Brief Report

Opioid Switching in Patients With Advanced Cancer Followed at Home. A Retrospective Analysis

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Abstract

Context. Opioid switching has been found to improve opioid responsiveness in different conditions. However, data on opioid switching performed at home are almost nonexistent, despite the fact that most patients are followed at home.

Objectives. The aim of this retrospective survey was to determine frequency, indications, usefulness, and safety of opioid switching when treating advanced cancer-related pain in patients followed at home.

Methods. A retrospective review of data from patients with advanced cancer followed at home by three home care teams for a period of two years was performed. Patients who had their opioids switched were selected. Reasons for switching opioid doses and routes of administration and outcomes were collected.

Results. Two hundred one (17%) of 1141 patients receiving "strong" opioids were switched. The mean Karnofsky Performance Status score was 35.6, and the median survival was 30 days. The most frequent reason to switch was for convenience, and the most frequent switch was to parenteral morphine. In most patients, a better analgesic response was observed. Patients who were switched to parenteral morphine had a shorter survival in comparison with other opioid sequences ($P < 0.0005$). After switching, opioid doses were increased by 23% and 41%, after a week and at time of death, respectively.

Conclusion. Opioid switching was useful for most patients in the home environment, at least in less complex circumstances, when done by experienced home care teams. Prospective studies are needed to provide information about the decision to admit to hospital for this purpose and the predictive factors that may relatively contraindicate transportation to a facility in severely ill patients. J Pain Symptom Manage 2013;45:298–304.

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Cancer pain, opioid switching, home care

Introduction

Management of cancer pain is one of the most important goals of palliative care. Opioids are the mainstay of moderate-to-severe cancer pain management, and most patients favorably respond to opioid therapy.[1]

Patients with advanced cancer spend most of their time at home. The home setting has been reported to be preferred by most patients and relatives and seems to be the favored place of death.[2] In a large sample of patients, a managed home care system has been found to enable patients to receive adequate pain treatment in the comfort of their own homes. Pain control was unsuccessful in a minority of patients.[3]

However, relieving pain may be problematic in some cases, particularly in the home care setting, where some facilities are unavailable and assistance is less intensive than in a hospice or in palliative care units. Despite a preference for care at home, patients are mainly transferred to hospital because of an acute medical event, an uncontrolled symptom, such as pain, imminent death, or the inability to provide needed care safely at home.[4]

Patients with cancer often require escalating doses of opioids to control their pain or overcome the development of tolerance to opioids.[5] This can result in untoward effects. Opioid switching has been found to improve opioid responsiveness in different conditions. Experience has shown that a failure to respond to one opioid does not mean failure to respond to all opioids, and opioid switching may allow better pain control and also decrease adverse effects.[6–11] Moreover, in some circumstances, a change in the route of delivery and/or drug is dictated by other factors in the home care setting, including convenience, patient preference, or concomitant problems, such as inability to swallow, cognitive failure, and intestinal transit failure.[12]

Unfortunately, data on opioid switching performed at home are almost nonexistent. The Home Care—Italy group recently has been established, with the intent to disseminate and implement information on cancer patients followed at home, given the paucity of existing data in this setting. The objective of this retrospective study was to determine frequency, indications, usefulness, and safety of opioid switching in treating cancer-related pain in patients followed at home.

Methods

We reviewed the charts of patients who were followed by three home palliative care teams in Turin, Genoa, and L'Aquila, for a period of two years (2008–2009). These teams belong to a home care network and share similar protocols and intervention modalities.

Patients were included in the study if they were receiving "strong" opioids for chronic cancer pain and were switched to another opioid. Patients were excluded if they were receiving opioids for reasons other than pain. The reasons for switching were collected: uncontrolled pain, adverse effects, or both, or convenience (i.e., switched for other reasons in an acceptable clinical situation, e.g., problems with swallowing or patient request). Demographic data and Karnofsky Performance Status score at the time of switching were recorded, as well as opioid doses and their initial conversion ratio. Doses and ratios after one week also were recorded.

