Therapy Switching in Patients Receiving Long-Acting Opioids

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BACKGROUND: Patterns of therapy switching in patients receiving long-acting opioids have not been well documented.

OBJECTIVE: To compare therapy switching among patients beginning treatment with controlled-release (CR) oxycodone, transdermal fentanyl, or CR morphine sulfate.

METHODS: Using a US healthcare claims database, we identified patients beginning treatment with CR oxycodone, transdermal fentanyl, or CR morphine sulfate between July 1, 1998, and December 31, 1999. We compiled claims for each patient for 6 months following therapy initiation and compared the incidence of therapy switching among the 3 groups. We also estimated total healthcare charges for patients who switched therapy versus those who did not.

RESULTS: We identified 1931, 668, and 449 patients beginning therapy with CR oxycodone, transdermal fentanyl, and CR morphine sulfate, respectively; 16.7%, 25.0%, and 35.9%, respectively, had cancer. For patients without cancer, rates of therapy switching at 6 months were 10.6% (CR oxycodone), 19.0% (transdermal fentanyl), and 26.0% (CR morphine sulfate); for those with cancer, rates were 23.8%, 24.6%, and 29.8%, respectively. Multivariate hazard ratios (vs CR morphine sulfate) for therapy switching in patients without cancer were 0.36 (95% CI, 0.27 to 0.47) for CR oxycodone and 0.69 (0.51 to 0.94) for transdermal fentanyl; for those with cancer, corresponding hazard ratios were 0.72 (0.50 to 1.03) and 0.76 (0.50 to 1.16). Total healthcare charges were significantly ($p < 0.01$) higher for patients who switched therapy than those who did not ($23 965 vs $14 299 in pts. without cancer; $58 259 vs $39 618 for those with cancer).

CONCLUSIONS: Patients without cancer who receive CR oxycodone or transdermal fentanyl are less likely to switch therapy than those receiving CR morphine sulfate. Total healthcare charges are higher for patients who switch therapy.

KEY WORDS: healthcare costs, opiod analgesics, pharmacotherapy..

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Long-acting opioids (eg, controlled-release [CR] oxycodone, transdermal fentanyl, CR morphine sulfate) are a core component of treatment for persistent moderate to severe pain.[1-5] Although long-acting opioids are generally well tolerated, the incidence and/or severity of adverse effects—particularly, itching,[6] hallucinations,[6] constipation,[7,8] and nausea[7]—may differ between agents. These differences may be clinically important, as they may give rise to differences in tolerability and persistency with prescribed treatment.

The time needed to titrate therapy and to achieve a desired analgesic effect also may differ between long-acting opioids.[2] It has been suggested, for example, that the initial dose of transdermal fentanyl may be too low, leading to greater numbers of patients requiring titration,[9,10] difficulties in titration,[11] and/or more frequent dosing than the recommended 3-day interval between applications.[12,13] Consistent with these observations, patients beginning treatment with transdermal fentanyl may have high levels of use of rescue medication.[14] Problems with dose titration may well lead to therapy switching as a consequence of undertreatment of pain.

These potential differences between long-acting opioids may have important economic implications. Patients who switch therapy due to adverse effects and/or problems with dose titration may incur higher costs due to additional office visits and the discarding of medication. Patients with inadequately managed pain also may have higher costs as a result of the need for additional pharmacotherapy and/or healthcare services (eg, hospitalizations).

The purpose of this study was to examine rates of therapy switching in clinical practice among patients beginning treatment with CR oxycodone, transdermal fentanyl, or CR morphine sulfate, using information from a large US healthcare claims database. We also compared healthcare charges for patients who switched long-acting opioid therapy versus those who did not.

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Methods

OVERVIEW

Using a large US health insurance claims database, we identified all patients who began therapy with CR oxycodone, transdermal fentanyl, or CR morphine sulfate between July 1, 1998, and December 31, 1999. The date of each patient's initial receipt of one of these agents was designated their index date, and patients were categorized into treatment groups according to the agent they received on this date. We then compiled all medical and pharmacy claims for each patient over the 6-month period following therapy initiation and compared the incidence of therapy switching among patients receiving the agents. We also compared total healthcare charges for patients who switched long-acting opioid therapy versus those who did not. Patients were stratified in all analyses according to whether or not they had cancer.

