

# Laxative prescribing in relation to opioid use and the influence of pharmacy-based intervention

M. L. Bouvy\*† PharmD, H. Buurma\*† PharmD and T. C. G. Egberts†‡ PhD

\*SIR Institute for Pharmacy Practice Research, Theda Mansholtstraat 5B, JE Leiden, †Department of Pharmacoepidemiology and Pharmacotherapy, Utrecht Institute of Pharmaceutical Sciences, University Utrecht and ‡Hospital Pharmacy 'Midden Brabant', TweeSteden Hospital and St Elisabeth Hospital, Tilburg, The Netherlands

## SUMMARY

**Introduction:** Opioid-induced constipation is a common problem and can cause serious complications. It is widely advised that laxatives should be started concurrently with opiates, unless there is a clear indication not to do so.

**Objective:** This study was undertaken to estimate how often laxatives were started concurrently with opiates and to describe the effect of pharmacy-based interventions to promote the use of laxatives in patients starting opioids.

**Methods:** Twenty-six community pharmacies identified all patients who received a first prescription for a strong opioid during January and February of 1998, 1999 or 2000. Pharmacists collected information on patient, drug and prescriber characteristics (age, gender, use of opiates and laxatives). A separate questionnaire was used to collect data on pharmacy-based interventions to promote the simultaneous prescribing of laxatives with the opiates.

**Results:** Overall, 37% of the patients receiving an opioid started taking laxatives within 5 days. The percentage of patients who received laxatives simultaneously with opioids increased from 31% in 1998 to 35% in 1999 and 42% in 2000. In 117 (43%) of the opioid prescriptions, pharmacy-based intervention had taken place before the prescription date. Of these, 48.7% was accompanied by a laxative. Opioid prescriptions ( $n = 152$ ) without a pharmacy based intervention were accompanied in 27.6%. After adjustment for covariates (including time trends), pharmacy-

based intervention increased the probability of concomitant laxative use 1.9 [95% CI 1.1–3.3] times.

**Discussion:** This study shows that the widely used guideline to start a laxative when prescribing an opioid is not always followed in daily practice. In addition, we showed that pharmacy-based intervention contributed to increasing laxative use in patients receiving opioids.

**Keywords:** intervention, laxatives, opioids, pharmacist, pharmacy practice research

## INTRODUCTION

Morphine and other strong opioids are still the most effective and commonly used analgesics in severe pain. Opioids are relatively safe drugs when used appropriately. While the potential for tolerance, dependence and respiratory depression are often exaggerated, the most commonly occurring side-effect, constipation, and its potential clinical sequelae are sometimes underestimated.

Opioids reduce gastrointestinal motility and consequently opioid-induced constipation is a common problem. Almost all patients on opioids report constipation as the major side-effect (1). A hospital survey showed that 87% of patients on strong opioids required the use of laxatives (2). Among patients using morphine 80% reported constipation (3). Opiate-induced constipation is not only bothersome but can cause abdominal pain, nausea and vomiting, and serious interference with drug administration and absorption. In addition, serious complications such as intestinal pseudo-obstruction may occur (4). Cancer pain may also be exacerbated (5). Although randomized clinical trials investigating whether the prophylactic use of laxatives in patients starting opioids is

Received 22 March 2001, Accepted 5 November 2001  
Correspondence: Marcel L Bouvy, SIR Institute for Pharmacy Practice Research, Theda Mansholtstraat 5B, 2331 JE Leiden, The Netherlands. Tel: +31 71 5766157; fax: ++ 31-71-5766251; e-mail: sir@stevenshof.nl

useful or not have not been performed, it is widely advised that laxatives should be started concurrently with opiates, unless there is a clear indication not to do so (6, 7). As the induction of constipation by opioids is so predictable, Dutch pharmacotherapy guidelines advise starting a laxative simultaneously with an opioid (8, 9). A pilot study in the Netherlands suggested that a substantial proportion of patients using opioids did not use laxatives concomitantly (10). Several pharmacy-based interventions may be used to promote the use of laxatives in patients starting opioids. For example, pharmacists can stimulate the concomitant use of opiates by proposing that patients starting opioids take laxatives. Pharmacists can also discuss the concurrent use of laxatives and opiates with physicians at appropriate meetings. Some Dutch pharmacists already participate in such activities.