The following parameters were collected for the first switch (Switch 1): 1) previous opioid, route, and dose; 2) initial doses of the second opioid and route; 3) the dose and route of the second opioid one week after performing the switch; 4) the outcome, classified as: a) good response, considered as good pain control (<4/10 on a numerical scale) if patients were switched for poor analgesia and/or acceptable improvement of adverse effects if patients had been switched for this reason; b) partial response (all the intermediate situations between a and c); and c) poor response, uncontrolled pain or adverse effects, need to further switch or other alternatives; 5) opioid, route of administration, and dose at time of death; and 6) survival. The same data were collected for further opioid switches (e.g., Switches 2, 3, and so on).

Statistical Analysis

Data were collected and analyzed using SPSS Software v. 14.0 (SPSS, Inc., Chicago, IL). Statistical analysis of quantitative and qualitative data, including descriptive statistics, was performed for all the items. Frequency analysis was performed with the Chi-squared test. The paired samples Student's *t*-test was used to compare initial with final opioid conversion ratios. The one-way analysis of variance was used for parametric analysis. All *P*-values were two-sided, and *P*-values of less than 0.05 were considered to indicate statistical significance.

Results

A total of 1682 consecutive patients followed at home during a two-year period were surveyed; 1141 patients (67.8%) were receiving "strong" opioids for chronic cancer pain. No patient was receiving opioids for reasons other than pain (e.g., dyspnea). Two hundred one patients were switched to other opioids (17.6%) during home care.

One, two, or three opioid substitutions were made for 201, 15, and two patients, respectively. Descriptive data are presented in Table 1. No statistical differences were found in patients who were switched. The most frequent reason to switch was for convenience, with a large number of patients switched from oral opioids, such as oral morphine (OR MOR) and oral oxycodone (OR OXY), to parenteral morphine (PR MOR) (52 patients) because they were no longer able to take oral medications, particularly in the last days of life. Uncontrolled pain was the second most frequent reason to switch (66 patients for uncontrolled pain and 27 patients for uncontrolled pain and other reasons). Sixteen and 22 patients were switched for adverse effects only and for adverse effects and other reasons, respectively. In most patients, the outcome was good or partial, with a minority of patients who were considered poorly responsive to opioid switching (Tables 2–7).

The sequences of the first switch are shown in Tables 2–7. Patients switched to PR MOR had a shorter survival (median 15 days) in comparison with other sequences (oral hydromorphone, OR MOR, and OR OXY) ($P < 0.0005$). After switching, opioid doses were modified during the course of treatment, with mean ± SD dose increments of $23.3 \pm 38.1\%$ and $41.4 \pm 70.1\%$, after one week and at the time of death, respectively.

A minority of patients were switched again ($n = 15$), and two patients were switched a third time. The most frequent reason for a further switch was inability to swallow ($n = 10$), and PR MOR was the preferred choice ($n = 8$).

Discussion

This retrospective study showed that opioid switching performed in patients followed at home is feasible and often yields favorable outcomes. Although it was not possible to assess the adequacy of the treatment in some cases, given the retrospective nature of this study, only four patients who could be assessed did not respond positively to the change of opioid or route of administration.

The frequency of opioid switching was 17.6%. As expected, the switching rate was lower than that observed in acute palliative care units,

Table 1
Characteristics of Patients Who Were Receiving Opioids and Who Were Switched

	Number of Patients	Patients Receiving Opioids	Patients Who Were Switched
Total	1682	1141	201
Age	68	70	69
Gender (male)	902	601	116
Karnofsky score (mean)	40.5	38.5	35.6
Primary tumor			
Lung	404	306	53
Gastrointestinal	313	208	43
Urogenital	252	132	32
Breast	143	71	17
Pancreas	134	65	17
Liver	60	37	8
Other	376	322	31