DATABASE

Data for this study were obtained from the Protocare Sciences Managed Care Database. The database is comprised of paid institutional, provider, and outpatient pharmacy claims derived from a variety of private healthcare plans. The database contains healthcare claims and enrollment data for approximately 3 million persons annually residing in over 20 states. Approximately one-quarter of persons in the database are aged ≥65 years.

The database includes patient demographic, eligibility, and vital status information, inpatient and outpatient diagnoses (in ICD-9-CM format[15]), inpatient and outpatient procedure information (in ICD-9-CM, Physician's Current Procedural Terminology, 4th ed. [CPT-4[16]], and Health Care Financing Administration Common Procedure Coding System [HCPCS] formats), outpatient drugs (identified by National Drug Code [NDC]) and associated therapy-days dispensed, billed charges, and dates of service for drugs and medical services.

SAMPLE SELECTION

Outpatient pharmacy claims were scanned to identify all persons who received CR oxycodone, transdermal fentanyl, or CR morphine sulfate during the study period. The date of each patient's initial receipt of one of these agents during this period was designated their index date, and patients were classified into treatment groups according to the particular agent they received on this date.

Patients were excluded if they had (1) received CR oxycodone, transdermal fentanyl, or CR morphine sulfate during the 6-month period preceding their index date (pretreatment), (2) received multiple long-acting opioids on their index date, (3) received <30 days of long-acting opioid therapy during the 6-month period following their index date (follow-up), (4) were not continuously eligible for health and drug benefits during pretreatment and follow-up, or (5) were enrolled in a Medicare supplemental or capitated health plan (the database does not include complete claims histories for these persons).

STUDY MEASURES

Attention was focused on the occurrence of therapy switching among patients using CR oxycodone, transdermal fentanyl, and CR morphine sulfate. Therapy switching was defined as receipt during follow-up of a long-acting opioid other than the one received on the index date. We also examined total medical care charges for patients who switched long-acting opioid therapy versus those who did not.

ANALYSES

Since patterns of therapy switching may differ for patients with cancer versus those without, we stratified the study sample according to whether patients had cancer (except squamous or basal cell skin carcinoma, as these rarely cause significant pain) (ICD-9-CM diagnosis codes 140.XX–172.XX, 174.XX–208.XX). Patients with ≥2 medical claims for cancer during pretreatment or ≥1 such claims ≤14 days prior to their index date were deemed to have cancer.

We assessed the comparability of CR oxycodone, transdermal fentanyl, and CR morphine sulfate patients at baseline. We then compared the prevalence of selected pain-related conditions based on the presence of ≥2 paid medical claims during pretreatment or ≥1 such claims within the 14-day period prior to the index date, with diagnoses shown in Table 1. We also compared the prevalence of other chronic comorbidities based on the presence of ≥2 paid medical claims during pretreatment with diagnoses shown in Table 1. Patient characteristics were compared across treatment groups using ANOVA for continuous variables and χ^2 tests for categorical variables.

Time to switching was assessed in terms of the number of days between the index date and the date of first receipt of another long-acting opioid. We focused attention on the first therapy switch only. Estimates of time to switch and the cumulative percentage of patients switching in the 3 groups were generated using Kaplan–Meier techniques[17]; the corrected group-

Table 1. ICD-9-CM Diagnostic Codes Used in Determining Prevalence of Pain-Related and Comorbid Conditions

Conditions	ICD-9-CM Diagnostic Codes
Pain-related conditions	
fibromyalgia	729.1X
low back pain	720.0X–720.2X, 721.3X, 721.42, 722.0X, 722.32, 722.52, 722.73, 722.83, 722.93, 724.02, 724.2X, 724.3X, 724.6X, 724.7X
other spinal pain (excluding low back pain and including neck)	720.XX–724.XX (excluding codes for low back pain; see above)
osteoarthritis	715.XX
other musculoskeletal pain	710.XX–714.XX, 716.XX–719.XX, 725.XX–729.XX (excluding 729.1X)
neuropathic pain	53.1X, 250.6X, 350.XX, 352.1X, 353.XX– 357.XX, 729.2X
Comorbid diseases	
chronic renal failure	ICD-9-CM 585.XX
congestive heart failure	428.0X
chronic obstructive pulmonary disease	491.XX, 492.XX, 496.XX
coronary heart disease	410.XX–414.XX
depression	296.2X–296.8X, 298.0X, 300.4X, 311.XX
diabetes	250.XX

ICD-9-CM = International Classification of Disease, 9th ed.

prognosis method[18] was employed to adjust these estimates for differences in selected covariates, including age (≥65 y vs younger), gender, the presence of selected chronic pain-related conditions and other chronic comorbidities, and pretreatment healthcare charges (≥median vs <median).