This study was undertaken to investigate how often laxatives were started concurrently with opioids in current clinical practice. We also studied the influence of various pharmacy-based interventions on the simultaneous prescribing of laxatives with opioids.

## METHODS

Twenty-six community pharmacies distributed throughout the Netherlands took part in this study. Pharmacies in the Netherlands keep complete patient medication records for several years. Patients usually visit the same pharmacy and it has been estimated that 95–99% of patients always collect their medications from the same pharmacy (11). The participating pharmacists selected all patients who received a first prescription for a strong opioid during January and February of 1998, 1999 or 2000. A first prescription was defined as the absence of a prescription for any strong opioid during the preceding 6 months. Pharmacists collected details about the patient, drug and prescriber (age, gender, use of opiates and laxatives) on a standard form. The concomitant use of laxatives was defined as the start of a laxative within 5 days after starting the opioid. Patients already using laxatives prior to starting an opioid were excluded from the analysis. A separate questionnaire was used to collect data on the type of pharmacy intervention used to promote the

simultaneous prescribing of laxatives when starting an opioid and the time of its implementation.

Data were analysed using SPSS 10.0 (SPSS inc. USA).

## RESULTS

The 26 pharmacies identified 318 patients who received a strong opioid for the first time during the study period. Of these patients 49 (15%) already used a laxative before the start of the opioid, leaving 269 patients for further analysis.

The majority of the patients were female and the mean age was 63 years (Table 1). Morphine (orally slow release) and fentanyl transdermally were the most commonly prescribed opioids.

Overall, 37% of the patients started a laxative within 5 days of receiving an opioid (Table 2). The percentage of patients who received laxatives simultaneously with opioids increased from 31% in 1998 to 35% in 1999 and 42% in 2000. There was no major difference in the use of laxatives between fentanyl users and morphine users. Specialists prescribed laxatives more often than general practitioners [55 vs. 32%; odds ratio 2.6 (1.5–4.8)].

The most common interventions were discussion of the topic in a pharmacotherapy meeting (educational) and notifying the prescriber in case the patient was prescribed an opioid but not a laxative as well. In 117 (43%) of the opioid prescriptions a pharmacy-based intervention had taken place before the opiate prescription date. Of

**Table 1.** Basic characteristics of patients included in the study ( $n = 269$ )

|                            | <i>n</i>    | %  |
|----------------------------|-------------|----|
| Female gender              | 164         | 61 |
| Mean age (SD)              | 63.2 (17.1) |    |
| Prescriber                 |             |    |
| General practitioner       | 213         | 79 |
| Specialist                 | 56          | 21 |
| Type of opioid             |             |    |
| Morphine                   | 189         | 70 |
| Fentanyl (transdermal)     | 53          | 20 |
| Other                      | 27          | 10 |
| Year of starting an opioid |             |    |
| 1998                       | 77          | 29 |
| 1999                       | 79          | 29 |
| 2000                       | 113         | 42 |

