

## Oxycodone – An Audit of its Prescription in a Local Hospital

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### Abstract

**Aim:** This study aims to evaluate the prescription patterns and side effects of oxycodone in a local hospital setting. **Materials and Methods:** This is a retrospective analysis of all patients who were prescribed oxycodone for acute or chronic pain from June to November 2007. Patients' names were obtained from the hospital pharmacy and data were collected with a set of questionnaire after review of their casenotes. Prescription was compared with other recommended opioid prescription guidelines. Side effects to oxycodone use were documented. **Results:** One hundred and thirty patients were prescribed oxycodone for the 6-month study period. Prescription by the orthopaedic surgeons was the highest, followed by the pain service. Most patients had a clear indication for use of oxycodone and appropriate dosing regimes. However, two thirds of the patients prescribed oxycodone were not reviewed with regard to their analgesia within 24 hours and one third did not have titration of the drug to their pain symptoms. Majority of the patients had outpatient follow-up within 4 weeks of discharge. Common side effects included nausea, vomiting and constipation. **Conclusion:** This is the first local audit that profiles oxycodone prescription patterns and its side effects. Prescription of oxycodone was appropriate for the majority of the study population. Patient assessment upon initiation of oxycodone therapy and titration of the drug to patients' pain symptoms was suboptimal. Oxycodone was well tolerated by the study population with minimal side effects. Further quality measures and ongoing education of clinicians will ensure future patients obtain safe and effective analgesia.

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**Key words:** Opioid prescription, Pain

### Introduction

Oral opioids have been increasingly used for treatment of both cancer and non-cancer pain.<sup>1-4</sup> Oxycodone is a synthetic opioid that has become recently available locally. Elsewhere in the world, its widespread use has been associated with dependence and problematic drug related behaviour.<sup>5-8</sup> Appropriate prescription will be essential to avert a similar outcome locally. Apart from a previous audit of morphine use in a hospice here in 2001,<sup>9</sup> we believe this is the second local audit of opioid prescription and first audit of oxycodone prescription for our patients. Results of this study will be a strong catalyst for future quality measures regarding oxycodone use.

Oxycodone has been effectively used for treatment of moderate to severe pain.<sup>10,11</sup> It is a synthetic opioid with mu-agonist and mild kappa-agonist properties, has a higher bioavailability compared with other oral opioids, and is almost twice as potent as morphine. This is available as

immediate-release oxycodone (OxyNorm<sup>®</sup>) and controlled-release oxycodone (OxyContin<sup>®</sup>).

### Materials and Methods

This retrospective audit was conducted in a 790-bedded multi-disciplinary local hospital with all major subspecialties except cardiothoracic, obstetrics and paediatrics. The study was carried out for patients who were prescribed oxycodone from June to November 2007. As oxycodone is a prescription drug under regulatory control, the hospital pharmacy keeps a list of patients who have been administered the opioid.

Approval by the hospital ethics committee was waived in view of the nature of our study. A literature search was performed in databases including Medline for international guidelines on opioid prescription. There were no specific ones found for oxycodone. Based on management strategies developed by the Australian Pain Society,<sup>1</sup> as well as consensus statements from the American Academy of Pain Medicine, American Pain Society<sup>12,13</sup> and the Canadian

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Pain Society,<sup>14</sup> pain consultants in the hospital drew up prescription statements on the use of oxycodone for acute and chronic pain. These were approved by the hospital Pharmacy and Therapeutics Committee in November 2006 and made available to all physicians in the hospital. A summary of the statements is shown in Figure 1.

Based on these statements, data extraction forms were formulated. Separate forms were used for acute and chronic pain. Patients' case files were reviewed, and data extracted by the pain service team. The information was then recorded onto a computer database. Data were analysed using SPSS.

**Results**

One hundred and thirty patients were prescribed oxycodone for the 6-month period from June to November 2007. Among these patients, 74 (56.9%) patients were treated for acute pain, and 56 (43.1%) patients had chronic pain, of whom 53 (94.6%) suffered from non-cancer pain and 3 (5.4%) suffered from cancer pain. For purposes of our clinical audit, chronic pain is defined as pain lasting for more than 3 months duration. Most had moderate to severe pain scores (91.9% of all patients).

