The Clinical Challenge of Opioid-induced Constipation: Insights from the Opioid-induced Constipation Clinical Audit

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Abstract

Objective: Constipation is the most common and often most debilitating adverse effect associated with opioid use. Opioid-induced constipation persists for the duration of therapy. The aims of this clinical audit were to investigate the GP management of opioid-induced constipation, gain insights on how to improve its management and determine if the audit could improve the management of opioid-induced constipation.

Methods: Using quantitative questionnaires, GPs prospectively evaluated their management of constipation in patients prescribed strong opioid analgesic for chronic non-cancer pain, across two audit cycles. The audited patients completed a quantitative survey after the initial GP visit and returned the completed survey to the GP in a sealed envelope. The patient questionnaire was used to assess consistency between patients' and GPs' evaluation and management of constipation. Following each cycle GPs received feedback and a decision support tool.

Results: Opioid-induced constipation was reported by 50.5% of patients, but its presence was underestimated by GPs, with GPs failing to recognise opioid-induced constipation in a third of patients. GP management of opioid-induced constipation improved during the audit with improvements in the frequency of assessment and the proactive management of constipation.

Conclusion: GPs need to regularly ask all patients taking opioid analgesics about the presence of constipation. Questioning should include both objective and subjective measures to assist the detection and assessment of opioid-induced constipation. The high prevalence of opioid-induced constipation necessitates proactive management at the time of opioid initiation and for the duration of opioid therapy.

Objectives

Constipation is the most common side effect of opioid therapy [1]. It is a consequence of opioids binding to mu-opioid receptors in the gastrointestinal tract, leading to decreased propulsive movement of bowel contents, decreased gut secretion of intestinal fluid and sphincter dysfunction [2,3]. The prevalence of opioid-induced constipation (OIC) in patients with chronic non-cancer pain (CNCP) ranges from 15% to 81% [3-7].

Unlike other opioid-related side effects, OIC does not improve over time, but persists for the duration of opioid therapy [1,8]. OIC is not a trivial complaint. If poorly managed it may lead to clinical sequelae, including faecal impaction with spurious diarrhoea, colonic pseudo-obstruction, abdominal pain, nausea and vomiting [9,10]. It has a negative impact on patient quality of life and undermines effective pain management [3].

Best clinical practice recommends that OIC be proactively managed and regularly monitored [1,11,12]. None the less a recent survey amongst Australian GPs, found that over one third of GPs either never or only occasionally assessed opioid-related side effects, including constipation, amongst their patients with CNCP [13]. This suggests that OIC may be undiagnosed and/or inadequately managed in Australian general practice.

The aims of this clinical audit were to investigate the GP management of OIC in patients taking a strong opioid for CNCP, to gain insights on how to improve the management of this common and persistent side effect and to determine if participation in the audit will improve the management of OIC.

Methods

The OIC clinical audit followed The Royal Australian College of General Practitioners (RACGP) five-step clinical audit process: needs assessment, audit cycle 1, review and reflection, audit cycle 2 and a further review and reflection. GPs participating in this prospective audit evaluated their management of OIC in 15 patients (10 in cycle 1 and 5 in cycle 2) who were taking a strong (Schedule 8) opioid analgesic for CNCP for at least 2 weeks prior to the audit. All patients provided consent to participate in the clinical audit. Following completion of each audit cycle, GPs received feedback in the form of an individualized report on their performance versus the audit criteria and a decision support tool that summarized laxative use and categorized patients according to whether they were currently constipated or not and the impact of OIC on quality of life and pain management. A brief educational report was also provided to GPs following the completion of cycle 1.

An educational committee comprising of six GPs and one

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gastroenterologist assisted with the development of the audit protocol, including setting the standards of care against which GP performance was evaluated (Table 1). The four audit criteria were developed from published reviews of the management of OIC, which represent best clinical practice [2,9-10]. GPs were recruited through the RACGP QI&CPD website, advertisements and by personal invitation.

Information about OIC and its management was collected from both the audited patients and GPs using quantitative questionnaires. Patient assessment of constipation was assessed using stool frequency, the Bristol Stool Scale and the Bowel Function Index [2]. To ensure that the patient surveys did not influence GPs' responses, patients were instructed to complete the survey after their appointment and return the completed form to the GP in a sealed reply-paid envelope.

The audit was accredited by the RACGP and approved by the Bellberry Human Research Ethics Committee.

Statistical Analysis

All data were captured in an Access database. Only data from GPs who completed both audit cycles within the first year of the audit commencing were included in this analysis. Analysis included basic descriptive statistics and comparisons between cycle 1 and 2 results using two-tailed t-tests.