The probability of therapy switching was assessed using multivariate Cox proportional hazards models.[17] Covariates entered into these models were as noted above. Patients were deemed to be at risk of therapy switching from their index date until either the date of receipt of another long-acting opioid or the end of follow-up, whichever came first.

To examine the impact of therapy switching on healthcare charges, we pooled patients across the 3 treatment groups and restratified them according to whether they switched therapy during follow-up. Charges of patients who switched therapy were then compared with those of patients who had not. ANCOVA was used to assess the significance of differences in mean total healthcare charges adjusting for differences in selected covariates between the 2 groups.

Continuous variables are reported as mean ± SD, while categorical variables are reported as proportions. All analyses were performed using PC-SAS v.8.0.[19]

Results

PATIENT CHARACTERISTICS

A total of 1931, 668, and 449 patients were identified who began therapy with CR oxycodone, transdermal fentanyl, and CR morphine sulfate, respectively; 16.7%, 25.0%, and 35.9%, respectively, had cancer. Among those without cancer, CR oxycodone patients were younger than transdermal fentanyl or CR morphine sulfate patients ($p < 0.01$) (Table 2). Transdermal fentanyl patients were most likely to be women. Pretreatment total healthcare charges were lowest for CR oxycodone patients; the prevalence of most chronic comorbid and pain-related conditions also was lowest for CR oxycodone patients. Among patients with cancer, there was no significant difference in either age or gender. Pretreatment total healthcare charges, however, were significantly higher among transdermal fentanyl patients versus those receiving CR oxycodone or CR morphine sulfate.

INCIDENCE OF THERAPY SWITCHING

Among patients without cancer, rates of therapy switching at 6 months were 10.6% for CR oxycodone, 19.0% for transdermal fentanyl, and 26.0% for CR morphine sulfate. Adjusted for covariates using the corrected group-prognosis method, similar results were obtained (CR oxycodone 10.5%; transdermal fentanyl 19.6%; CR morphine sulfate 26.6%). Median time to switching was 63 days for CR oxycodone, 57 days for transdermal fentanyl, and 44 days for CR morphine sulfate.

Among patients with cancer, rates of therapy switching were 23.8% for CR oxycodone, 24.6% for transdermal fentanyl, and 29.8% for CR morphine sulfate. On an adjusted basis, similar results were obtained (CR oxycodone 23.6%; transdermal fentanyl 24.2%; CR morphine sulfate 31.1%). Median time to switching was 77 days for CR oxycodone, 52 days for transdermal fentanyl, and 26 days for CR morphine sulfate.

Table 2. Characteristics of Patients Receiving Long-Acting Opioids by Presence of Cancer

