Health Care Resource Use and Costs in Opioid-Treated Patients with and without Constipation in Brazil

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ABSTRACT

Objective: To estimate the prevalence of constipation concomitant to opioid treatment and related resource use and costs from the private payer perspective. Methods: In this retrospective database analysis, patients receiving opioid therapy were identified from a longitudinal insurance claims database. An algorithm was used to identify patients receiving opioid therapy with coincident constipation-related claims according to ICD-10 codes, targeted procedures, and opioid use criteria. Results were compared using analysis of variance with a significance level of 0.05. Results: A total of 23,313 patients were classified as opioid-treated patients (22.2%) and 6678 of them had events related to constipation (29.0%). Compared with opioid-treated patients without constipation, incremental mean total costs per month per patient were 261.18 BRL (P < 0.001). The average cost per month for opioid-related constipation patients was 787.84 BRL, significantly higher than other patients (P < 0.001 for all comparisons). Among cancer patients, 24.4% was receiving opioids and 27.0% of those had constipation-related claims. As expected, the opioid therapy prevalence was significantly higher when compared to all patients (2.2% vs. 24.4%, P < 0.001). Cancer patients had, in average, higher costs than did noncancer patients in all four subgroups. Conclusions: Patients with constipation coincident with opioid treatment exhibited a significantly higher economic burden than did patients without the condition. These results indicate that reducing opioid-induced constipation could lead to potential cost savings for the health care system.

Keywords: analgesics, constipation, costs and cost analysis, drug toxicity, opioid.

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Introduction

Opioids are the mainstay therapy for patients with moderate to severe pain. According to the Brazilian Society for Study of Pain [1], the prevalence of chronic pain is about 30% within the country and noncancer pain is responsible for 60% to 70% of chronic pain cases. For these patients opioid treatment must be very carefully monitored and is generally reserved for refractory cases. Thus, it is estimated that about 10% of patients with chronic pain will eventually receive opioid treatment. Of these, 70% had moderate pain, indicating the use of a weak opioid and 30% strong or very strong pain with indication of strong opioids [2]. Pain is present in 30% of cancer patients undergoing chemotherapy and in 60% to 90% of those with advanced cancer [3].

Although effective in pain management [4], opioid therapy is frequently complicated by side effects [5]. With continued use, patients usually develop tolerance to those side effects, except constipation, which is the most common and usually the most debilitating side effect reported by patients, with a median frequency of 30% among noncancer patients (range 12%–52%) [6]. The prevalence in cancer patients is even higher [7], reaching 63% [8], and laxatives are required by 87% of terminally ill cancer patients taking oral strong opioids and by 74% of those receiving weak opioid therapy [9,10].

Constipation is also associated with a serious negative effects on patients’ health-related quality of life (HRQoL) and on society in terms of health care resource use and work productivity loss [11]. Patients with constipation have more hospital admissions, emergency room visits, home health services, nursing home care, physician visits, and laboratory tests, as well as higher mean all-cause costs for emergency, physician visits, nursing facilities, home health care, and prescription drug services compared to patients without constipation [12]. Further, it is known that constipation usually persists for as long as opioid therapy is administered [8].

In Brazil, opioid consumption was estimated at 1.1520 mg per capita, showing an average prescription below the world average

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consumption (5.5708 mg per capita) and indirect evidence of inadequate pain control in the country [13]. Despite these variations, a large number of patients are currently receiving opioid therapy for chronic pain worldwide. To date, no studies evaluating the prevalence of constipation in patients using opioids have been published in Brazil; neither their related management resource use nor costs.

This study aimed to estimate the prevalence of constipation concomitant to opioid treatment and to compare resource use and costs in opioid-treated patients with and without constipation, from the private payer perspective in Brazil.

**Methods**

**Data source**

Patients receiving opioid therapy were identified from a longitudinal insurance claims database (Axismed Database) consisting in 1,057,033 individuals observed during a 35-month period (December 2004 to December 2007). This database comprises about 3% of the population covered by health insurance plans across all five geographic regions in Brazil (national coverage). Its general data include patient demographics, medical claims, and enrollment date. Medical claims information includes date, type of procedure, provider specialty, amount paid, and diagnosis code using International Classification of Diseases, 10th revision (ICD-10) [14]. Average patient exposition time was 21.84 months.

**Study population**

An algorithm was developed through evidence-based clinical rules and expert opinion to identify patients receiving opioid therapy with coincident constipation-related claims according to ICD-10 codes and constipation-related procedures. Patients were initially segmented according to the presence of opioid therapy records. To be subsequently classified as a patient with constipation concomitant to opioid therapy, patients with evidence of opioid analgesics use had to meet at least one of the following eligibility criteria: at least one medical claim with an ICD-10 code potentially related to constipation (i.e., K59.0, K59.9, or R19.4) and/or at least one medical procedure potentially related to constipation (e.g., enemas or manual, endoscopic, or surgical fecal impaction removal).