Results

A total of 64 GPs completed the audit within the first year and provided data on 956 patients (638 in cycle 1 and 318 in cycle 2). The rate of return of patient surveys was excellent at 98.7% (n=944). The characteristics of the audited patients are summarised in Table 2. Most patients were prescribed a single opioid to manage CNCP. The three most commonly prescribed opioids in cycle 1 were oxycodone (28.2%), buprenorphine (24.0%) and modified-release oxycodone/naloxone (16.9%). In audit cycle 2 these same three opioids were the most commonly prescribed, however the use of modified-release oxycodone/naloxone significantly increased and was the most commonly prescribed opioid (24.8%, P=0.004), followed by oxycodone (24.5%) and buprenorphine (18.9%).

The mean GP performance against the four audit criteria are shown in Figure 1. The only criteria that GPs performed well relative to the acceptable standard was criteria 3, the provision of lifestyle advice. Performance across all criteria improved significantly in cycle 2. This improvement was reflected in the percentage of individual GPs who achieved the acceptable standards across the audit criteria. For example, 35.9% of GPs informed 100% of their patients about the risk of constipation prior to initiating opioid therapy in cycle 1, in cycle 2 this increased to 65.6% (P=0.001). In cycle 1, 7.8% of GPs co-prescribed

Audit criteria	Ideal standard	Acceptable standard
1. Patients prescribed opioid analgesics are informed of the potential side effect of constipation prior to commencing opioid therapy.	100%	100%
2. At the time when opioid therapy is commenced, patients are co-prescribed a therapy to prevent/manage OIC.	100%	80%
3. At or before opioid therapy is commenced, patients are provided with lifestyle advice to help manage constipation.	100%	70%
4. The presence and management of constipation is regularly assessed in patients prescribed opioid therapy (i.e. at every appointment where the patient's pain is reviewed).	100%	80%

Table 1: OIC clinical audit evaluation criteria.

	Cycle 1 (n=638)	Cycle 2 (n=318)
Gender		
Male	264 (41.4%)	120 (39.2%)
Female	344 (53.9%)	184 (60.1%)
Not specified	30 (4.7%)	2 (0.7%)
Age		
18-30 years	13 (2.0%)	4 (0.3%)
31-50 years	120 (18.8%)	43 (14.1%)
51-60 years	126 (19.7%)	62 (20.3%)
61-70 years	102 (16.0%)	63 (20.6%)
71-80 years	137 (21.5%)	72 (23.5%)
81+ years	118 (18.5%)	61 (19.9%)
Not specified	22 (3.4%)	1 (0.3%)
Schedule 8 opioid use		
Taking only one Schedule 8 opioid	562 (88.1%)	279 (87.7%)
Taking two or more Schedule 8 opioids	76 (11.9%)	39 (12.3%)
Taking other medications known to cause constipation	300 (47.0%)	116 (36.5%)*
Codeine	102 (16.0%)	41 (12.9%)
Tricyclic antidepressants	113 (17.8%)	47 (14.8%)
Anticonvulsants	56 (8.8%)	15 (4.7%)
Other	85 (13.4%)	26 (8.2%)
GP reported the patient was constipated prior to commencing current opioid therapy	106 (16.6%)	65 (20.4%)
*P=0.002 versus cycle 1.		

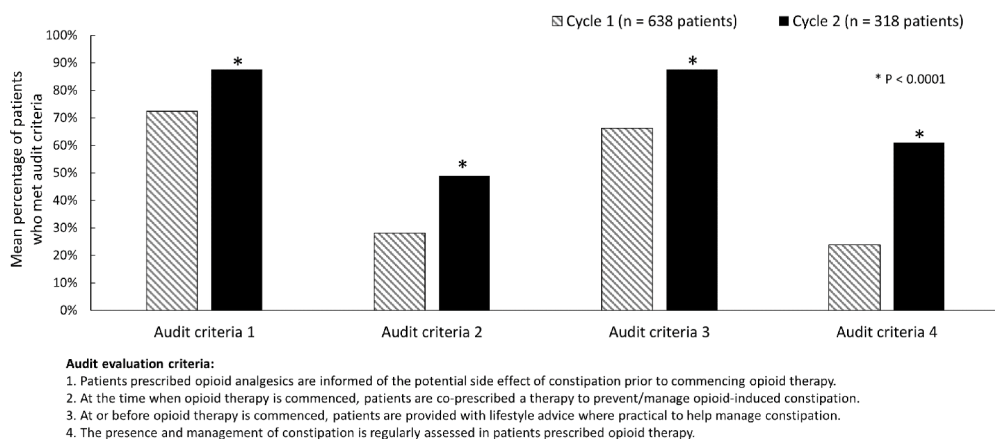**Table 2:** Patient characteristics.

