td>3.1</td>
<td>3.5</td>
<td>2.9</td>
<td>3.4</td>
<td>3.0</td>
</tr>
<tr>
<td>95% CI</td>
<td></td>
<td>1.5–5.1</td>
<td>1.5–6.9</td>
<td>1.6–5.2</td>
<td>1.6–7.0</td>
<td>1.4–5</td>
</tr>
<tr>
<td>The difficulty of defecation:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td></td>
<td>92</td>
<td>12</td>
<td>11</td>
<td>9</td>
<td>60</td>
</tr>
<tr>
<td>Mean [0–4]</td>
<td></td>
<td>2.1</td>
<td>2.1</td>
<td>2.1</td>
<td>2.3</td>
<td>2.1</td>
</tr>
<tr>
<td>95% CI</td>
<td></td>
<td>1–3.4</td>
<td>1.1–3.8</td>
<td>0.9–4.0</td>
<td>0.8–4.0</td>
<td>1–3.5</td>
</tr>
<tr>
<td>Too few stools:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td></td>
<td>92</td>
<td>12</td>
<td>11</td>
<td>9</td>
<td>60</td>
</tr>
<tr>
<td>Mean [0–4]</td>
<td></td>
<td>1.5</td>
<td>1.8</td>
<td>1.4</td>
<td>1.2</td>
<td>1.6</td>
</tr>
<tr>
<td>95% CI</td>
<td></td>
<td>0.4–2.9</td>
<td>0.7–3.5</td>
<td>0.1–3.6</td>
<td>0.1–3.3</td>
<td>0.4–3</td>
</tr>
<tr>
<td>Too hard stools:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td></td>
<td>92</td>
<td>12</td>
<td>11</td>
<td>9</td>
<td>60</td>
</tr>
<tr>
<td>Mean [0–4]</td>
<td></td>
<td>1.5</td>
<td>1.4</td>
<td>1.4</td>
<td>1.0</td>
<td>1.7</td>
</tr>
<tr>
<td>95% CI</td>
<td></td>
<td>0.6–2.7</td>
<td>0.6–2.8</td>
<td>0.2–3.5</td>
<td>0.3–2.4</td>
<td>0.7–2.8</td>
</tr>
<tr>
<td>The feeling of an incomplete bowel movement:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td></td>
<td>92</td>
<td>12</td>
<td>11</td>
<td>9</td>
<td>60</td>
</tr>
<tr>
<td>Mean [0–4]</td>
<td></td>
<td>1.4</td>
<td>1.6</td>
<td>0.9</td>
<td>1.1</td>
<td>1.5</td>
</tr>
<tr>
<td>95% CI</td>
<td></td>
<td>0.4–2.7</td>
<td>0.8–2.9</td>
<td>0–2.7</td>
<td>0–3.3</td>
<td>0.5–2.9</td>
</tr>
<tr>
<td>Straining or squeezing to try to pass bowel movements:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td></td>
<td>91</td>
<td>12</td>
<td>11</td>
<td>9</td>
<td>59</td>
</tr>
<tr>
<td>Mean [0–4]</td>
<td></td>
<td>2.0</td>
<td>1.9</td>
<td>2.4</td>
<td>1.9</td>
<td>2.0</td>
</tr>
<tr>
<td>95% CI</td>
<td></td>
<td>0.8–3.5</td>
<td>0.5–4.0</td>
<td>1–4.0</td>
<td>0.5–4.0</td>
<td>0.9–3.4</td>
</tr>
<tr>
<td>The necessity of use of laxatives:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td></td>
<td>91</td>
<td>12</td>
<td>11</td>
<td>8</td>
<td>60</td>
</tr>
<tr>
<td>Mean [0–4]</td>
<td></td>
<td>2.1</td>
<td>2.5</td>
<td>2.0</td>
<td>1.6</td>
<td>2.1</td>
</tr>
<tr>
<td>95% CI</td>
<td></td>
<td>0.9–3.5</td>
<td>1.3–4.0</td>
<td>0.6–4.0</td>
<td>0.9–3.1</td>
<td>0.8–3.7</td>
</tr>
</tbody>
</table>

No statistical difference was for mean values. OXN – oxycodone/naloxone group, ITP – itopride group, OXN+ITP – oxycodone/naloxone + itopride group, CTRL – control group.
Itopride increases the effectiveness of the management of opioid-induced constipation in palliative care patients: an observational non-interventional study

The main finding of this study is that adding itopride to laxative therapy decreased the necessity to use laxatives. On the other hand, using oxycodone/naloxone did not affect the use of laxatives. What is more, the combined use of oxycodone/naloxone and itopride did not increase the effectiveness of the preventive management of OIC.

The findings confirm the sparse clinical evidence available so far [31].

In conclusion, all strategies of OIC prevention seem equally effective in clinical practice. Itopride, but not naloxone, appeared effective in reducing the use of laxatives in OIC. However, using oxycodone/naloxone or itopride could be associated with decreasing the necessity of interventive and burdensome methods, such as manual stool evacuation or enemas.

The conclusions should be taken with caution because it was not a prospective blinded study. We should treat these results as preliminary. We suggest that an RCT would be valuable to confirm the value of itopride in the strategy of prevention and treatment of OIC.

Conflict of interest

The authors declare no conflict of interests.

References


