

Information on risk of constipation for Danish users of opioids, and their laxative use

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Abstract *Background* While it is well known that use of opioids often cause constipation, little is known about the information given to patients regarding this potential side-effect and their use of laxatives to prevent it. *Objective* To assess the degree of information provided by the prescriber to users of opioids by the time of the first prescription regarding the risk of constipation. *Method* Interviews with patients filling an opioid at a community pharmacy were performed by the dispensing pharmacist or pharmaconomist at the pharmacy. Information collected concerned the patient, the opioid, information received regarding constipation, current constipation and current laxative treatment. *Results* A total of 286 interviews were completed. Overall, 28.3 % remembered having received information about the risk of constipation by the time of the first prescription. Excluding 49 first-time opioid users, we found 91 laxative users and 146 non-laxative users, of whom 73.6 and 4.8 %, respectively, currently experienced constipation. *Conclusion* Only a small proportion of patients with a prescription

for opioids remembered having had information on potential constipation caused by opioids and having received any recommendation on how to use laxatives to prevent constipation. Interventions should focus on whether constipation is present and on rational use of laxatives.

Keywords Constipation · Denmark · Laxative · Opioids · Patient information · Prescribing

Impact of findings on practice

- More and probably better information regarding the risk of constipation should be provided to users of opioids.
- Information on laxatives to opioid users in the pharmacy should focus on the rational use of the laxative medicines.

Introduction

In comparison with other countries, Denmark has a high consumption of opioids [1]. Roughly 400,000 persons in Denmark (5.5 million inhabitants) were at some point during 2011 treated with opioids [2]. Constipation is a well-known and common side-effect of treatment with opioids, and for many years, recommendations for prescribing opioids have emphasised the fact that co-treatment with laxatives is mandatory [3, 4]. Still, many hospitalisations are often caused by opioid-induced constipation [5]. Nevertheless, most studies on consumption of laxatives have focused on abuse and overuse, while less focus has been on insufficient use.

In Denmark, all citizens are registered with a general practitioner (GP), with free access to consultation and

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treatment, and the GP is usually the first contact for patients in need of medical services [6]. The vast majority of the opioid consumption is prescribed in primary care. However, very little is known about the extent to which GPs' prescribing of opioids is accompanied by recommendation of using laxatives. Hence, we conducted a cross-sectional study comprising patients filling prescriptions for opioids at a community pharmacy.

Aim of the study

To investigate the prevalence of information provided by the prescriber by the time of the first opioid prescription regarding the risk of constipation as well as the prevalence of constipation and laxative use among users of opioids.

Method

The study was based on structured interviews. Informants comprised users of opioids consecutively recruited at a Danish community pharmacy.

Setting

The study was conducted at Copenhagen Sønderbro Pharmacy, which is one of the three largest pharmacies in Denmark with 73 employees in the main pharmacy and 25 employees in the associated dose-dispensing production unit, producing medicine packages individually packed for each administration time. The trained employees include 15 pharmacists, 46 pharmacists¹ and 16 pharmacist or pharmacist students. Sønderbro Pharmacy is open day and night and serves an average of 1,300 patients per day and fills 300,000 prescriptions (460,000 packages) per year.

Data collection

Eight persons employed at the pharmacy (two pharmacists and six pharmacists) collected data for the study. Patients were asked to participate in the study by the dispensing pharmacist or pharmacist when filling a prescription for any opioid for their own use. Both prevalent opioid users and new users were included. If the patient agreed to participate, a short structured interview was completed.

The interviews were performed directly at the counter, using a questionnaire specifically designed for the purpose

of this study. Data from the interviews were recorded in a database accessible from all PCs at the pharmacy. The dispensing pharmacist/pharmacists were instructed to ask the questions one by one and to enter the information directly into the database. Information comprised patient characteristics, type of opioid, whether the patient by the time of the first opioid prescription had received information about constipation as a potential side-effect and, lastly, current laxative treatment.

The database was based on Microsoft SharePoint and was pilot-tested before implementation. The pilot test only led to minor changes, i.e. rephrasing some of the questions and a slightly changed order of the questions.

