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Differences in pain characteristics between oncology outpatients taking analgesics on an around-the-clock compared to on an as-needed basis

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Differences in Pain Characterisitcs Between Oncology Outpatients Taking Analgesics on an Around-the-Clock Compared to on an As-Needed Basis

by

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THESIS

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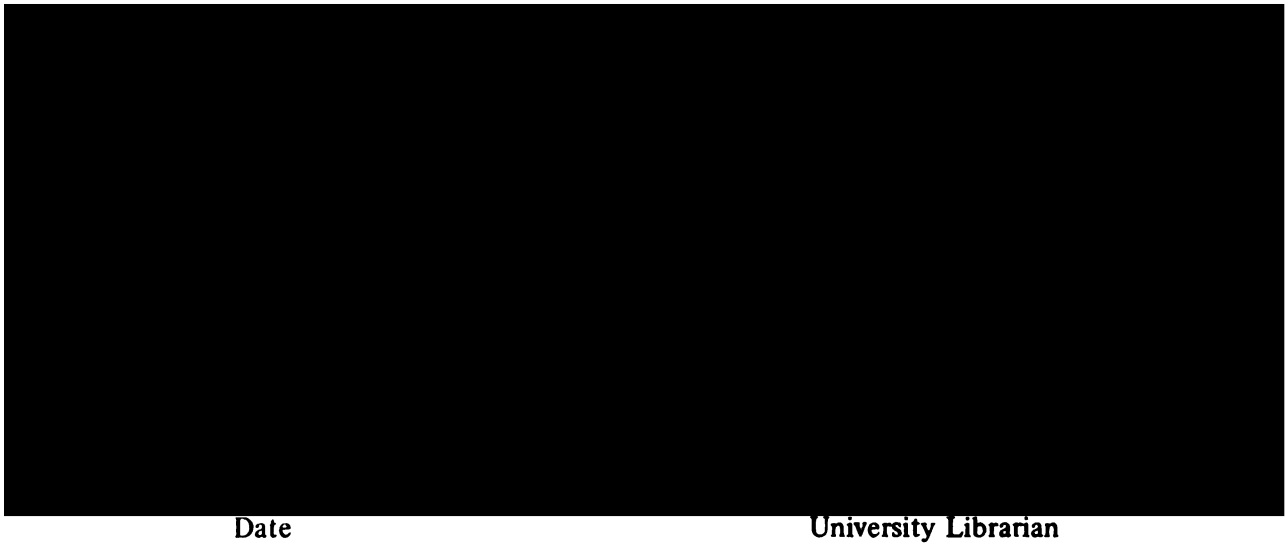

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For my mom and dad

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Differences In Pain Characteristics Between Oncology Outpatients Taking Analgesics On An Around-The-Clock Compared To On An As-Needed Basis
Kayee Alice Mack

Abstract

Background: Clinical management of chronic cancer-related pain is based on the Cancer Pain Guideline recommendations that analgesic medications be administered on an around-the-clock (ATC) basis, rather than on an as-needed (PRN) basis. However, no studies could be found that evaluated for differences in pain intensity scores, over time, in oncology outpatients with chronic pain from bone metastasis who were taking analgesic medications on an ATC as compared to a PRN basis.

Objective: To determine if there were differences in pain intensity scores, pain duration, opioid prescription and consumption and total analgesic prescription and consumption between oncology outpatients with pain from bone metastasis who were taking opioid analgesics on an ATC compared to PRN basis over 5 weeks.

Methods: This study is part of a large randomized clinical trial (RCT) that is testing the effectiveness of a self-care intervention called the PROSELF©: PAIN CONTROL PROGRAM compared to standard care in improving the management of pain from bone metastases. Data from adult oncology patients (n=88) in both the standard care arm and treatment arm of the RCT were used in this analysis. Patients were recruited from 7 outpatient sites.

Results: Four separate two-way RM-ANOVAs found no significant differences between the two groups of patients in average, least, or worst pain intensity scores or in the number of hours per day that the patients experienced significant pain over the 5 weeks of data collection. Significant differences were found in the total dose of opioids prescribed and taken between the 2 groups over the 5 weeks of data collection. The

average total opioid dose prescribed and taken was significantly greater for the ATC group than the PRN group.

