

Development

The impact of opioid and laxative prescribing habits on constipation in the primary care setting before and after the introduction of SIGN 44: *Control of pain in patients with cancer*

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The constipating effect of opioids used in cancer pain is widely acknowledged. Opioids account for about a half of constipation in cancer patients, making constipation one of the most prevalent side effects of cancer analgesia. Scottish Intercollegiate Guidelines Network (SIGN) guideline 44 (7.4.1) states explicitly that the appropriate intervention for opioid-induced constipation is a combination of softening and stimulating prophylactic laxatives. Previous literature suggests such practice is not commonplace, implicating a knock-on negative effect to patients' quality of life and highlighting the need for audit in this area. An audit of bowel management in Fife primary care was carried out comparing laxative prescribing practice before and after the publication of SIGN 44: *Control of pain in patients with cancer*. The data for the audit included all opioid prescriptions including both cancer and non-cancer patients. It was found that publication of SIGN 44 had no significant effect on adherence to the guideline by general practitioners in Fife, at six-, 12- and 18-months post-publication. Implications for quality of life and improving bowel management are discussed.

Key words: cancer; constipation; laxatives; opioids; pain; primary care; SIGN 44

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Cancer is one of the leading causes of death in the UK. One in three of the population will develop cancer at some stage in their lives and one in four will die of the disease (Potter *et al.*, 2003). Distressing symptoms may occur as a result of the disease process itself, during treatment, or from lack of adequate symptom control. Pain is one of the most frequent and disturbing symptoms of cancer. The World Health Organization's (WHO) classic three-step ladder stipulates that opioids are the

appropriate analgesia for moderate to severe cancer pain (Cherny, 2001). Although opioids are a mainstay of cancer pain management, they are not without adverse side effects.

This audit has addressed the consequences of opioid analgesic use in the treatment of cancer pain. The adverse effects of opioids, opioid-induced constipation, quality of life, cancer care, and quality control in the form of audit procedures and the Scottish Intercollegiate Guidelines Network (SIGN) guidelines are discussed. The prescribing habits of general practitioners (GPs) in Fife pre- and post-publication of SIGN 44: *Control of pain in patients with cancer* will be investigated and specifically,

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SIGN 44 (7.4.1) which addresses prophylactic co-prescribing of stimulant and softening laxatives with opioids (SIGN, 2001; 2004).

Adverse effects of opioids

The incidence and severity of side effects from the administration of opioids can play an important role in the success or failure of management in patients with cancer pain. In clinical practice, opioid pharmacotherapy for cancer pain hinges on finding a satisfactory balance between analgesia and side effects. Side effects such as constipation impair quality of life and can be reduced by limiting the dosage of opioid analgesics to patients (McNicol *et al.*, 2003). Until recently, constipation had been understood only in terms of the physical symptoms, regarded as trivial and was not fully recognized as a complex, interactive problem. Treatment has not always been simple. It has been reported that a combination of softening and stimulating laxatives is more likely to maintain normal bowel function at the lowest dose with the least side effects compared to other or no laxatives (Sykes, 1996; Klaschik *et al.*, 2003; McNicol *et al.*, 2003).

Opioid-induced constipation

Patients do not develop tolerance to opioid-induced constipation and a prophylactic bowel regimen is recommended at initiation of therapy (Bouvy *et al.*, 2002). The constipating effect of opioids is widely acknowledged where opioids account for about 25–50% of constipation found in terminally ill cancer patients (Fallon and O'Neil, 1997; Sykes, 1998; McQuay, 1999; McMillan and Weitzner, 2000; Foss, 2001; Klaschik *et al.*, 2003; McNicol *et al.*, 2003). It is not just the experience of constipation itself, but also the symptoms that stem from constipation that are problematic for the patient (Pappagallo, 2001; Pearce *et al.*, 2001).