Figure 1: Mean GP performance versus audit criteria.

a therapy (opioid antagonist or laxative) to manage constipation in at least 80% of their patients at the time of opioid initiation and this increased to 26.6% in cycle 2 (P=0.006). The regular assessment of constipation in at least 80% of patients was achieved by 17.2% of GPs in cycle 1 and 51.6% of GP in cycle 2 (P=0.0001).

Constipation, as measured by combining all patient data sources the Bowel Function Index, stool frequency and the Bristol Stool Scale, was very common amongst the patients prescribed strong opioids with 50.5% (477/944) of patients across both audit cycles reporting symptoms of being constipated. The prevalence of OIC did not differ significantly between the two audit cycles (cycle 1, 52.4% cycle 2, 46.7%). For patients audited in both cycles, OIC affecting quality of life or pain management occurred in 20.8% (196/944) of patients. The prevalence of OIC differed between the different methods of assessing constipation. It was lowest, when based only on stool frequency (11.2%) and highest when assessed with the Bowel Function Index (43.1%).

There was a marked difference in the presence of OIC as reported by patients and GPs. Half of patients reported symptoms of OIC, but GPs believed that only 22.8% of their patients were currently constipated. There was a trend for improved GP awareness of OIC in cycle 2, with a higher level of agreement between GP and patient reporting of current constipation, increasing from 61% in cycle 1 to 67% in cycle 2 (P=0.075).

To investigate any dose relationship for OIC, the oral morphine equivalent dose per day was calculated [14] and opioids were grouped as being low (≤ 40 mg/day), medium (41-100 mg/day) or high dose (>100 mg/day). There was no dose relationship with respect to OIC as the prevalence of OIC was 52.9% amongst patients taking low doses compared to 51.5% for high doses (P=0.744). There was potentially a relationship between opioid dose and problematic OIC (impacting quality of life or pain management) (Figure 2).

The use of opioid antagonists and laxatives increased significantly from cycle 1 to cycle 2 (16.9% to 24.8%, P=0.004; and 42.9% to 50.0%, P=0.041 respectively). The majority of patients taking laxatives where using them regularly (every day or second day). The three most commonly used laxatives were osmotic laxatives (16.5%), the combination of a stool softener plus a stimulant laxative (7.7%) and bulk-forming agents (7.4%). The laxative used was most commonly

that recommended by their GP; 69.1% in cycle 1 increasing to 78.0% in cycle 2 (P=0.048). 47.2% of patients were very or completely satisfied with their laxatives, whilst 12.8% patients were not satisfied or only a little satisfied.

Discussion

The GP assessment and management of OIC improved as result of participating in this clinical audit. The greatest improvements were observed for the co-prescribing a therapy to manage OIC (opioid antagonist or laxative) at the time of opioid initiation and for increasing the frequency of the assessment of OIC. Despite these improvements, there is need for increased focus on the proactive management of OIC as this occurred in less than half of patients audited in cycle 2, whilst best practice recommends that OIC is anticipated and proactively managed in all patients [9,10,15].

In this Australian GP patient population with CNCP, OIC was very common occurring in 50.5% of patients. GPs underestimated the prevalence of OIC, only identifying 22.8% of patients as being currently constipated. Specific reasons for this underestimation cannot be directly elucidated from the audit; however constipation is a subjective experience [2] and if its assessment is limited to objective measures, such as stool frequency, then many patients with constipation may not be identified. Many patients may not discuss constipation with their GP or under-report their symptoms due to embarrassment or a lack of awareness that OIC may result in adverse clinical outcomes. Taking a history of constipation and regularly asking about OIC are essential steps to overcoming this clinical barrier [16]. Even though this audit focused on OIC associated with the use of strong opioids, GPs need to apply the same principles to patient's prescribed weak opioids in particular codeine due to its high propensity to cause constipation.

The audit used a combination of objective and subjective measures to evaluate constipation [2]. This included gathering information about the frequency of bowel movements, stool consistency and color, concomitant symptoms, diet and fluid intake and medication use, including laxatives [17]. Asking patients the questions from the validated Bowel Function Index [18] identified the presence of constipation in more patients than via stool frequency or the Bristol Stool Scale. Hence, GPs should consider routinely asking all patients