Conclusion: ATC group patients did not report better levels of pain control than PRN group patients did over 5 weeks. Further research is needed to explain the lack of difference in the pain intensity measures between the two groups, while ATC group patients were prescribed 7 times more opioid analgesics and were taking 21 times more analgesics than PRN group patients.

Key Words: Analgesics, opioids, cancer pain.

Christine Miaskowski, RN, PhD, FAAN

Effective cancer pain management is based on the fundamental principle that continuous pain requires continuous relief (McCabe, 1997). Clinical practice as well as guidelines published by the World Health Organization (WHO) and the Agency for Health Care Policy and Research (AHCPR) support this principle. The WHO guideline recommends that the appropriate scheduling of analgesic medications means that "the drug must be given 'by the clock' and not merely when the patient complains of pain" (pp.14, 22) (WHO, 1996). Similarly, the around-the-clock (ATC) administration of analgesics for persistent cancer-related pain, rather than on an "as needed" basis, is recommended in the Cancer Pain Guideline developed by an expert panel for the AHCPR. (Jacox et al., 1994). This guideline recommendation is based on level A evidence [i.e., "data deriving its strength from the findings of clinical trials"] (Jacox et al., 1994). However, no studies are cited in the AHCPR Cancer Pain Guideline to support this level A recommendation for ATC dosing of analgesics.

The use of ATC dosing to manage chronic cancer pain originated with the hospice movement. In a groundbreaking descriptive study of cancer-related pain conducted at St. Christopher's Hospice (1974), Twycross evaluated the use of diamorphine in 500 patients with advanced malignant disease. This descriptive study attempted to answer questions about the most appropriate method of drug administration, optimal dosing of diamorphine, and the potential risks for the development of tolerance and physical dependence to diamorphine. Significant clinical data were generated on the optimal dosing of opioid analgesics, the use of the oral route, and the lack of impairment of mental faculties in patients who received ATC dosing of diamorphine. In addition, the findings from this study suggested that fears of tolerance, addiction, and physical

dependence were unwarranted. Based on clinical experience with the management of cancer pain in the hospice setting, ATC dosing of opioid analgesics became an established approach for the management of chronic cancer pain. This approach was based on the belief that the continuous administration of pain medication would yield optimal pain relief. This work lead to the development of sustained/controlled release opioid preparations and transdermal delivery systems that reduced the frequency with which patients needed to administer opioid analgesics.

Studies of optimal dosing of analgesics for cancer-related pain

While ATC dosing of analgesic medications for cancer-related pain is the established credo, because constant blood levels of the analgesic are maintained, no randomized clinical trials (RTCs) were found that compared changes in pain intensity scores over time in patients with cancer-related pain who were randomized to an ATC dosing regimen compared to a PRN dosing regimen. Most of the analgesic studies of cancer-related pain that were conducted over the past 25 years were done to evaluate the new sustained/controlled release formulations of morphine or the transdermal delivery of fentanyl. These analgesic studies can be grouped into two broad categories, namely: studies that compared the effectiveness of two long-acting drug formulations (Beyssac et al., 1998; Broomhead et al., 1997; Bruera et al., 1999; Citron et al., 1998; Gourlay et al., 1997; Hagen & Babul, 1997; Heinrich-Nols et al., 1999; Peat et al., 1999; Raber et al., 1999; and Wong et al., 1997); and studies that compared the effectiveness of short-acting to long-acting formulations (Grond et al., 1999; Hummel et al., 1996; Reuben et al., 1999; Salzman et al., 1999). All of these studies controlled the dosing schedule of the

analgesic medications. An evaluation of an optimal dosing schedule was precluded by the studies' design.

An exhaustive review of the analgesic studies for cancer-related pain is beyond the scope of this paper. However, current exemplar studies that are illustrative of the two categories of studies listed above are summarized below.