The individuals in the database were then classified in four groups: nonopioid-treated without constipation (NONC), nonopioid-treated with constipation (NOWC), opioid-treated without constipation (ONC), and opioid treated with constipation (OWC). To ensure more detailed analysis reflecting relevant clinical questions, individual with oncologic ICD-10 codes were separately analyzed, once opioid therapy and opioid-related constipation prevalence is usually higher among cancer patients.

**Outcomes measures**

Resource use and costs were collected for each individual during the 35-month follow-up period using a top-down approach [15]. Once individuals were followed for varying amounts of time, these variables (i.e., total costs, costs segmented by category, and resource use segmented by category) were then converted to per member/month units dividing the results for all patients by the person-months of follow-up. Resource use results are presented as average consumption per month of six claims groups: outpatient procedures, consultations, tests and therapies, hospitalization, emergency department visits, and others. Hospitalizations are reported as hospital days. Costs were collected as reported in the administrative database, reflecting the amount effectively paid by each health insurance plan. Costs are presented in Brazilian reals (BRL), using reference values for 2009.

**Statistical analyses**

Medical resource use and costs in patients with constipation coincident with opioid therapy (OWC) were compared with the outcomes observed in the other three groups (NONC, NOWC, and ONC). The per member per month outcomes were compared using analysis of variance, with corresponding P values reported with a significance level of 0.05. If the analysis of variance test indicated a statistically significant difference, further post hoc analyses were performed. SAS (version 9, 2002, SAS Institute Inc., Cary, NC) statistical software was used to perform all analyses.

**Results**

**All patients**

In our study, 23,313 patients were classified as opioid-treated patients (2.2% of total population) and 6678 of them had events or ICD-10 codes related to constipation, resulting in a constipation prevalence of 29.0% among opioid-treated patients. The mean age of OWC patients was 51.58 ± 19.35 years, 65.0% was women, 1.0% had cancer diagnosis, and the mean follow-up per individual ranged from 20.03 to 24.44 months in each group. Table 1 in Supplemental Materials found at: doi:10.1016/j.jval.2011.05.019 summarizes the baseline characteristics of the study sample, including average costs (mean ± SD) and resource use (mean ± SD) per patient during the follow-up. Mean cost per patient ranged from 2,122 BRL (NONC) to 17,206 BRL (OWC) and the average cost per patient for the entire sample was 2,486 BRL.

Table 2 in Supplemental Materials found at: doi:10.1016/j.jval.2011.05.019 compares average cost and resource use per month of OWC patients with the other three subgroups. Compared to opioid-treated patients without constipation, average incremental costs per month per patients with the condition were 261.18 BRL ($P < 0.001$). The average cost per month for OWC patients was 787.84 BRL, significantly higher than ONC (526.66 BRL), NOWC (284.47 BRL), and NONC patients (90.17 BRL) ($P < 0.001$ for all comparisons). Patients with claims related to both conditions had significantly more days in hospital per month (0.25 vs. 0.497, $P < 0.001$), outpatient office visits (1.04 vs. 1.59, $P < 0.001$), outpatient procedures (4.69 vs. 14.05, $P < 0.001$) and tests and therapies (31.95 vs. 36.66, $P < 0.001$) than did patients without opioid-related constipation claims.

**Cancer patients**

Cancer patients were considered as a separate subgroup due to the expected higher prevalence of both conditions (opioid therapy and constipation) among those individuals. Oncology ICD-10 codes were identified for 9873 individuals, representing 1.0% of the total population. Among those, 24.4% was receiving opioid therapy and 27.0% of those had constipation-related claims. As expected, the opioid therapy prevalence was significantly higher among cancer patients when compared to all patients (2.21% vs. 24.4%, $P < 0.001$). Among opioid-treated patients the prevalence of constipation was similar in both groups (29.0% for all patients and 27.0% for cancer patients), regardless of cancer status. Table 3 in Supplemental Materials found at: doi:10.1016/j.jval.2011.05.019 presents the costs and resource use results for the cancer population, considering the same subgroups previously described. Cancer patients had, on average, higher costs than did noncancer patients in all four constipation and opioid status categories. The absolute difference between ONC and OWC patients, however, remains stable when compared to the observed difference in all patients’ analysis (263.21 BRL vs. 261.18 BRL, respectively). When segmented costs were analyzed, OWC patients resulted in higher costs due to tests and therapies and hospital days, but did not for other categories.
Opioid-related constipation has multidimensional influences on a patient’s health status and consequently results in complex burdens for health care systems. To relieve constipation, patients often abandon their opioid medication, potentially impairing analgesia. Therefore, the burden of constipation can be not only from the direct influence of its symptoms on HRQoL and constipation-related health care resources consumption, but also from medical resources to relieve the pain and the side effects of treatments taken to relieve the condition.