Quality of life

Constipation is not just an unpleasant physical symptom, but is a consequence of poor pain management that may have a ripple effect, causing much distress and affecting quality of life (McMillan and Small, 2002). Generally, good pain management

corresponds with higher quality of life scores compared with poor pain management (Ahmedzai, 1995; Isikhan *et al.*, 2001; Chang *et al.*, 2002; Chochinov *et al.*, 2002; McMillan and Small, 2002; Zaza and Baine, 2002). Additionally, research has indicated that unmanaged side effects such as constipation can increase the chance of hospitalization. It has been reported that constipation was one of four factors that significantly and independently predicted hospice in-patient care (Addington-Hall *et al.*, 1998).

The impact of constipation on quality of life extends beyond the patient themselves. In a review of the literature, Pearce *et al.* (2001) conclude that direct costs as well as indirect costs are substantial to families and often go unacknowledged. The complexity of the reported costs attached to cancer and cancer care included clinic visits, transport, food, prescriptions, over-the-counter medication, child-care, loss of wages, home care and accessing support.

Cancer care

Improving cancer and specialist palliative care services has been recognized as central priorities for National Health Services (NHS) Scotland (Scottish Executive, 2001). As GPs in the UK have a central role in cancer treatment and palliative care, it has been suggested that the concept of good cancer pain management should be embedded in a framework of palliative care, taking into consideration, all the different aspects of symptom management (Cherny, 2001). In the UK, it has been reported that 80% of GPs were prepared to manage cancer pain on their own (Lang *et al.*, 1992; Seamark *et al.*, 1996), despite limited relevant palliative care knowledge (Seamark *et al.*, 1996). Similarly in the US, knowledge and implementation of accepted palliative care practices is haphazard, both with GPs and in hospice care (Barclay *et al.*, 2002). Knowledge and practice of health professionals outside the UK and the US in the care of patients with cancer is also lacking (Von Roenn *et al.*, 1993; Nissen *et al.*, 2001; Bouvy *et al.*, 2002). Worldwide, there seems to be a distinct lack of knowledge and practice in the pain management of patients with cancer.

Quality control

The SIGN was formed in 1993 'to improve the quality of health care for patients in Scotland by

reducing variation in practice and outcome, through the development and dissemination of national clinical guidelines containing recommendations for effective practice based on current evidence' (SIGN, 2001: 1). SIGN 44: *Control of pain in patients with cancer* was published to improve the quality of life for cancer patients. Specifically, Paragraph 7.4.1 states categorically 'Patients receiving an opioid must have access to regular prophylactic laxatives. A combination of stimulant and softening laxative will be required.' (SIGN 44, Evidence Level III, 2000). Local and national audit projects provide invaluable assistance in the implementation of guidelines and indeed, SIGN actively works to encourage and facilitate audit by providing a 'gold standard' against which clinical practice can be judged.

An initial feasibility study investigating the ability to audit the effect of the implementation of SIGN 44 (7.4.1) in the primary care setting in Fife using General Practice Administrative Service Scotland (GPASS) computer databases failed to result in an adequate audit. Limitations included an incomplete data set, an inability to obtain time frames for prescriptions, poor recording habits and small GP participation numbers. However, the results indicated further investigation was warranted and so more accurate data was required. The Common Services Agency (CSA) statistics division are sent all individual prescriptions dispensed in Fife by community pharmacies. They are then processed and stored electronically. The data supplied by the CSA was considered sufficient for this audit.

Aim

This investigation aimed to compare current practice in Fife against the standard laid out in SIGN 44 Paragraph 7.4.1.

The specific objectives were the following:

1. To identify prevalence of opioid prescriptions with prophylactic laxative prescriptions pre-publication of the SIGN guideline and at six-, 12- and 18-months post-publication.
2. To identify prevalence of opioid prescriptions alone.
3. To identify prevalence of all laxative prescriptions (both stimulant and/or softening) pre-publication of the SIGN guideline at six-, 12- and 18-months post-publication.

4. Feedback to the specialist palliative care team to improve care and information to patients.
5. Suggest future recommendations and improvements.