Figure 2: Relationship between opioid dose and constipation.
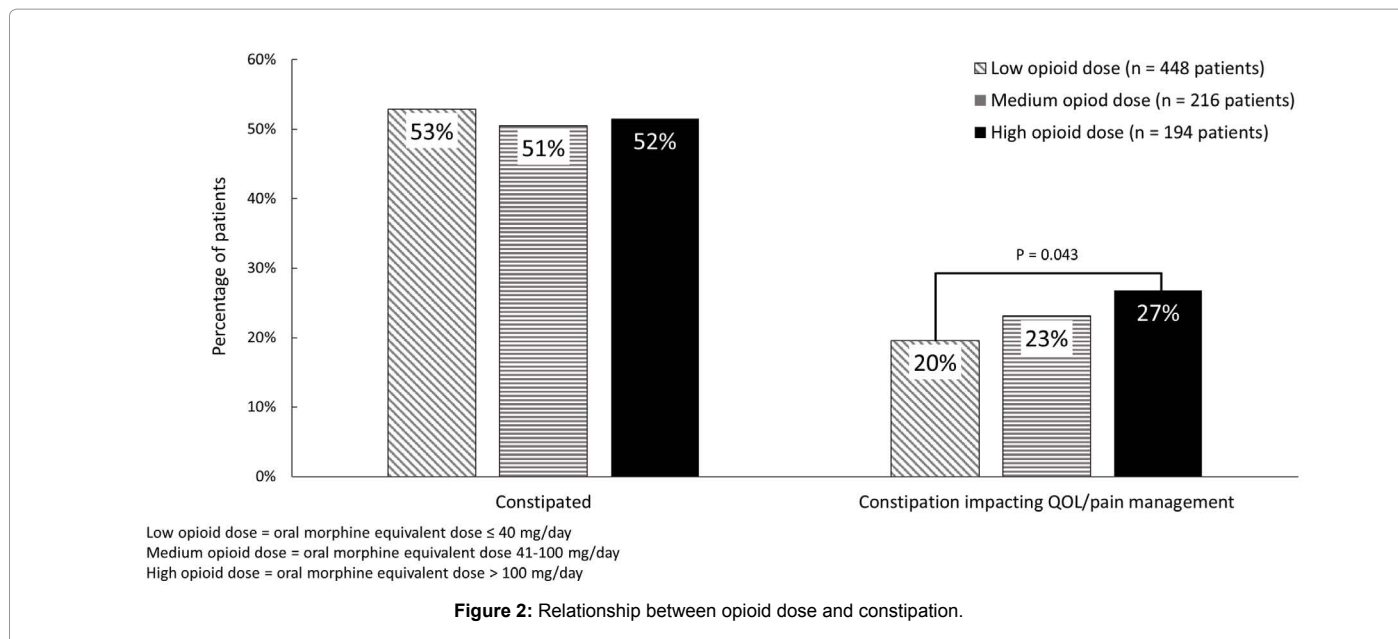
taking opioids about the ease or difficulty of defaecation, feelings of incomplete bowel evacuation and the patient's personal judgement of constipation.

One in five patients had OIC which was significantly affecting their quality of life and/or pain management. This is concerning, as these patients were receiving standard care yet many were suffering from a manageable side effect. This level of interference is lower than has been reported in other surveys [3].

Management options for OIC include life style measures, the use of laxatives, the co-administration of locally acting (enteric) opioid antagonists and opioid rotation [19]. All patients should be advised of life style measures (adequate fluids, fibre, exercise), however these measures alone are rarely effective to relieve OIC [10]. Laxatives have traditionally been used first line, but they often provide suboptimal relief, with 50% of patients failing to achieve a satisfactory response [10,19,20]. Reducing the opioid dose is not an effective strategy as the dose required to induce OIC is often less than that required for adequate analgesia [19]. In addition, as demonstrated in this audit, OIC was just as common in patients taking low or high opioid doses. Rotation to an opioid that is potentially less constipating is an appealing management strategy. However in this audit, there were no clear differences in the propensity of individual opioids to cause OIC, including transdermal opioids. The use of locally acting opioid antagonists, such as the combination of modified-release oxycodone/naloxone is an effective method of reducing the incidence and burden of OIC [21-23].

The main limitation of this research is in the nature of a clinical audit. It took two snapshots of clinical management and even though GP performance improved, it's unknown if this translated into improved patient outcomes. Similarly the longevity of the improved clinical practice is unknown.

Conclusions

OIC is common affecting 1 in 2 Australian patients prescribed strong opioids. GPs failed to recognize OIC in a third of their patients. GPs need to regularly ask all patients taking opioid analgesics about the presence of constipation. Questioning should include both objective measures, e.g. stool frequency, and subjective measures e.g. ease of defaecation, feelings of incomplete bowel movements and the patient's personal judgement of constipation.

OIC needs to be proactively managed from the time of opioid initiation and for the duration of opioid therapy. To paraphrase an old aphorism, 'the hand that writes the opioid, should simultaneously write the treatment for OIC'.

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