The observed prevalence of constipation in our sample was quite similar to data reported by a meta-analysis focused in older patients without cancer (29.03% vs. 30.00%, respectively) [1]. The subgroup analysis of cancer patients showed a slightly lower prevalence (27.0%), which is different than results previously described, achieving 63% [8]. The published data refer to the higher rate reported by hospice cancer patients in the United States. A study published in 2001 [16] with 593 cancer patients treated by a pain service showed a 23% prevalence of constipation and this symptom was assessed as being frequently caused by the analgesic regimen. Furthermore, much of the variation in the frequency of constipation in patients treated with opioids can be attributed to study design and population heterogeneity: age, sex, base pathology, type of opioid administered, its dose and duration, and subjective perception of constipation.

Our findings indicated that, on average, opioid-treated patients were significantly more costly than patients without opioid-related events, and patients with constipation-related claims resulted in higher medical costs than those without constipation. The incremental costs observed for patients with constipation-related claims coincident with opioid therapy, when compared to opioid-treated nonconstipated patients, were about 260 BRL per individual per month either for cancer patients or for the entire sample. The similar findings for both subgroups can indicate that the observed difference probably reflects the actual absolute difference in costs due to constipation.

The effects of constipation in patients using opioids has already been studied in other countries showing similar results. A literature review was conducted to identify national and international cost-of-illness and prevalence studies addressing the burden of opioid-related constipation using a mix of controlled vocabulary and free text terms for constipation, opioid therapy, prevalence, and costs. PubMed and LILACS databases were searched and only US and European studies were found [7,9–12,17–22].

In the United States, Bell et al. [11] evaluated the effects of opioid-induced constipation on health care resource use, work productivity, and HRQoL with data from 2430 individuals, of whom 359 reported constipation. Opioid-induced constipation patients reported significantly more physician visits and alternative care visits. Significantly greater productivity loss and significantly lower HRQoL were observed in the constipated group, both signals of subjective perception of constipation.

Iyer et al. [12] also compared the opioid use patterns, resource use, and costs of 39,485 US patients receiving opioid therapy who had constipation with those who did not. Patients with constipation had statistically significant higher resource use and all-cause costs compared to patients without constipation. Those studies showed that opioid-related constipation has a significant influence on costs and resource use in developing countries and it seems reasonable to believe that this association between higher health care resource consumption and opioid-related constipation could be observed in other similar countries, but there is still a lack of evidence concerning this issue in Brazil or Latin America. As stated before, average opioid prescription in Brazil is considered below the world average consumption and this is indirect evidence of inadequate pain control in the country [13]. In addition, resource use and medical costs are directly related to patients’ access to the health care system, reimbursement and coverage processes, local therapeutic patterns, and clinical guidelines, all of which are expected to be significantly different across countries, particularly if they have different health care system organizations.

Study limitations include potential selection bias due to retrospective analysis of administrative database, misclassification of patients (ICD-10 codes are not homogeneously used in Brazilian clinical practice, particularly for general conditions such as constipation), and the lack of more detailed baseline clinical information in the original database to provide clinical and demographic variables that could be used to control for confounders. Trying to minimize those limitations, the opioid-treated patients were compared with nonopioid-treated patients and cancer patients were separately analyzed. We hypothesized that higher prevalence of cancer among OWC patients could lead to higher costs due to cancer treatments (e.g., chemotherapy, radiation therapy, and surgery) and not directly to opioid-related constipation. These hypotheses can be rejected once the same difference in costs was observed when only cancer patients were compared. In addition, opioid-treated patients are more likely to be in palliative care (i.e., not receiving high-cost cancer treatment).

Retrospective claims database studies are still a novel field of research in Health Economics and Outcomes Research in Brazil and there is a recognizable absence of data concerning patients with private health care plans coverage. Our findings provided the first local overview of the burden associated to opioid-related constipation in Brazil. Further research is needed to validate those findings through primary data collection, preferably in a prospective fashion.

Conclusions

Patients with constipation coincident with opioid treatment exhibited a significantly higher economic burden than did patients without the condition. These results indicate that reducing opioid-induced constipation could lead to potential cost savings for the health care system.

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Supplemental Materials

Supplemental material accompanying this article can be found in the online version as a hyperlink at doi:10.1016/j.jval.2011.05.019, or if hard copy of article, at www.valueinhealthjournal.com/issues (select volume, issue, and article).

References