Method

The five Local Healthcare Co-operatives (LHCCs) in Fife (Dunfermline, West Fife, Glenrothes, Kirkcaldy/Levenmouth, North East Fife) were approached and four agreed to participate in the study. Data from the CSA in Edinburgh was accessed and contained prescriptions dispensed in Fife pharmacies from January 2000 to December 2001. This scanned data included prescriptions from all but one of the GP practices in the four LHCCs who agreed to participate. Thus 42 of the 43 GP practices from four LHCCs were involved in the audit. GP practices in the data set from the CSA were not named to maintain confidentiality. The prescription data from CSA also included non-cancer patients with pain. At the time that the CSA data for this project was collected, it was not possible to differentiate cancer and non-cancer patients.

The criteria for inclusion were all opioid prescriptions for pain. The data was then divided into four categories: prescriptions that contained, opioid alone, opioid plus a stimulant laxative, opioid plus a softening laxative, and opioid plus a combination of stimulant and softening laxative. Methadone prescriptions were excluded from the data because the Fife Palliative Care Service reported that methadone is rarely used at the moment as a cancer pain analgesic. Nor was a distinction made between strong and weak opioids as SIGN 44 (7.4.1) makes no distinction between opioid strength.

The data was then divided into four time periods:

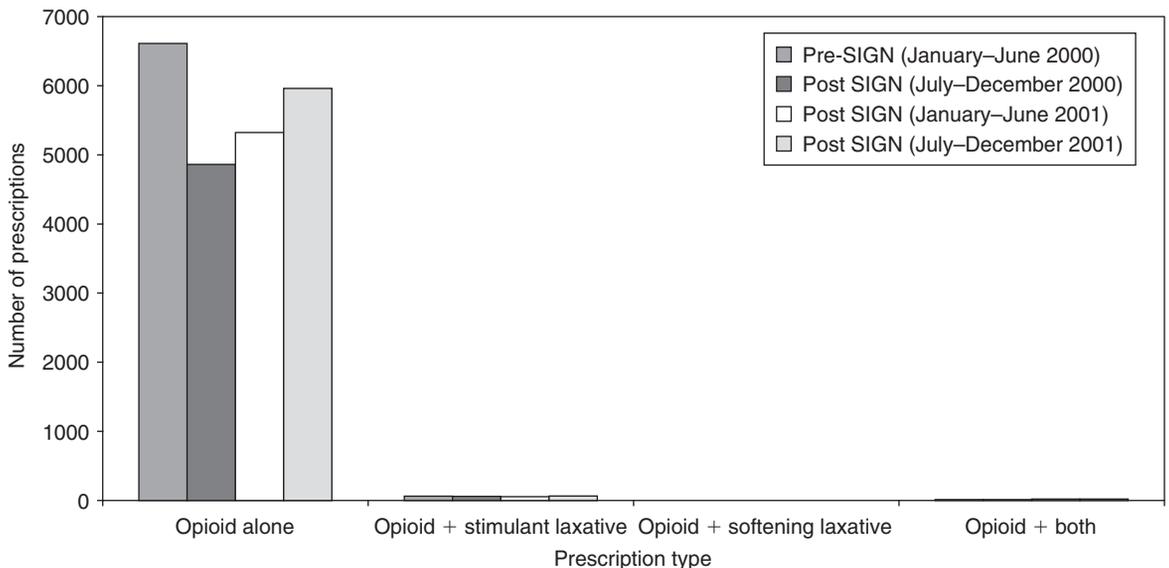
- six-months pre-SIGN 44 publication (January–June 2000)
- six-months post-SIGN 44 publication (July–December 2000)
- 12-months post-SIGN 44 publication (January–June 2001)
- 18-months post-SIGN 44 publication (July–December 2001)

Results

A summary of all opioid prescriptions is displayed in Table 1. The data from individual GP practices has

Table 1 Summary of opioid prescriptions across all LHCCs, pre- and post-publication