**Table 2.** Determinants of the concomitant use of laxatives in patients starting an opioid ( $n = 269$ )

|                                    | Concomitant laxative |      | Odds ratio<br>[95% confidence<br>interval] |
|------------------------------------|----------------------|------|--|
|                                    | <i>n</i>             | %    |  |
| All patients ( $n = 269$ )         | 99                   | 36.8 |  |
| Year of prescription               |                      |      |  |
| 1998 ( $n = 77$ )                  | 24                   | 31.2 | 1 (reference)                              |
| 1999 ( $n = 79$ )                  | 28                   | 35.4 | 1.2 [0.6–2.4]                              |
| 2000 ( $n = 113$ )                 | 47                   | 41.6 | 1.6 [0.9–2.9]                              |
| Type of opiate                     |                      |      |  |
| Morphine ( $n = 189$ )             | 80                   | 42.3 | 1 (reference)                              |
| Fentanyl transdermal ( $n = 53$ )  | 17                   | 32.1 | 0.6 [0.3–1.1]                              |
| Other ( $n = 27$ )                 | 2                    | 7.4  | 0.1 [0.0–0.5]                              |
| Prescriber                         |                      |      |  |
| General practitioner ( $n = 213$ ) | 68                   | 31.9 | 1 (reference)                              |
| Specialist ( $n = 56$ )            | 31                   | 55.4 | 2.6 [1.5–4.8]                              |
| Any pharmacy based strategy        |                      |      |  |
| No ( $n = 152$ )                   | 42                   | 27.6 | 1 (reference)                              |
| Yes ( $n = 117$ )                  | 57                   | 48.7 | 2.5 [1.5–4.1]                              |

those prescriptions, 48.7% had a laxative co-prescribed, whereas with opioid prescriptions without pharmacy intervention the corresponding figure was only 27.6% [odds ratio 2.5 (95% CI 1.5–4.1)]. After adjustment for type of opiate, type of prescriber and time trends, pharmacy intervention increased the probability of concomitant laxative use 1.9 (95% CI 1.1–3.3) times.

## DISCUSSION

This study shows that the guideline to start a laxative when prescribing an opioid is not always followed in clinical practice. In addition, we showed that pharmacy intervention increased laxative co-prescription.

Use of laxatives with every opioid co-prescription seems neither feasible nor necessary. There may be good reasons for avoiding co-prescribing of laxatives, for example, when patients already have severe diarrhoea. However, several studies have shown that laxatives are necessary for the vast majority of patients receiving opioids (1–3, 7). It was not the aim of our study to identify which particular type of intervention was the most effective. The most important message is that possible adverse events can be prevented by pharmacist intervention in concert with physicians.

## REFERENCES

1. Robinson CB, Fritch M, Hullett L *et al.* (2000) Development of a protocol to prevent opioid-induced constipation in patients with cancer: a research utilization project. *Clinical Journal of Oncology and Nursing*, **4**, 79–84.
2. Sykes NP. (1998) The relationship between opioid use and laxative use in terminally ill cancer patients. *Palliative Medicine*, **12**, 375–382.
3. Nilsson JLG, Andersson A, Kalvemarmark S *et al.* (2000) Surveys of drug-related therapy problems of patients using medicines for allergy, asthma and pain. *International Journal of Pharmaceutical Practice*, **8**, 198–203.
4. Murthy BV, Ion F, Winstanley JR. (1998) Intestinal pseudo-obstruction associated with oral morphine. *European Journal of Anaesthesiology*, **15**, 370–371.
5. Glare P, Lickiss JN. (1992) Unrecognized constipation in patients with advanced cancer: a recipe for therapeutic disaster. *Journal of Pain and Symptom Management*, **7**, 369–371.
6. Cameron JC. (1992) Constipation related to narcotic therapy. A protocol for nurses and patients. *Cancer Nursing*, **15**, 372–377.
7. Levy MH. (1996) Pharmacologic treatment of cancer pain. *New England Journal of Medicine*, **335**, 1124–1132.
8. Tongeren JHM. (1992) Symptoombehandeling bij patienten in de terminale fase van ongeneeslijke aandoeningen: obstipatie en het gebruik van laxantia. *Gebu*, **26**, 35–36.

9. Rosmalen CFH, Thomas S, van der Laan JR, van Lennep MJ, Vink R. (1996) Farmacotherapie voor de huisarts; achtergronden. Utrecht, The Netherlands: Nederlands Huisartsen Genootschap
10. Dik E, Diepenmaat B. (1999) Suggesties voor therapieverbetering. *Pharmaceutisch Weekblad*, **134**, 1348–1352.
11. Herings HR. (1993) PHARMO. A record linkage system for postmarketing surveillance of prescription drugs in the Netherlands. Dissertation, Utrecht University, Utrecht.