The usage of the immediate and prolonged release formulations were different for acute and chronic pain

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1. Oxycodone is indicated for moderate to severe pain.
  2. The only route of administration available locally is oral. The initial regime prescribed should be the lowest available dose, e.g. oxycodone immediate release 5 mg 4 hourly prn, oxycodone controlled release 10 mg bd, etc.
  3. When prescribing oxycodone, start with a fixed dose of oxycodone controlled release given 12 hourly. Always leave instructions for treatment of breakthrough pain, e.g. oxycodone immediate release 5 mg 4 hourly prn.
  4. Oxycodone should be prescribed for a limited duration with clearly defined goals for treatment.
  5. Oxycodone should only be prescribed by 1 doctor, or one team of doctors.
  6. Dose modification should be considered in elderly patients, patients with significant pulmonary disease, organ dysfunction, and patients who are taking other sedating drugs concomitantly.
  7. Patients should be reviewed within 24 hours of starting therapy, aim to titrate the oxycodone dose so that the mean number of breakthrough pain episodes is  $\leq 2$  per day.
  8. Patients with acute pain may be prescribed a short course (<2 weeks) of oxycodone, but those with chronic pain may need a longer course. Patients should ideally be reviewed within 4 weeks upon discharge for their pain control.
  9. Laxatives should be prescribed together with oxycodone to prevent constipation.
  10. Antiemetics should be prescribed as needed
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Fig. 1. Oxycodone prescription statements.

patients. For chronic pain patients, all had immediate-release oxycodone, and 62.5% had controlled-release oxycodone. As for acute pain patients, 83.8% had immediate-release oxycodone, 54.1% had controlled-release oxycodone. As anticipated, a greater proportion of chronic pain patients had prolonged release formulation compared with acute pain patients.

The demographics of the patients are shown in Table 1.

Oxycodone is most commonly prescribed by the Orthopaedic surgeons, accounting for 56 out of 74 (75.7%) acute pain patients and 33 out of 56 (58.9%) chronic pain patients. The pain physicians came second, accounting for 9 (12.2%) acute pain patients and 16 (28.6%) chronic pain patients (Figs. 2 and 3).

Of the 74 patients who had acute pain, 73 (98.6%) had an established diagnosis for pain and 70 (94.6%) had a clear indication for starting oxycodone. This is defined by moderate to severe pain, failed pharmacotherapy (including weak opioids like tramadol and codeine), or pain despite intervention or physiotherapy. Of the 56 patients with chronic pain, 55 (98.2%) had an established diagnosis for

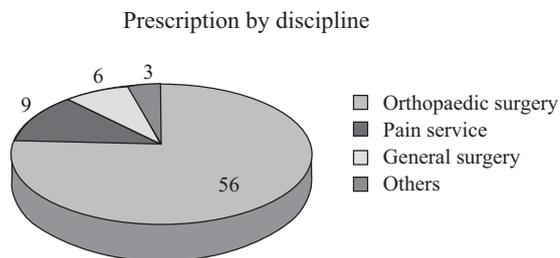


Fig. 2. Oxycodone prescription for acute pain patients. (The numbers in the pie chart reflects the number of acute pain patients prescribed oxycodone)

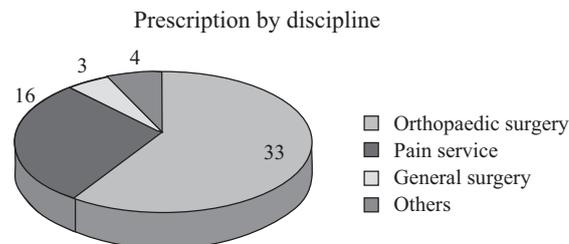


Fig. 3. Oxycodone prescription for chronic pain patients. (The numbers in the pie chart reflects the number of chronic pain patients prescribed oxycodone.)

Table 1. Patient Demographics

	Acute pain (n = 74)	Chronic pain (n = 56)
Age (range), y	51.6 (18 to 93)	52.8 (19 to 95)
Gender		
Male	39 (52.7%)	30 (53.6%)
Female	35 (47.3%)	26 (46.4%)
Race		
Chinese	47 (63.5%)	35 (62.5%)
Malay	10 (13.5%)	10 (17.8%)
Indian	4 (5.4%)	8 (14.3%)
Others	13 (17.6%)	3 (5.4%)
Pre-existing liver/renal impairment	2 (2.7%)	0 (0%)

Table 2. Indications for Starting Oxycodone

	Acute pain (n = 74)	Chronic pain (n = 56)
No clear indication for oxycodone therapy	4 (5.4%)	3 (5.4%)
Oxycodone therapy indicated:		
1. Moderate to severe pain	70 (94.6%)	53 (94.6%)
2. Failed non opioid therapy	68 (91.9%)	51 (91.1%)
3. Pain despite intervention or physiotherapy	38 (51.4%) 46 (62.2%)	33 (58.9%) 41 (73.2%)

pain. Fifty-three out of 56 (94.6%) chronic pain patients had a clear indication for starting oxycodone therapy. Among the 3 patients who did not have a clear indication for oxycodone prescription, 1 suffered from cancer pain and 2 had non-cancer pain (Table 2).