Table 2
Patients Switched From TD FEN to Oral Opioids

$n = 39$	Dose of Previous Opioid (mg) (Mean [SD])	Initial Dose of Second Opioid (mg)	Initial Ratio	Dose at One Week of Second Opioid (mg)	Final Ratio After One Week	Dose at Death (mg)	Outcome
7	TD FEN 2.0 (1.2)	OR OXY 87 (51)	0.027 (0.015)	OR OXY 116 (78)	0.023 (0.016)	240 (0)	$A = 2$ $B = 4$ $C = 1$
8	TD FEN 1.1 (0.6)	OR MOR 106 (77)	0.013 (0.008)	OR MOR 106 (74)	0.012 (0.007)	151 (97)	$A = 8$
23	TD FEN 2.18 (1.28)	PR MOR 84 (56)	0.029 (0.010)	PR MOR 88 (61)	0.028 (0.010)	102 (75)	$A = 15$ $B = 2$ NA = 6
1	TD FEN 1.8 (0.0)	OR HYD 28 (0)	0.06 (0)	OR HYD 36 (0)	0.05 (0)	36 (0)	$B = 1$

TD FEN = transdermal fentanyl; OR OXY = oral oxycodone; A = good response; B = partial response; C = poor response; OR MOR = oral morphine; PR MOR = parenteral morphine; OR HYD = oral hydromorphone; NA = not available.

where stringent admission criteria more frequently require opioid switching.[1,12–16] In the home setting, it is likely that the decision to switch usually was dictated by the progressive worsening of the clinical situation, preventing oral administration of opioids, as suggested by the shorter survival in this group of patients.

Although patients had variable courses, many required an increase in the opioid dose at time of death, in comparison with the doses used for switching. The mean percentage increment was about 40%. This observation could be attributed to many factors, including metabolic derangement, increasing pain, the development of dyspnea, or psychological distress occurring at the end of life. This also is confirmed by the high rate of switching because of the inability to swallow.

The limited number of patients for each opioid sequence prevented further analysis regarding the relationship with the causes of opioid switching. Most patients were switched from the most common opioids used as first choice, including transdermal fentanyl, OR OXY, and OR MOR, reflecting the attitudes of the opioid market in the country.

Although there was not a precise initial conversion ratio "per protocol," given the retrospective nature of the study, the ratios initially used worked very well, although the doses often needed changing after one week. This highlights the use of a prudent initial conversion ratio, based on safety reasons in a setting like home care. The final conversion ratios were in line with previous studies performed in other settings.[12]

Many patients were switched for convenience rather than for improving analgesia or to address adverse effects, with a large number of patients switched from oral opioids, such as OR MOR and OR OXY, to PR MOR. It is notable that many patients were switched

Table 3
Patients Switched From OR OXY to Other Opioids

$n = 72$	Dose of Previous Opioid (mg) (Mean [SD])	Initial Dose of Second Opioid (mg)	Initial Ratio (Mean)	Dose at One Week of Second Opioid (mg)	Final Ratio After One Week	Dose at Death (mg)	Outcome
11	Dose OR OXY 63.6 (29.7)	TD FEN 1.0 (0.5)	68.9 (37.6)	0.8 (0.3)	88.9 (69.4)	1.1 (0.6)	$A = 7$ NA = 4
9	Dose OR OXY 32.2 (30.7)	OR MOR 59.7 (51)	0.53 (0.11)	50.8 (33.7)	0.69 (0.7)	52.1 (35.8)	$A = 7$ $B = 2$
52	Dose OR OXY 95.9 (114)	PR MOR 68 (64)	1.48 (1.11)	65 (42)	1.16 (0.52)[a]	78 (65)	$A = 27$ $C = 1$ NA = 24

OR OXY = oral oxycodone; TD FEN = transdermal fentanyl; A = good response; NA = not available; OR MOR = oral morphine; B = partial response; PR MOR = parenteral morphine; C = poor response.
[a] $P < 0.05$.