A review of the most recent studies that compared controlled-release morphine tablets (Beyssac et al., 1998; Broomhead et al., 1997; Bruera et al., 1999; Citron et al., 1998; Gourlay et al., 1997; Hagen & Babul, 1997; Heinrich-Nols et al., 1999; Peat et al., 1999; Raber et al., 1999) and/or the transdermal fentanyl patch (Wong et al., 1997) yielded ten published, well-controlled, repeated-dose trials. Collectively, these studies consistently utilized a ten-point scale to assess pain, captured baseline pain intensity data, and routinely administered morphine tablets and/or the transdermal fentanyl patch every 12 hours as the primary analgesic. The primary objective of these studies was to compare the effectiveness of different routes of administration and formulations of opioid analgesics (e.g., oral capsule or tablet, suspension, suppositories, bioadhesive buccal tablet, and transdermal patch), relative bioavailability, and adverse effects (such as side effects when used with and without concominant food intake). The use of PRN scheduling is briefly discussed in the context of using intermediate-release analgesics as rescue medications for breakthrough pain. Studies that did not report pain assessment scores were not reviewed.

A smaller group of studies that compared the effectiveness of immediate-release morphine to controlled-release morphine were reviewed for relevance to ATC versus PRN administration. Four studies (e.g., Grond et al., 1999; Hummel et al., 1996; Reuben

et al., 1999; Salzman et al., 1999) were found that compared the effectiveness of controlled-release formulations to immediate-release formulations. All of these studies administered the immediate-release formulations every 4 to 6 hours and the controlled-release formulations every 12 or 24 hours. These studies were conducted primarily to investigate the efficacy of different formulations and their adverse effects. Patients with pain of malignant and non-malignant origin as well as healthy volunteers were included in these studies. None of these studies addressed the issues of tolerance, breakthrough pain, or the assessment of pain over time.

Because no studies could be found that evaluated for differences in pain intensity scores, over time, in oncology outpatients who were taking analgesic medications on an ATC as compared to a PRN basis, we decided to examine this question in oncology outpatients who were experiencing pain from bone metastasis. Therefore, the purposes of this study were to determine if there were differences in pain intensity scores (average, least, and worst) and pain duration (hours per day in pain) between oncology outpatients who were taking opioid analgesics on an ATC compared to a PRN basis. In addition, differences in opioid prescription and consumption (expressed in morphine equivalents) and total analgesic prescription and consumption (expressed as a Medication Quantification Scale (MQS) score) were examined between the two groups over 5 weeks. In order to classify patients into the ATC group versus the PRN group, we calculated mean adherence scores (i.e., the amount of opioid analgesic taken/amount of opioid analgesic prescribed x 100) for each of the 5 weeks of data collection. Patients were classified in the ATC group if they had an ATC opioid analgesic prescribed and if they took 80% or more of their prescribed ATC dose of opioid analgesic for each of the 5

weeks of data collection. Patients were classified into the PRN group if they took their prescribed opioid dose on a PRN basis for each of the 5 weeks of data collection.

Methods

Sample and settings

This study is part of a large RCT that is testing the effectiveness of a self-care intervention called the PROSELF©: PAIN CONTROL PROGRAM compared to standard care in improving the management of pain from bone metastases. Data from patients in both the standard care arm and treatment arm of the RCT were used in this analysis. Eighty-eight patients were recruited from seven outpatient settings in Northern California. One site is a university-based cancer center, two are community-based oncology practices, one is an outpatient radiation therapy center, one is an oncology outpatient practice in a large health maintenance organization, one is a veteran's administration facility, and one is a military hospital.

The participants were adult oncology outpatients (> 18 years) who were able to read, write, and understand English. On enrollment, all patients had a Karnofsky Performance Status (KPS) score of ≥ 50; had an average pain intensity score of ≥ 2.5; and had radiographic evidence of bone metastasis.

Instruments

Patients completed a demographic questionnaire, the KPS rating, the interference items from the Patient Outcomes Questionnaire, a daily pain diary, and a daily pain medication diary. In addition, each patient's medical record was reviewed for disease and treatment information.

Demographic questionnaire. The self-report demographic questionnaire obtained information on the patient's age, gender, marital status, living arrangements, educational level, ethnicity, and employment status. Baseline information was obtained about the patient's pain problem, including pain right now, average daily pain, pain at its worst, pain at its least, as well as number of hours per day and number of days per week that pain interfered with the patient's ability to function. Patients recorded the length of time they were in pain, whether pain limited their work activities, and the percentage of pain relief they experienced in the past week.