Patients with chronic pain had more psychological issues than those with acute pain. Nine out of 74 (12.2%) patients with acute pain had psychological issues, as compared with 12 out of 56 (21.4%) patients with chronic pain. All were under review by a psychiatrist. Psychological issues were defined as past or ongoing substance abuse, presence of psychiatric illnesses such as depression, anxiety, or schizophrenia (Table 3). One chronic pain patient had a history of heroin abuse.

All acute pain patients had only 1 doctor or a team of doctors handling the opioid prescription. However, there were 9 patients (16.1%) within the chronic pain group who had 2 or more different doctors prescribing them with oxycodone. Generally most patients had only 1 type of opioid prescribed at any point in time (95.9% of acute pain patients, 96.4% of chronic pain patients). The lowest possible dose was started for all acute pain patients, and

Table 3. Psychological Issues in Patients Prescribed Oxycodone

	Acute pain (n = 74)	Chronic pain (n = 56)
Substance abuse	0 (0%)	1 (1.8%)
Anxiety/Depression	9 (12.2%)	12 (21.4%)
Schizophrenia	0 (0%)	1 (1.8%)

Table 4. Side Effects to Oxycodone Therapy

	Acute pain (n = 74)	Chronic pain (n = 56)
Nausea and vomiting	3 (4.1%)	3 (5.4%)
Constipation	4 (5.4%)	0 (0%)
Sedation	0 (0%)	1 (1.8%)

96.4% of chronic pain patients.

An appropriate interval of dosing (at least 2 to 4 hourly for immediate-release oxycodone, 12 hourly for controlled-release oxycodone) was noted in 69 (93.2%) patients with acute pain, and 48 (85.7%) patients with chronic pain. Dosing interval was adjusted for elderly patients, patients with significant cardiorespiratory comorbidities, liver or renal impairment and those with other central nervous system depressant drugs on board.

Only 48 (64.9%) acute pain patients were reviewed within 24 hours after prescription of oxycodone. Thirty-eight (67.9%) chronic pain patients were reviewed within 24 hours. These were all inpatients prescribed oxycodone during admission. Fewer inpatients had the opioid titrated to their pain symptoms over the next 24 to 48 hours (29.7% of acute pain patients and 39.3% of chronic pain patients), reflecting a less than ideal pain management strategy.

The number of acute pain patients requiring oxycodone for more than 2 weeks is 28 out of 74 (37.8%), all the chronic pain patients were prescribed oxycodone for more than 2 weeks. Majority were reviewed as outpatients within 4 weeks upon discharge: 71 (95.9%) patients with acute pain and 47 (83.9%) patients with chronic pain. This is an arbitrary time frame that the authors think is reasonable to reassess the patient within the practical constraints of the outpatient clinic setting.

If prescription exceeded 2 weeks, evidence of weaning before termination was seen in 53 (71.6%) patients with acute pain. Weaning was not applied to chronic pain patients due to the short duration of review as part of the methodology of this audit. A high rate of eventual follow-up was observed. Seventy-two (97.3%) patients with acute pain and 55 (98.2%) patients with chronic pain returned for outpatient review.

The common side effects experienced were nausea, vomiting and constipation. None of the affected patients were prescribed anti-emetics or laxatives initially. One patient suffered from sedation. Half (51.4%) of the acute pain patients and two thirds (69.6%) of the chronic pain patients had laxatives prescribed with oxycodone. Table 4 lists out the side effects to oxycodone therapy. There were no other significant side effects than those mentioned above.

## Discussion

It has become increasingly acceptable for patients with chronic non-malignant pain to be treated with opioids. Up to two thirds of oxycodone prescriptions for chronic pain in this audit came from disciplines other than the pain service, reflecting a greater awareness among non-pain specialists on the use of opioids for chronic non-malignant pain.

We chose to audit oxycodone because it is a relatively new opioid available locally and our hospital prescription statements were designed exclusively for this medication. With the introduction of longer acting opioids and greater physician willingness to use them, opioid prescription has increased exponentially in the United States and other parts of the world. Oxycodone has become arguably the most abused prescription opioid in the United States.<sup>6</sup> We hope that this audit will serve as a timely reminder for appropriate prescription of this drug.

Previous audits had utilised general guidelines to assess opioid prescribing.<sup>11,15</sup> As there are no specific guidelines for oxycodone prescription to the best of our knowledge, our hospital prescription statements were used for purposes of the audit.

Majority (94.6%) of our chronic pain patients were being treated for non-cancer pain. The small percentage of cancer patients in our sample population can be explained by the paucity of oncology and palliative care units in our hospital rendering them to be transferred to other tertiary cancer centres.