Table 4
Patients Switched From OR MOR to Other Opioids

$n = 54$	Dose of Previous Opioid (mg) (Mean [SD])	Initial Dose of Second Opioid (mg)	Initial Ratio	Dose at One Week of Second Opioid (mg)	Final Ratio After One Week	Dose at Death (mg)	Outcome
17	OR MOR 57.1 (39.3)	TD FEN 0.8 (0.4)	72 (33.9)	TD FEN 0.9 (0.5)	58.3 (32.7)	1.2 (0.6)	$A = 15$ $B = 1$ NA = 1
4	OR MOR 51.2 (40.9)	OR OXY 56.2 (53)	1.13 (0.3)	OR OXY 76.2 (75)	1.02 (0.5)	70 (71)	$A = 4$
27	OR MOR 72.5 (70.9)	PR MOR 26.7 (21.6)	2.51 (0.9)	PR MOR 33.2 (30.1)	2 (0.7)[a]	38 (34.4)	$A = 24$ $B = 2$ EXITUS = 1
2	OR MOR 17.5 (3.5)	TD BUP 0.8 (0)	21.9 (4.4)	TD BUP 0.8 (0)	21.9 (4.4)	0.8 (0)	$A = 2$
4	OR MOR 33.7 (20.5)	OR HYD 9.0 (5)	3.75 (1.0)	OR HYD 9.0 (5)	3.75 (1.0)	15 (5)	$A = 4$

OR MOR = oral morphine; TD FEN = transdermal fentanyl; A = good response; B = partial response; NA = not available; OR OXY = oral oxycodone; PR MOR = parenteral morphine; TD BUP = transdermal buprenorphine; OR HYD = oral hydromorphone.
[a] $P < 0.05$.

to the parenteral route. This probably reflects attitudes about changing the route of administration in the last days of life, when patients are expected to be unable to swallow.

Data regarding opioid switching at home are lacking for comparison with the present data. In a multicenter prospective study, about 75% of patients assessed were outpatients or, more often, home care patients. The true opioid switching rate was about 12% and was higher in the inpatient setting.[17] Interestingly, change to the parenteral route accounted for a further 30% of opioid substitutions.

Of interest, methadone was practically excluded from opioid switching. Dosing of this drug can be challenging for practicing physicians.[18] This is true as well in the home care setting, where monitoring is obviously less likely than in a hospital setting.

There are only two studies assessing opioid switching at home, both of which involved changes to methadone. In an early experience in patients followed at home or as outpatients, a rapid switching from OR MOR to small doses of methadone was effective by using an initial conversion ratio of 5:1.[19] In another study, 14 home care patients were switched from about 120 mg/day of OR MOR equivalents to a stable dose of 40 mg/day of methadone. Ten patients improved after switching to methadone, but one patient developed severe delayed toxicity, and another one received an initial dose 10 times higher than that prescribed for four days.[20]

There are other data pertinent to outpatient switching to methadone. In a retrospective analysis of 29 heavily pretreated patients, the starting dose of methadone was about 25 mg

Table 5
Patients Switched From TD BUP to Other Opioids

$n = 22$	Dose Previous Opioid (mg) (Mean [SD])	Initial Dose of Second Opioid (mg)	Initial Ratio	Dose at One Week of Second Opioid (mg)	Final Ratio After One Week	Dose at Death (mg)	Outcome
8	TD BUP 1.5 (0.2)	TD FEN 1.4 (0.5)	1.26 (0.41)	TD FEN 1.7 (0.8)	1.06 (0.37)	2.0 (0.8)	$A = 6$ $B = 1$ $C = 1$
4	TD BUP 1.62 (0.33)	OR OXY 55 (19)	0.03 (0.01)	OR OXY 62.3 (33)	0.03 (0.01)	120 (0)	$A = 3$ NA = 1
5	TD BUP 0.88 (0.33)	OR MOR 58 (39)	0.019 (0.01)	OR MOR 70 (40)	0.017 (0.01)	62 (25)	$A = 5$
4	TD BUP 1.1 (0.6)	PR MOR 31.3 (23.2)	0.04 (0.03)	PR MOR 47.5 (45.9)	0.020 (0.0)	37.5 (30.7)	$A = 2$ NA = 2
1	TD BUP 0.8 (0.0)	OR HYD 16 (0)	0.05 (0)	OR HYD 16 (0)	0.05 (0)	16 (0)	$A = 1$

TD BUP = transdermal buprenorphine; TD FEN = transdermal fentanyl; A = good response; B = partial response; C = poor response; OR OXY = oral oxycodone; NA = not available; OR MOR = oral morphine; PR MOR = parenteral morphine; OR HYD = oral hydromorphone.