Data were analysed using descriptive statistics. Chi square test was used to test whether factors were associated with the level of information given. We examined the association between the degree of information and the indication for use (categorized as "pain from the musculoskeletal system (including arthritis)", "neuropathic pain (including headache)" and "other reasons"), the length of opioid treatment (<1, 1–3, or >3 months) as well as the type of prescriber (GP, doctor on call, emergency ward physician, or hospital physician). These factors were selected in advance. All analyses were performed using Stata Release 11.0 (StataCorp, College Station, TX, USA).

Approval

The study was approved by the Danish Data Protection Agency. An approval from an ethics committee was not required according to Danish law.

Results

A total of 286 subjects redeemed a prescription for an opioid and completed the questionnaire survey. The mean age of participants was 58.0 years (range 21–92; SD 15.2) and 55.9 % were women (Table 1). 237 (82.9 %) were prevalent opioid users while 49 (17.1 %) were first-time opioid users.

The most common opioids were tramadol (n = 122, 42.7 %), morphine (n = 44, 15.4 %) and codeine (n = 27, 9.4 %). The remaining 52 (18.2 %) prescriptions were distributed with <20 for each of the remaining opioids. Some 41 (14.3 %) subjects used different opioids in combination. The majority of users (n = 232, 81.1 %) used opioids due to musculoskeletal pain (Table 1). In 56.6 % of the cases, the prescription was issued by the patients' GP, in 37.4 % by hospital physicians and in 6.0 % by other physicians (emergency service doctors and private practicing specialists).

¹ A pharmacist is equivalent to a pharmacy technician but with a substantially longer education (3 years).

Table 1 Basic characteristics among the participants

	Number of patients (%) (n = 286)
Male	126 (44.1)
Female	160 (55.9)
Age (range)	58.0 (21–92)
Opioid	
Tramadol	122 (42.7)
Morphine	44 (15.4)
Codeine	27 (9.4)
Oxycodone	17 (5.9)
Ketobemidone	12 (4.2)
Transdermal opioids ^a	8 (2.8)
Other	15 (5.2)
Using only one opioid	245 (85.7)
Using more than one opioid	41 (14.3)
Indication	
Musculoskeletal pain	232 (81.1)
Neuropathic pain and headache	21 (7.34)
Cancer pain	5 (1.8)
Other	28 (9.8)
Pattern of use ^b	
Daily dosage	211 (76.2)
As needed (daily)	47 (17.0)
As needed (not daily)	19 (6.8)
Duration of treatment ^c	
First prescription	49 (17.3)
<1 month	15 (5.3)
1–3 months	29 (10.3)
3+ months	190 (67.1)

^a Includes fentanyl and buprenorphine

^b Nine values missing

^c Three values missing

Table 2 Use of laxatives and prevalence of constipation among 237 users of opioids (excluding 49 first-time users)

Laxative users	
Constipated	67 (28.3)
Not constipated	24 (10.1)
Not laxative users	
Constipated	7 (3.0)
Not constipated	139 (58.6)

Excluding first-time users (n = 49, 17.1 %), 91 of 237 subjects (38.4 %) reported using laxatives (Table 2). Among the 91 laxative users, 67 (73.6 %) reported currently experiencing constipation. Among the 146 non-users, the corresponding figure was 7 (4.8 %). The most commonly used laxatives were osmotic laxatives (n = 41)

and stimulant laxatives (n = 21); 53.0 % of laxative users used the drug on a daily basis. Laxative users were slightly older than non-users (mean age 62 years vs. 56 years).

Overall, 81 (28.3 %) subjects remembered having received information about risk of constipation, and 38 (13.3 %) subjects were prescribed laxatives or instructed to request them at the time of the first opioid prescription. The prevalence of information was found to be similar among the sub-group of laxative users and non-users (both 28 %). Individuals receiving information about the risk of constipation at the time of the first prescription most often reported receiving this information from the pharmacy (41.4 %), from different sources (not specified) (12.0 %) and from standard written information from the manufacturer (3.9 %).