There were a number of acute pain patients who required therapy with controlled-release oxycodone. Due to the retrospective nature of the audit, it was difficult to glean the exact reasons for choice of the prolonged formulation. Depending on the nature of the pain, some patients may need prolonged release formulation even for the treatment of acute pain. Controlled-release oxycodone has been shown to be efficacious in treatment of both acute pain (e.g. postoperative pain and visceral pain) and chronic pain.<sup>11</sup>

Proper prescription and clearly defined goals of treatment will lead to better analgesia and patient satisfaction with an improved side effect profile. Ideally, oxycodone should be prescribed to responsible patients, with no history of substance abuse or psychiatric disorder, have

a well-defined basis for pain and failed other modes of pharmacotherapy or interventional therapy despite drug compliance. Of the sample population, 5.4% did not have a clear indication for initiation of opioid therapy. Amongst them, 4 suffered from acute pain and 3 from chronic pain. This is undesirable practice because the risks of opioid prescription may outweigh its benefits. As there are no external figures for comparison, this result can serve as a baseline for future audits to monitor for indiscriminate opioid prescription, particularly for chronic non-malignant pain. Ongoing physician education is important to avoid opioid prescription and dependence in patients whom such therapy is unwarranted.

Patient selection is important to decrease the likelihood of problematic drug-related behaviour. Only 1 patient in the chronic pain group had history of substance abuse. 12.2% of the patients with acute pain and 21.4% of the patients with chronic pain had a background history of anxiety or depression. One chronic pain patient had schizophrenia. All these patients were on appropriate psychiatric follow-up. The low incidence of psychological issues may be attributed to the fact that as majority of the chronic pain patients were prescribed oxycodone by non-pain physicians, attendance to psychological issues may not have been the primary priority.

Patients should only have 1 dedicated physician prescribing their opioids. However, 16.1% of chronic pain patients had more than 1 doctor/team of doctors prescribing opioids at any one time, which can potentially increase the risk of opioid overdose and abuse. This may be secondary to poor communication among attending physicians as well as a lack of monitoring system from the hospital pharmacy when this audit was conducted. With the recent implementation of electronic drug prescription, the pharmacy may now be able to flag out patients who are receiving opioids from more than one physician. Dose adjustments were made for patients with organ dysfunction and those on concomitant sedative drugs. We recommend that all complicated cases should receive more attention and multi-disciplinary co-management with the pain service so as to improve their analgesic therapy.

Only two thirds of patients were reviewed within 24 hours after starting on oxycodone and one third of the patients had titration of oxycodone to their pain symptoms, revealing a great shortcoming in our prescription practice. This could be due to titration of opioid therapy having a low priority in the daily medical management, lack of knowledge in pain assessment by attending physicians or poor documentation. Further physician education on pain assessment and management is recommended, particularly for physicians who have just joined the hospital. Most patients were reviewed within 4 weeks of discharge from hospital. Regular reviews and clearly defined goals for

treatment, e.g. improvement in pain scores or level of function, will help to achieve better patient satisfaction and reduction of unwanted side effects. Patients who were discharged with a short course (<2 weeks) of oxycodone may also benefit from an early outpatient review in case pain persists.

Nausea, vomiting and constipation were common side effects. The low incidence of side effects could be explained by a cautious dosing regime – utilisation of the lowest possible dose and appropriate dosing interval. However, it is also likely that this is due to under reporting by patients and/or under recording by physicians when these side effects were not actively sought for in a retrospective study such as this. Although side effects were experienced by only a handful of patients, they could be improved if patients were more judiciously prescribed anti-emetics and laxatives. For high-risk patients, a lower starting dose should be considered and the opioid titrated upwards in small increments.

There are certain limitations in our audit. As this is a retrospective review, it is difficult to assess the reasons why certain acute pain patients required strong opioid treatment for more than 2 weeks. Our study was not designed to assess the efficacy of opioid therapy, which would be interesting especially in the group of chronic pain patients being treated for non-cancer pain. We also did not examine fully the interaction between oxycodone, its adverse effects and functional recovery of our patients. For future quality measures, it is anticipated that improvements can be made after taking into account the above considerations.

## Conclusion

This audit shows that prescription was sub-optimal in our hospital compared with pre-existing opioid prescription guidelines. Adherence to single physician prescription, a multi-disciplinary approach to pain management and prompt review of patients given strong opioids will help improve current prescription practices. From this audit, quality measures that are recommended include physician education to reinforce strict adherence to prescribing guidelines, improved communication among attending physicians and involvement of hospital pharmacy to monitor errant

prescriptions. The results here can serve as a baseline for subsequent audits to ensure that future patients receive safe and satisfactory analgesia.

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