Prescriptions	Pre-SIGN (January–June 2000)	Post-SIGN		
		(July–December 2000)	(January–June 2001)	(July–December 2001)
A Opioid alone	5341	4662	5039	5588
Opioid + stim lax	63	59	54	64
Opioid + soft lax	0	0	0	0
Opioid + both	14	14	21	20
B Opioid alone	10301	8437	8787	9580
Opioid + stim lax	109	120	157	140
Opioid + soft lax	0	0	0	1
Opioid + both	77	31	24	21
C Opioid alone	7327	7296	7189	7439
Opioid + stim lax	85	76	54	81
Opioid + soft lax	0	0	0	0
Opioid + both	54	40	55	37
D Opioid alone	4490	–	4584	5302
Opioid + stim lax	49	–	47	48
Opioid + soft lax	0	–	0	0
Opioids + both	33	–	19	30

**Figure 1** Prescriptions for LHCC A during the audit period

been pooled by LHCC and displayed pre- and post-publication of SIGN 44.

Data was not available for LHCC D for the post-SIGN period, July–December 2000.

It is clear that the publication of SIGN 44 made little difference to the prescribing habits of GPs in

the four LHCCs in Fife. The number of prescriptions in all categories varied only marginally across all LHCCs.

As an example, Figure 1 shows the number of prescriptions from one LHCC (LHCC A) during the audit period.

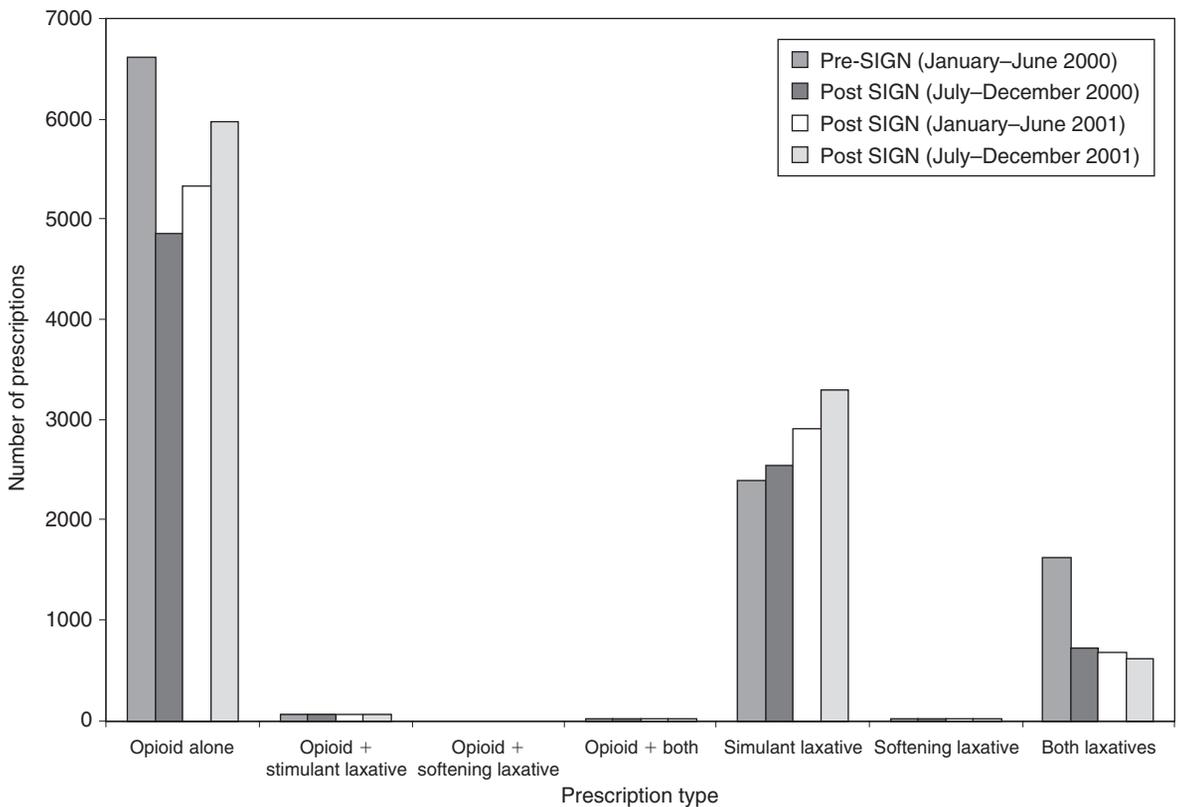


Figure 2 Prescriptions for opioids alone as well as laxatives alone for LHCC A

For the audit period, subsequent data on prescriptions of laxatives alone was also collated. Although SIGN 44 is very explicit, further consideration was given to the number of ‘opioid alone’ and ‘laxative alone’ prescriptions.