	Without Cancer				With Cancer			
Variable	CR Oxycodone (N = 1608)	Transdermal Fentanyl (N = 501)	CR Morphine Sulfate (N = 288)	p Value	CR Oxycodone (N = 323)	Transdermal Fentanyl (N = 167)	CR Morphine Sulfate (N = 161)	p Value
Age (y), mean ± SD	57.4 ± 16.9	64.7 ± 17.7	60.3 ± 16.5	<0.01	64.4 ± 12.3	64.3 ± 13.7	65.3 ± 12.1	0.68
Female (%)	59.0	69.3	53.8	<0.01	47.4	53.9	47.8	0.36
Chronic comorbid condition, n of pts. (%)								
chronic renal failure	15 (0.9)	9 (1.8)	7 (2.4)	0.06	6 (1.9)	2 (1.2)	2 (1.2)	0.80
congestive heart failure	71 (4.4)	45 (9.0)	28 (9.7)	<0.01	15 (4.6)	10 (6.0)	7 (4.3)	0.75
COPD	125 (7.8)	54 (10.8)	34 (11.8)	0.02	46 (14.2)	31 (18.6)	25 (15.5)	0.46
coronary heart disease	132 (8.2)	69 (13.8)	31 (10.8)	<0.01	33 (10.2)	17 (10.2)	8 (5.0)	0.13
depression	96 (6.0)	32 (6.4)	15 (5.2)	0.80	9 (2.8)	5 (3.0)	4 (2.5)	0.96
diabetes	169 (10.5)	80 (16.0)	43 (14.9)	<0.01	55 (17.0)	29 (17.4)	25 (15.5)	0.89
Chronic pain-related conditions, n of pts. (%)								
fibromyalgia	138 (8.6)	23 (4.6)	19 (6.6)	0.01	10 (3.1)	4 (2.4)	1 (0.6)	0.23
low back pain	583 (36.3)	158 (31.5)	95 (33.0)	0.12	63 (19.5)	23 (13.8)	41 (25.5)	0.03
neuropathic pain	185 (11.5)	53 (10.6)	45 (15.6)	0.09	19 (5.9)	7 (4.2)	8 (5.0)	0.72
osteoarthritis	263 (16.4)	81 (16.2)	49 (17.0)	0.95	22 (6.8)	8 (4.8)	15 (9.3)	0.27
other musculoskeletal pain	609 (37.9)	194 (38.7)	114 (39.6)	0.83	98 (30.3)	46 (27.5)	45 (28.0)	0.76
other spinal pain	622 (38.7)	148 (29.5)	113 (39.2)	<0.01	79 (24.5)	37 (22.2)	31 (19.3)	0.43
Pretreatment healthcare costs ($), mean ± SD	11 445 ± 24 607	18 426 ± 36 894	18 667 ± 48 117	<0.01	33 657 ± 38 817	46 089 ± 51 362	34 968 ± 38 836	<0.01

COPD = chronic obstructive pulmonary disease; CR = controlled release.

Hazard ratios obtained using a Cox multivariate proportional hazards model are shown in Table 3.

THERAPY SWITCHING AND HEALTHCARE CHARGES

Among the 2397 patients without cancer, 341 (14.2%) switched long-acting opioid therapy during follow-up. Those who switched therapy were more likely to be women and to have low back pain and other spinal pain (Table 4). Adjusted mean total healthcare charges during follow-up were $9666 higher among those who switched therapy compared with those who did not (Table 5). Inpatient care accounted for 59.1% of the total charges among patients who switched therapy and 54.5% among those who did not. Charges for pain-related pharmacotherapy were greater among patients who switched long-acting opioid therapy compared with those who did not.

Among 651 patients with cancer, 25.5% switched therapy during follow-up. Patients who switched therapy were more likely to have other spinal pain compared with those who did not switch. Adjusted mean total healthcare charges during follow-up were $18 641 higher among those who switched therapy compared with those who did not. Inpatient care comprised 48.2% of total charges among patients who switched therapy and 42.2% among those who did not. Charges for pain-related pharmacotherapy were greater among patients who switched long-acting opioid therapy.

Discussion

Our findings indicate that patients beginning treatment with CR oxycodone or transdermal fentanyl are less likely to switch therapy than those treated initially with CR morphine sulfate. In multivariate analyses controlling for differences in baseline characteristics, patients without cancer who were receiving CR oxycodone or transdermal fentanyl were found to be 64% and 31%, respectively, less likely to switch therapy than CR morphine sulfate patients. Among patients with cancer, those receiving CR oxycodone or transdermal fentanyl were approximately 25% less likely to switch therapy, although this result did not achieve statistical significance.

Similar to research on therapy switching in other therapeutic areas,[20,21] we also found that patients who switch long-acting opioid therapy have significantly higher healthcare charges than those who do not. This finding persists after adjustment for covariates such as age, preexisting diagnoses, and pretreatment healthcare charges. Charges for inpatient and outpatient care, as well as for pain-related medications, were significantly higher for cancer and noncancer patients who switched therapy. While we cannot establish causality with our study design, our findings do raise the interesting possibility that better pain management may lead to reduced rates of therapy switching and lower healthcare costs.

