CMRO

Current Medical Research & Opinion Vol. 27, No. 12, 2011, 2357–2360

0300-7995
doi:10.1185/03007995.2011.635197

Article ST-0328.R1/635197

Brief report

Outcome of opioid switching 4 weeks after discharge from a palliative care unit

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Key words:
Cancer pain – Long-term therapy – Opioid switching

Accepted: 21 October 2011; published online: 3 November 2011
Citation: Curr Med Res Opin 2011; 27:2357–2360

Abstract

Despite the favorable effects reported with opioid switching performed in a specialized unit in the short term, data on long-term basis are poor, particularly after discharging patients home or in other settings.

Research design and methods:
The aim of this prospective study was to evaluate the long-term outcome of patients who were switched in an acute palliative care unit at a high volume of opioid switching. A consecutive sample of patients who underwent opioid substitution during admission in an acute palliative care unit were assessed for a period of 1 year. Patients were followed-up for 4 weeks after being discharged. Patients were contacted by phone or visited at the outpatient clinic 4 weeks after discharge. Epidemiological data, pain mechanisms, reason for switching, number of opioid substitutions during admission, drugs, doses and routes of administration, opioid treatment at discharge, pain intensity, distress score (DS) calculated as a sum of symptom intensity, were recorded after 2 weeks (T2) and 4 weeks (T4).

A total of 76 patients underwent an opioid substitution in the period taken into consideration. Seventeen patients were excluded as they died in the unit or underwent an alternative procedure after unsuccessful opioid trials. A total of 50 patients were consecutively assessed and discharged after performing an opioid switching. The mean age was 63 (±11) years, and 29 were males. Of the 31 patients, 29 patients were switched during admission once and twice or more, respectively. In all, 32 patients had a complete assessment at T2 and T4. In 13 patients the switching was definitive, as they maintained the same drug and the same dose. Other patients required the same changes to opioid therapy, including doses and drugs. Only a minority of patients worsened their pain and/or symptom control in the subsequent assessments after discharge.

Conclusions:
Opioid switching performed in acute pain relief and palliative care is an effective method of improving the balance between analgesia and adverse effects, even for prolonged periods of time, following discharge to another setting of care. However, for different reasons, some of patients may lose this benefit. Additional studies using different models of care should be performed in order to gather further information about the long-term outcome of opioid switching.

Introduction

The majority of patients with cancer pain can be adequately treated with oral analgesics usually provided 'around the clock' with rescue doses for breakthrough pain. Nevertheless, some patients develop uncontrolled adverse effects, including generalized myoclonus, delirium, nausea and vomiting, or encounter severe sedation before achieving adequate analgesia during dose titration. In other patients dose escalation of one opioid may provide poor clinical benefit. The substitution of another opioid for a previous one in order to obtain a more favorable clinical response has largely been reported as opioid switching[1].

Sequential therapeutic trials with different opioids have been claimed to improve the balance between analgesia and adverse effects in difficult pain conditions. Opioid switching is going to be a popular approach, although data on the use of this practice are poor and difficult to determine and controlled studies are a difficult to undertake in this setting[2]. According to available data, opioid switching will result in clinical improvement in 50–80% of patients with cancer pain who present with a poor response to one opioid[1]. Despite the favorable effects reported with opioid switching performed in a specialized unit in the short term[3], data on longer-term results are poor, particularly after discharging patients home or other settings. The aim of this prospective study was to evaluate the long-term outcome of patients who were switched in an acute palliative care unit at a high volume of opioid switching.

Patients and methods

A consecutive sample of patients who underwent opioid substitution successfully during admission in an acute palliative care unit were assessed for a period of 1 year.

Informed consent and institutional approval were obtained. Opioid switching was performed according to local protocols described elsewhere[3].

Patients were followed up for 4 weeks after being discharged. Patients who died in the unit after switching or patients who underwent alternative procedures because of an unsuccessful switching, were excluded. After discharge, patients were contacted by phone or visited at the outpatient clinic at 1-week intervals for 4 weeks to gather information about the clinical situation and to offer eventual changes in the treatment according to the clinical condition.