Table 6
Patients Switched From OR HYD to Other Opioids

$n=8$	Dose of Previous Opioid (mg) (Mean [SD])	Initial Dose of Second Opioid (mg)	Initial Ratio	Dose at One Week of Second Opioid (mg)	Final Ratio After One Week	Dose at Death (mg)	Outcome
1	OR HYD 8.0 (0.0)	TD FEN 0.6 (0)	13.3 (0)	TD FEN 0.6 (0)	13.3 (0)	0.9 (0)	$A=1$
2	OR HYD 15 (9.9)	OR OXY 40 (0)	0.37 (0.25)	OR OXY 52 (16)	0.28 (0.10)	—	$A=1$ $B=1$
2	OR HYD 14 (14.1)	PR MOR 90 (42)	0.13 (0.09)	PR MOR 90 (42)	0.13 (0.09)	190 (155)	$A=2$
3	OR HYD 16 (13.8)	PR MOR 43.3 (32.1)	0.36 (0.07)	PR MOR 25.0 (7.1)	0.33 (0.09)	43.3 (32.1)	$A=3$

OR HYD = oral hydromorphone; TD FEN = transdermal fentanyl; A = good response; OR OXY = oral oxycodone; B = partial response; PR MOR = parenteral morphine.

and the final dose after titration was 243 mg. The duration of titration was 32 days.[21] Retrospective data on 89 rotations to methadone conducted in an outpatient setting of a comprehensive cancer center have been recently reviewed. Patients receiving about 100 mg of OR MOR equivalents were switched to oral methadone. The methadone dose at the first and the second follow-up visits was 15 mg/day and 18 mg/day, respectively. The interval between the first prescription and the two follow-up visits was about 15 days. This approach provided an overall success rate of 85%.[22] It is likely that these ambulatory patients were in a different condition than the patients reported in this survey; performance status was likely to be higher than in a sample that had a mean survival of about four weeks and required a rapid solution to the problem.

There are some limitations to this study, including the retrospective design and the relatively low number of patients who were switched. The home care teams participating in this study were chosen according to the quality of the service offered to patients and families, similar programs, and experience in research and are not representative of the level of home care in Italy. These data cannot be generalized, as there is no global information on the clinical activities of home care in Italy.

Opioid switching may improve opioid response. Although the present survey has limitations, it suggests that opioid switching in the home environment by experienced home care teams is feasible for most patients, at least in less complex circumstances. Prospective studies are needed to provide more information about the approach, including the factors that would support a decision to admit to hospital and those that would relatively contraindicate transportation in severely ill patients.

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Table 7
Patients Switched From PR MOR to Other Drugs

$n=6$	Dose of Previous Opioid (mg) (Mean [SD])	Initial Dose of Second Opioid (mg)	Initial Ratio	Dose at One Week of Second Opioid (mg)	Final Ratio After One Week	Dose at Death (mg)	Outcome
3	PR MOR 50 (60)	TD FEN 0.7 (0.5)	55.6 (38.5)	TD FEN 1.1 (0.6)	36.1 (26.8)	1.4 (0.7)	$A=2$ $B=1$
1	PR MOR 60 (0)	OR OXY 60 (0)	1 (0)	OR OXY 120 (0)	0.5 (0)	160 (0)	$A=1$
2	PR MOR 10 (0)	OR MOR 25 (7)	0.42 (0.1)	OR MOR 48 (16)	0.22 (0.07)	65 (7)	$B=2$

PR MOR = parenteral morphine; TD FEN = transdermal fentanyl; A = good response; B = partial response; OR OXY = oral oxycodone; OR MOR = oral morphine.

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