Table 3. Multivariate Cox Proportional Hazards Analysis of Factors Associated with Long-Acting Opioid Switching by Presence of Cancer

	Without Cancer			With Cancer		
Variable	**HR**	**95% CI**	**p Value**	**HR**	**95% CI**	**p Value**
Index LAO vs CR morphine sulfate						
controlled-release oxycodone	0.36	0.27 to 0.47	<0.01	0.72	0.50 to 1.03	0.07
transdermal fentanyl	0.69	0.51 to 0.94	0.02	0.76	0.50 to 1.16	0.20
Age (≥65 vs <65 y)	0.85	0.68 to 1.08	0.18	0.85	0.62 to 1.17	0.32
Male (vs female)	0.81	0.65 to 1.02	0.81	0.80	0.59 to 1.09	0.16
Chronic comorbid condition						
chronic renal failure	1.47	0.68 to 3.17	0.33	0.74	0.18 to 3.09	0.68
congestive heart failure	0.87	0.54 to 1.39	0.87	1.21	0.56 to 2.60	0.62
COPD	1.21	0.85 to 1.74	0.29	0.83	0.52 to 1.32	0.43
coronary heart disease	0.80	0.54 to 1.19	0.27	0.96	0.52 to 1.76	0.89
depression	1.10	0.73 to 1.65	0.66	0.60	0.19 to 1.90	0.38
diabetes	0.91	0.65 to 1.27	0.56	1.29	0.86 to 1.93	0.22
Chronic pain-related conditions						
fibromyalgia	1.07	0.72 to 1.58	0.74	1.14	0.41 to 3.14	0.81
low back pain	1.33	1.03 to 1.70	0.03	0.97	0.63 to 1.50	0.89
neuropathic pain	1.04	0.76 to 1.44	0.79	1.02	0.51 to 2.04	0.96
osteoarthritis	1.00	0.74 to 1.34	1.00	0.94	0.50 to 1.77	0.85
other musculoskeletal pain	1.10	0.87 to 1.38	0.43	0.75	0.52 to 1.09	0.13
other spinal pain	1.13	0.88 to 1.45	0.34	1.75	1.18 to 2.60	0.01
Pretreatment healthcare charges (≥median vs <median)	1.24	0.97 to 1.6	0.08	0.84	0.56 to 1.26	0.41

COPD = chronic obstructive pulmonary disease; CR = controlled release; LAO = long-acting opioid.

We note several limitations of our study. First, since our study was based on a retrospective analysis of health insurance claims data, we do not know why patients were started on a particular long-acting opioid versus another or why they switched therapy. While the latter may reflect differences in adverse effects, tolerability, and dose titration as hypothesized, it also may be due to differences in the characteristics of patients who received these drugs and/or those of the providers who prescribed them (ie, it may be the result of confounding). While we attempted to control for potential confounders in multivariate analyses, limitations inherent in claims data no doubt precluded us from controlling completely for such factors. For example, transdermal fentanyl and CR morphine sulfate may be preferentially prescribed to patients in the later—and hence more painful—stages of their disease. Additionally, pretreatment healthcare charges were higher among patients receiving transdermal fentanyl and CR morphine sulfate than those on CR oxycodone, suggesting a greater need for healthcare services among the former groups. Transdermal

Table 4. Characteristics of Patients Receiving Long-Acting Opioids Switching and Not Switching Therapy by Presence of Cancer