The following data were recorded: epidemiological data, pain mechanisms, reason for switching, number of opioid substitutions during admission, drugs, doses and routes of administration, opioid treatment at discharge, pain intensity (numerical scale 0–10), opioid-related symptoms, including nausea and vomiting, drowsiness, confusion, and constipation by using a scale from 0 to 3 (absent, slight, moderate, severe). A distress score (DS) was calculated as a sum of symptom intensity. Although never validated, this score has been previously used in different studies for determining the 'weight' of adverse effects. The aim of using a sum of intensities is justified by the high variability of symptom intensity in individual patients. This score is able to determine a general improvement of symptoms. The evaluation of the changes in intensity of a single symptom, different for each patient, makes a global evaluation and statistics for a group of patients practically impossible. Moreover, it is not unusual to switch a patient for more than one symptom. Changes in DS have been already used to assess outcome of switching. On the other hand an important decrease in the principal symptom which required the switching is another parameter to take into consideration. Thus, these parameters have been used to assess opioid switching[3]. Symptoms were assessed by the patient, whenever possible. However, patients who had severe cognitive failure, a proxy evaluation was taken into account. Daily doses of opioids, pain and DS were recorded at discharge (T0) and after 2 weeks (T2) and 4 weeks (T4).

Descriptive statistics were used to summarize the data. Data were collected and analyzed by SPSS Software 14.0 version (SPSS, Inc., Chicago, IL, USA). Statistical analysis of quantitative and qualitative data, included descriptive statistics, was performed for all the items. Frequency analysis was performed with Pearson's chi-square test. The paired Wilcoxon signed-rank test was used to compare pain intensity scores and symptom intensity scores over weekly periods. All *p*-values were two-sided and *p*-values less than 0.05 were considered to indicate statistical significance.

Results

A total of 67 patients underwent an opioid substitution in the period taken into consideration. In all, 17patients were excluded as they died in the unit or underwent alternative procedure after unsuccessful opioid trials. A total of 50 patients were consecutively assessed and discharged after opioid switching had been performed. In all, 14 patients were switched for adverse effects, 17 patients for uncontrolled pain,17 for both, and two for convenience.

The mean age was 63 (±11) years, and 29 were males. Primary diagnosis was in a rank order: lung (16), genitourinary (13), gastrointestinal (7), breast (6), other (8). The median Karnofsky status of patients who were discharged after a successful opioid switching was 40 (range 30–70).

A total of 31 and 29 patients were switched during admission once and twice or more, respectively. The majority of patients (29) were finally switched to methadone (two of them to intravenous methadone).

Thirteen patients were not evaluated because they died before T2, were receiving low doses of opioids (less than 60 mg of oral morphine equivalents), discontinued opioid treatment, or were lost in follow-up. Five patients died or were lost in follow-up between T2 and T4, and could not be assessed at T4. One of these patients, who was receiving 130 mg/day of intravenous methadone, was transferred to a hospice, where he was switched to oral oxycodone because of unavailability of intravenous methadone. One patient was discharged on transdermal fentanyl 0.6 mg/day. The same dose was maintained successfully at T2. The patient was then lost in follow-up. One patient was discharged on hydromorphone 16 mg/day, maintaining the same dose successfully at T2 and died before T4. One patient was

discharged on oral methadone 60 mg/day. At T2 he was receiving methadone 45 mg and hydromorphone 16 mg/day and died before T4. Finally, one patient was discharged on methadone 12 mg/day, maintaining the same dose at T2, and died before T4.

A total of 32 patients had a complete assessment at T2 and T4. Data regarding this group of patients are presented in Table 1. In 13 patients the switching was definitive, as they maintained the same drug and the same dose. Other patients required the same changes to opioid therapy, including doses and drugs. Pain intensity, DS, and number of patients whose pain was not considered effectively controlled, at T0, T2, and T4, are presented in Table 2. A minority of patients had their pain uncontrolled in the subsequent assessments after discharge. However, a significant change in pain intensity and DS was observed at T2 and T4.