Figure 2 displays prescriptions of opioids alone as well as laxatives alone for LHCC A in addition to the combination prescriptions. Although there was an increase in the number of prescriptions, this is no way matched the number of opioid prescriptions.

It would appear that the results of this audit demonstrate that the introduction of SIGN guideline 44 made little difference to an existing lack of prophylactic laxative prescribing by GPs in Fife for patients receiving an opioid for cancer pain. However, the results can only be considered tentatively, because the prescription data used in the audit included both cancer and non-cancer patients.

Limitations

The data set from the CSA included both initial and subsequent prescriptions of opioid use. It may have been more useful had only ‘first prescriptions’ been included in the data set. Although SIGN 44 is very explicit in terms of the regular prophylactic co-prescribing of both stimulant and softening laxatives, a possible explanation for the discrepancy between the number of opioid and laxative prescriptions is that the opioid supplied may have been for a shorter time frame than the laxative in the initial prescription, with subsequent prescriptions listing opioids only. The prescription numbers therefore may not be an accurate measure of adherence to the guideline for auditing purposes.

The criteria for prescription inclusion in the audit, ‘if the script contained an opioid used in cancer pain analgesia or contained an opioid used in cancer pain analgesia along with a softening and/or

stimulating laxative' was also problematic. The prescription data supplied by the CSA could not differentiate cancer and non-cancer patients. Therefore, our criteria for prescription inclusion could not be satisfied.

Discussion

Given that the goal of clinical guidelines is the improvement of clinical decision making and the quality of care for patients it would appear that this goal has not been achieved in this audit. There are significant issues concerning the quality of pain management, lack of bowel management and indeed impaired quality of life for cancer patients when constipation is overlooked or mismanaged.

Education of GPs and health professionals needs to be highlighted as an area to be addressed if clinical effectiveness is to improve (Seamark *et al.*, 1996). More research is needed which specifically addresses quality of life with cancer pain patients. Little of the current research on quality of life looks solely at cancer pain and the impact that has on quality of life (McNicol *et al.*, 2003). Very few studies have been conducted that have focused on a physical symptom such as constipation and investigated the impact it has on quality of life as an independent factor. However, constipation seems to be implicated as a predictor of poor quality of life and a factor leading to symptom distress. Clearer links between constipation and quality of life need to be established. Given the vast literature on quality of life and indeed the prevalence and severity of constipation in cancer patients, there is a significant motive to investigate this further.

Moreover, it would not be enough to simply investigate the relationship between constipation and quality of life. Action must be initiated. If best practice is the aim of patient care then adhering to guidelines and clinical governance standards is essential. Possible barriers to adherence to published guidelines need to be investigated further. Are practitioners too busy? Is there peer and/or patient resistance? Is there insufficient access to patient data? Are there administrative obstacles or financial problems? Is there insufficient information and education available? Do practitioners simply forget? These questions remain unanswered, but are important considerations if improved patient care is to be achieved. The process of audit itself will need to continue to be developed and implemented.

Conclusion

The question of whether the introduction of SIGN 44 improved practice in bowel management has most unequivocally been answered. The practice of prescribing a prophylactic combination of softening and stimulating laxative in concurrence with an opioid has not been shown to improve post-publication of SIGN 44. Possible future action points in the direction of better GP education, improved prescribing habits and practices, better documentation of prescriptions, awareness of constipation, and further research into constipation and quality of life.

Furthermore, the results highlight the importance of audit in evaluating what is going on in current practice. Unfortunately, there is a lack of previous research on the actual prescribing practice of laxatives in recent years in Britain. This study has attempted to address this. Despite the considerable limitations, the results suggest that in Fife, the introduction of SIGN 44 has made little difference to existing prescribing habits in the primary care setting.

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