	Without Cancer			With Cancer		
Variable	Not Switching (N = 2,056)	Switching (N = 341)	p Value	Not Switching (N = 485)	Switching (N = 166)	p Value
Age (y), mean ± SD	59.4 ± 17.3	58.6 ± 17.1	0.44	64.9 ± 12.7	63.6 ± 12.4	0.26
Female (%)	59.7	65.7	0.04	47.6	53.6	0.18
Chronic comorbid condition, n of pts. (%)						
chronic renal failure	24 (1.2)	7 (2.1)	0.19	8 (1.7)	2 (1.2)	0.69
congestive heart failure	123 (6.0)	21 (6.2)	0.90	24 (5.0)	8 (4.8)	0.95
COPD	176 (8.6)	37 (10.9)	0.17	80 (16.5)	22 (13.3)	0.32
coronary heart disease	201 (9.8)	31 (9.1)	0.69	45 (9.3)	13 (7.8)	0.57
depression	117 (5.7)	26 (7.6)	0.16	15 (3.1)	3 (1.8)	0.38
diabetes	251 (12.2)	41 (12.0)	0.92	77 (15.9)	32 (19.3)	0.31
Chronic pain-related conditions, n of pts. (%)						
fibromyalgia	150 (7.3)	30 (8.8)	0.33	11 (2.3)	4 (2.4)	0.92
low back pain	689 (33.5)	147 (43.1)	<0.01	90 (18.6)	37 (22.3)	0.29
neuropathic pain	235 (11.4)	48 (14.1)	0.16	25 (5.2)	9 (5.4)	0.89
osteoarthritis	334 (16.3)	59 (17.3)	0.63	34 (7.0)	11 (6.6)	0.87
other musculoskeletal pain	771 (37.5)	146 (42.8)	0.06	147 (30.3)	42 (25.3)	0.22
other spinal pain	733 (35.7)	150 (44.0)	<0.01	99 (20.4)	48 (28.9)	0.02
Index LAO, n of pts. (%)						
CR oxycodone	1,437 (69.9)	171 (50.2)	<0.01	246 (50.7)	77 (46.4)	0.35
transdermal fentanyl	406 (19.8)	95 (27.9)	<0.01	126 (26.0)	41 (24.7)	0.35
CR morphine sulfate	213 (10.4)	75 (22.0)	<0.01	113 (23.3)	48 (28.9)	0.35
Pretreatment healthcare charges ($), mean ± SD	13,274 ± 31,256	16,771 ± 29,266	0.05	36,331 ± 38,845	39,623 ± 52,271	0.46

COPD = chronic obstructive pulmonary disease; CR = controlled release; LAO = long-acting opioid.

Table 5. Healthcare Charges for Patients Receiving Long-Acting Opioids Switching and Not Switching Therapy by Presence of Cancer

	Without Cancer ($) Mean ± SD			With Cancer ($) Mean ± SD		
Parameter	Not Switching (N = 2056)	Switching (N = 341)	p Value	Not Switching (N = 485)	Switching (N = 166)	p Value
Inpatient care	7,792 ± 25 210	14 167 ± 25 558	<0.01	16 710 ± 38 007	28 081 ± 38 241	<0.01
Outpatient care	4,979 ± 8622	7770 ± 8741	<0.01	21 393 ± 27 658	28 136 ± 27 828	0.01
Medications						
pain-related	813 ± 968	1170 ± 982	<0.01	675 ± 764	1060 ± 769	<0.01
other	716 ± 977	857 ± 991	0.02	840 ± 1019	982 ± 1025	0.13
TOTAL	14 299 ± 28 166	23 965 ± 28 553	<0.01	39 618 ± 49 114	58 259 ± 49 417	<0.01

fentanyl and CR morphine sulfate patients may have been sicker and/or in greater pain and therefore may have been more predisposed to switch therapy. The degree to which residual confounding affects our results is therefore unknown, and caution is accordingly warranted in interpretation of our findings.

We also note that, while healthcare charges are higher among patients who switch long-acting opioid therapy in comparison with those who do not, it does not necessarily follow that therapy switching is the cause of these higher charges. Causation may run in the opposite direction. For example, higher charges may reflect disease progression and/or unrelieved pain, which may give rise to therapy switching. While it is not possible for us to ascertain the direction of causation, our results nonetheless are not inconsistent with our a priori hypotheses. Additional research is needed to determine the exact relationship between therapy switching and healthcare costs.

Finally, we note that the database we employed contains information only on drugs that are dispensed through retail pharmacies. Thus, to the extent that patients received long-acting opioids via other channels (eg, inpatient), we might have underestimated the rate of therapy switching. We believe, however, that patients typically receive these medications through retail pharmacies and that the magnitude of any bias that this may have introduced is small.

Summary

Patients without cancer who are beginning treatment with CR oxycodone or transdermal fentanyl are less likely to switch therapy than those treated initially with CR morphine sulfate. Our findings may be of economic significance, as healthcare charges are significantly higher among patients who switch therapy compared with those who do not.