Discussion

Although evidence for the efficacy of opioid switching is lacking, this practice may be useful in cancer patients with an unacceptable balance between analgesia and adverse effects[2]. Opioid switching may occur more frequently in an acute palliative care unit, possibly because of the more selective population with relevant clinical problems, particularly uncontrolled pain, or high doses of opioids. Moreover, since it is well-recognized that drug tolerance represents the most frequent cause of opioid escalation and sometime of opioid hyperalgesia, opioid switching may be considered as an efficacious way of preventing these phenomena during opioid therapy of chronic cancer pain. It has been reported that opioid switching rate may be as high as 34% of patients admitted for pain control[3]. While opioid switching may improve the balance between analgesia and adverse effects in most cases and patients can be discharged in a relative state of stabilization, the duration of such a condition may be short-lived or unstable, particularly when patients are then followed-up in other settings. This study showed that opioid switching maintains its efficacy after patients' discharge. Most patients reported an adequate pain control and a large proportion of them remained stable for 4 weeks, maintaining the same drug and the some dose. However, about one-half of patients may require further assessment, as they may need to change the dose, or in a minority of cases to switch to another drug. Moreover a trend in the increase of pain intensity and DS was observed. Regrettably, some patients lost their pain control, although the reasons for this – for example inadequate treatment or loss of responsiveness – are unclear. Of interest, the decision to change opioid therapy has multiple influences, based on the care setting following patient discharge from the acute palliative care unit, including hospice care, GP care, home palliative care program, or poor family compliance, independently of phone advice or visits from the original hospital team.

Data about the long-term outcome of opioid switching performed in hospital are virtually non-existent, and data on switching performed at home did not provided such information. In a pharmacoepidemiological study from a national Norwegian prescription database of 168 cancer patients who were switched to methadone, 22% of patients received prescriptions of other opioids and more than 75% received subsequent dispensed prescriptions of methadone. This suggests that a large proportion of cancer patients experience a lasting benefit from switching to methadone. The study also reported that many treatment options had not been exhausted prior to the switch to methadone[4]. One retrospective study provided information on a long-term period after opioid switching and was performed in an outpatient setting. Switching to methadone was considered effective in about 85% of patients at either the first follow-up visit (on average 13 days after switching) and the

Table 1. Number of patients who maintained the same opioid and the same doses or required changes in therapy between T0 and T2, T2 and T4, and between T0 and T4.

	T0–T2	T2–T4	T0–T4
Maintaining the same dose	16	19	13
Increasing the dose	5	7	8
Decreasing the dose	8	1	4
Switch to another opioid	3	4	7
Adding another opioid		1	1*

*One patient had a dose increment and another opioid was added at T4(n.4).

Table 2. Mean pain intensity and distress score (DS) in patients with assessments at T0, T2 and T4. No. of patients with a NRS of 0–5 versus 6–10.

	T0	T2	T4	*p*-value
Pain intensity (mean ± SD)	2.6 (1.6)	3.7 (1.9)	3.6 (2.4)	0.007 T2 vs. T0* 0.025 T4 vs. T0*
DS (mean ± SD)	5.2 (2.5)	7.4 (4.8)	7.4 (3.4)	0.007 T2 vs. T0* 0.002 T4 vs. T0*
No. of patients with pain 0–5/6–10	32/0	28/4	25/7	0.022†

*Paired Wilcoxon signed-rank test.
†Pearson's chi-square test.

second follow-up visit (on average 28 days after switching). One month after switching, 84% of patients continued receiving methadone. Doses of methadone were low, ranging from 18 to 20 mg/day[5]. Moreover, this group of ambulatory patients was presumably seen at an early stage of disease, giving the low rate of deaths in the period considered, which was different from the overall population examined in this study.

The principal limitations of this study were the short survival of patients and the assessment performed in a setting where the responsibility of the subsequent treatment may reside with other people, including GP, hospice, or home palliative care program, despite continuous phone contact by a hospital team. Of interest, half of patients were coming from distant provinces. In some cases availability of drugs may be limited in these situations. Finally, relatives may have played a negative role because of cultural attitudes. Thus, the choice of the subsequent treatment depends on several variables. These problems were expected and are probably insurmountable, reflecting the reality of what happens in this category of patient. Thus, a more strict collaboration is advisable to provide the best care for advanced cancer patients who move from a specialized setting to another. Nevertheless the treatment was effectively long-lasting in the majority of patients

In conclusion, opioid switching performed in an acute pain relief and palliative care is an effective method of improving the balance between analgesia and adverse effects, even for prolonged periods of time, after being discharged to another setting of care. However, for a variety of different reasons, some of them may lose this benefit. More studies using different models of care should be performed to gather further information about the long-term outcome of opioid switching.

Transparency

Declaration of funding
S.M. declares no conflict of interest and has received no payment in preparation of this manuscript.

Declaration of financial/other relationships
The peer reviewers on this manuscript have disclosed that they have no relevant financial relationships.

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