The underlying indication for opioid use was statistically significantly associated with the level of information ($p = 0.04$). A total of 71.7 % of persons receiving opioids due to musculoskeletal pain said that they had not received any information. This was the case for 45.0 % in the group receiving opioids because of nerve pain (including headache) and for 63.0 % in the group receiving opioids for other reasons (pain due to cancer, intestinal pain, dental pain and as a cough suppressant). Having the prescription issued by a hospital physician was associated with higher prevalence of information compared to having the prescription issued by other physicians ($p = 0.03$).

No statistical associations between duration of opioid use and recommendation on use of laxatives ($p = 0.70$) were found.

Discussion

The majority of users of opioids did not seem to have received information from the prescriber about the risk of constipation, nor had they been instructed to use laxatives. Prevalence of constipation among laxative non-users was very low (4.8 %) compared to among laxative users (73.6 %).

The main strength of the study is the use of the pharmacy staff as interviewers, which secures a more detailed collection of data and better supports the informant compared to for example a written survey. Furthermore, as the patients are used to discussing their pharmacological treatment with the pharmacy staff, it is conceivable that they are more willing to answer the questions asked by the pharmacy staff. Recall bias denominates the systematic error caused by differences in the accuracy or completeness of the data retrieved. In our study, it may be important that the opioid prescribing often occur in scenarios where much important information, i.e. on consequences of the disease, cause, prognoses and information on self-care, is

given to the patients, and far from everything is likely to be understood or remembered. Hence, many patients may not remember or have understood the importance of using laxatives along with opioid treatment. Further, it is likely that those opioid users with constipation for various reasons may state that they have not received information on how to avoid constipation. All in all, the consequence of this possible recall bias is an underestimation of the frequency of having received information on constipation and on use of laxatives. Hence, it is likely that, to some degree, we may have underestimated the frequency of patients having received information on possible side-effects of opioids.

Furthermore, we did not evaluate the quality of the information received, but merely asked whether the patient felt that he/she had received information or not. Hence, future studies should also address the quality and extent of information given, as these issues are likely to be vital for the impact of the core messages.

The prevalence and costs of opioid-induced admissions and readmissions are generally not known. A Danish hospital has documented that 2.4 % of all re-admissions in 2010 were due to constipation (unpublished results). One should bear in mind that the cost of treatment with laxatives is probably negligible compared to the cost of a readmission to hospital. It is well known that proper use of laxatives can prevent constipation, and that no particular strategy or laxative combination is likely to be superior, but studies comparing different strategies for constipation management are lacking [7]. Nevertheless, responsibility for information about side-effects, including constipation, primarily lies with the healthcare professionals who initiate the treatment. Standardised and structured information about side-effects, e.g. when the prescription is written by the GP or at discharge from the hospital, may help to prevent admissions due to constipation. As it is known that oral information is easily forgotten [8], supplementary written information should be considered. However, producing written information that can be readily understood and be usable by a broad range of patients is a huge challenge [9]. A central player in this field is the pharmacy staff [10, 11]. This study showed that the pharmacy is the most common source of information about side-effects. However, given the fact that a quarter of the respondents reported of currently being constipated, i.e. experiencing a drug-related problem, underlines the fact that there is still need for improvement. In 2011, 407,881 Danes used opioids [2], corresponding to 7 % of the population. Better management of this drug-related problem is therefore crucial when considering the sheer number of patients. An important aspect of laxative use is whether constipated opioid users use the laxative correctly. As an example, only

38 of the 67 constipated users of laxative reported using the drug on a daily basis. The next step should be to focus on the quality of information provided and on how to provide effective information on management of constipation, rather than merely on whether any information has been given.

Conclusion

Only a small proportion of patients with a prescription for opioids remembered having had information on potential constipation caused by opioids, or having received recommendation on how to use laxatives to prevent constipation. Interventions should focus on whether constipation is present and on rational use of laxatives.

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Conflicts of interest The authors report no conflict of interest.

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