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References

1. Parrott T. Using opioid analgesics to manage chronic noncancer pain in primary care. J Am Board Fam Pract 1999;12:293-306.
2. Pappagallo M. Aggressive pharmacologic treatment of pain. Rheum Dis Clin North Am 1999;25:193-213.
3. The use of opioids for the treatment of chronic pain: a consensus statement from American Academy of Pain Medicine and American Pain Society. www.ampainsoc.org/advocacy/opioids.htm (accessed 2002 Apr 2).
4. Jacox A, Carr DB, Payne R. New clinical-practice guidelines for the management of pain in patients with cancer. N Engl J Med 1994;330: 651-5.
5. American Pain Society. Guideline for the management of pain in osteoarthritis, rheumatoid arthritis, and juvenile chronic arthritis. Glenview, PA: American Pain Society, 2002:54-92.
6. Mucci-LoRusso P, Berman BS, Silberstein PT, Citron ML, Bressler L, Weinstein SM, et al. Controlled-release oxycodone compared with controlled-release morphine in the treatment of cancer pain: a randomized, double-blind, parallel-group study. Eur J Pain 1998;2:239-49.
7. Allan L, Hays H, Jensen NH, Le Polain de Waroux B, Bolt M, Donald R, et al. Randomised crossover trial of transdermal fentanyl and sustained release oral morphine for treating chronic non-cancer pain. BMJ 2001;322:1-7.
8. Radbruch L, Sabatowski R, Loick G, Kulbe C, Kasper M, Grond S, et al. Constipation and the use of laxatives: a comparison between transdermal fentanyl and oral morphine. Palliat Med 2000;14:111-9.
9. Breitbart W, Chandler S, Eagel B, Ellison N, Enck RE, Lefkowitz M, et al. An alternative algorithm for dosing transdermal fentanyl. Oncology 2000;14:695-705.
10. Donner B, Zenz M. Transdermal fentanyl: a new step on the therapeutic ladder. Anticancer Drugs 1995;6:39-43.
11. Johanson GA. New routes of opiate administration. Am J Hosp Palliat Care 1992;9:4-5.
12. Donner B, Zenz M, Strumpf M, Raber M. Long-term treatment of cancer pain with transdermal fentanyl. J Pain Sympt Manage 1998;15:168-75.
13. Korte W, de Stoutz N, Morant R. Day-to-day titration to initiate transdermal fentanyl in patients with cancer pain: short- and long-term experiences in a prospective study of 39 patients. J Pain Sympt Manage 1996;11:139-46.
14. Robards M. Transdermal fentanyl in the hospice: a survey of rescue dosing and pain control. Am J Hosp Palliat Care 2001;18:47-50.
15. Professional ICD-9-CM code book. 6th ed. Reston, VA: St. Anthony Publishing, 2000.
16. Current procedural technology. 4th ed. Chicago: American Medical Association, 2000.
17. Allison PD. Survival analysis using the SAS system: a practical guide. Cary, NC: SAS Institute, 1995:29-60,111-84.
18. Ghali WA, Quan H, Brant R, van Melle G, Norris CM, Faris PD, et al. Comparison of 2 methods for calculating adjusted survival curves from proportional hazards models. JAMA 2001;286:1494-7.
19. SAS/STAT user's guide, version 8, 4th ed. Volumes 1 & 2. Cary, NC: SAS Institute, 1992.
20. Hughes D, McGuire A. The direct costs to the NHS of discontinuing and switching prescriptions for hypertension. J Hum Hypertens 1998;12: 533-7.
21. Hensley PL, Nurnberg HG. Formulary restriction of selective serotonin reuptake inhibitors for depression: potential pitfalls. Pharmacoeconomics 2001;19:973-82.

EXTRACTO

TRASFONDO: Los patrones de conversión de terapia en los pacientes usando opiáceos de larga duración no han sido bien documentados.

OBJETIVO: Comparar la conversión de terapia entre pacientes iniciandose en terapia con oxicodona de liberación controlada (OLC), fentanil transdermal (FT) o sulfato de morfina de liberación controlada (MLC).

METODOS: Usando un banco de datos de reclamos de servicios de salud en los Estados Unidos, identificamos pacientes iniciandose en terapia con OLC, FT, o MLC entre 1/7/98 y 31/12/99. Coleccionamos los reclamos para cada paciente durante 6 meses luego de iniciada la terapia, y comparamos la incidencia de cambio en terapia entre los tres grupos. Además, estimamos el costo total en los servicios de salud entre los que cambiaban de terapia y los que no cambiaban.

RESULTADOS: Identificamos 1931, 668 y 449 pacientes que comenzaron terapia con OLC, FT, y MLC respectivamente; 16.7%, 25.0%, y 35.9% tenían cáncer. En aquellos pacientes que no tenian cáncer, la tasa de cambio de terapia luego de 6 meses fue de 10.6% (OLC), 19.0% (FT), y 26.0% (MLC); la razón de cambio entre pacientes con cáncer fue 23.8%, 24.6%, y 29.8%. Las tasas de riesgo multivariadas (TR) (vs MLC) para el cambio en la terapia en pacientes sin cáncer fue 0.36 (95% intervalo de confianza, 0.27–0.47) para OLC y 0.69 (0.51–0.94) para FT; para aquellos con cáncer las TR correspondientes fueron 0.72 (0.50–1.03), y 0.76 (0.50–1.16). El costo total del cuidado de salud fue

significativamente más alto ($p < 0.01$) entre pacientes a quienes se les cambiaba la terapia y los que no ($23 965 vs $14 299 en los pacientes sin cá Therapy Switching in Patients Receiving Long-Acting Opioids cáncer y $58 259 vs $39 618 en los paciente con cáncer).

CONCLUSIONES: Pacientes sin enfermedad maligna tratados con OLC o FT son menos propensos a requerir cambios en su terapia comparados a los que se inician con MLC. Los costos totales de los servicios de salud son más altos entre los pacientes a quienes se les cambia la terapia.

Mitchell Nazario

RÉSUMÉ

AVANT-PROPOS: Les modalités de transfert des patients sous narco-analgésie chronique ne sont pas décrites dans la littérature.

OBJECTIF: Comparer les transferts thérapeutiques chez les patients traités initialement avec de l'oxycodone à libération contrôlée (OLC), du fentanyl par voie transdermique (FT), ou du sulfate de morphine à libération contrôlée (SMLC).

METHODES: En utilisant une base de données américaine de réclamations pour des soins de santé, les auteurs ont identifié les patients qui avaient débuté un traitement avec de l'OLC, FT, ou SMLC entre le 1/7/98 et le 31/12/98. Ils ont colligé ces réclamations pour chaque patient durant les 6 mois suivant l'initiation de la thérapie, et ont comparé l'incidence de transfert thérapeutique entre les 3 groupes. Ils ont aussi estimé les dépenses totales de santé pour les patients ayant transféré vers un autre opiacé par rapport à ceux qui sont demeurés avec le traitement initial.

RESULTATS: Les auteurs ont identifié 1931, 668, et 449 patients qui ont amorcé la thérapie avec l'OLC, le FT, et le SMLC, respectivement; 16.7%, 25%, et 35.9% avaient un cancer. Pour les patients sans cancer, le taux de transfert de thérapie était de 10.6% (OLC), 19.0% (FT), et 26.0% (SMLC) à 6 mois; pour ceux avec un cancer, les taux étaient de 23.8%, 24.6%, et 29.8%. L'analyse multivariée pour le risque (vs SMLC) de transfert chez les patients sans cancer était de 0.36 (intervalle de confiance 0.27–0.47) pour l'OLC et 0.69 (0.51–0.94) pour le FT; pour les patients avec cancer, les valeurs correspondantes étaient de 0.72 (0.50–1.03) et 0.76 (0.50–1.16). Les dépenses totales de santé étaient significativement plus élevées pour les patients qui ont dû transférer de thérapie ($p < 0.01$) par rapport à ceux qui ont poursuivi la thérapie initiale (23 965$ vs 14 299$ chez les patients sans cancer, et 58 259$ vs 39 618$ pour ceux avec un cancer).

CONCLUSIONS: Les patients sans cancer recevant l'OLC ou le FT sont moins sujets à un transfert de thérapie que ceux recevant le SMLC. Les dépenses de santé sont plus élevées pour les patients qui doivent changer de thérapie.

Marc Parent