KPS rating scale. The KPS rating was designed to measure the patient's ability to accomplish normal activities of daily living or their need for help and nursing care (Karnofsky, 1977). The KPS rating, used in this study, was a patient self-report measure that consisted of a series of eight items for ranking functional status that ranged from 30 (disability with hospitalization needed) to 100 (adequate health status with no complaints and no evidence of disease). Reliability and construct validity of the KPS has been established and it has been shown to be a global indicator of the functional status of patients with cancer. (Karnofsky, 1977)

Interference items from the Patient Outcomes Questionnaire. Interference items were taken from the Patient Outcomes Questionnaire that was developed by the Quality Improvement Committee of the American Pain Society (American Pain Society Quality of Care Committee, 1995). The interference items determined how the cancer-related pain interfered with the person's ability to perform eight activities. On each of the interference items, patients were asked to circle a number from 0 to 10 to indicate the degree to which pain interfered with different activities. Zero was labeled 'does not

interfere' and 10 was labeled 'completely interferes.' A total interference score was calculated as the sum of the responses to the eight items.

Daily pain diary. The daily pain diary consisted of descriptive numeric rating scales of pain intensity and a measure of pain duration. A descriptive numeric rating scale of pain intensity is a horizontal row of numbers ranging from 0 to 10 with verbal descriptors below several of the numbers (0 = none, 2 = mild, 5 = moderate, 8 = severe, and 10 = excruciating). Patients were asked to rate three separate measures of pain intensity (i.e., average pain, worst pain, least pain) for the previous twenty-four hours prior to bedtime. To obtain information on the duration of pain, patients were asked to indicate how many hours of the day (0-24) the pain lasted.

All of the measures in the daily pain diary were used in our previous studies (e.g., Burrows, Dibble, & Miaskowski, 1998; Glover, Dibble, Dodd, & Miaskowski, 1995; Miaskowski & Dibble, 1995; Miaskowski, Zimmer, Barrett, Dibble, & Wallhagen, 1997). In addition, a number of researchers have found that numeric rating scales are valid and reliable measures of perceived pain intensity. A numeric rating scale is a simple and sensitive measure of pain intensity and has yielded reproducible results with many types of patients in many settings (Downie et al., 1978; Huskinsson, 1974; Ohnhaus & Adler, 1975).

Daily medication diary. The daily pain medication diary provided information on opioid, non-opioid, and adjuvant pain medications that the patients took on an around-the-clock (ATC) and on an as needed basis (PRN). The research nurse recorded the name, dose, and administration schedule for all of the pain medications that the patients' physician had prescribed and any over-the-counter medications the patients were taking

for pain. The research nurse completed this section of the pain medication diary for each week of the study. Patients recorded the times they took their pain medications on a daily basis. If a change in the pain medication prescription occurred, patients were instructed to make the change on their pain medication diary. The research nurse verified the patients' current pain medication regimen at each study visit and checked the diary entries for completeness.

Data collection procedures

Patients were approached in an outpatient setting by a recruitment nurse who explained the study procedures and obtained informed consent. Patients completed the demographic questionnaire and KPS rating at the time of enrollment into the study. Patients were randomized into either the treatment group or the standard care group. At Weeks 1, 3, and 6, different research nurses saw patients in each group in their homes. Telephone interviews were conducted at Weeks 2, 4, and 5. Patients were taught to complete the pain diary and the pain medication diary on a daily basis prior to bedtime. The research nurses reviewed the diary for completeness during each study visit and reminded the patients to complete the diary with each phone call. Using this approach, we achieved a 98% adherence rate with completing the diaries. This study was approved by the Committee on Human Research at the University of California, San Francisco and at each of the study sites.

Data Analysis

Descriptive statistics and frequency distributions were generated for the patients' demographic and disease-related characteristics. Daily ratings of pain intensity and duration were averaged on a weekly basis. All opioid analgesics were converted to

morphine equivalents. Total daily doses of opioid analgesics, prescribed and taken on an ATC and PRN basis, were calculated and then averaged for each week of the study.

In order to classify patients into the ATC group or the PRN group, we calculated mean adherence scores (daily amount of opioid analgesics taken/daily amount opioid analgesics prescribed x 100) for each of the 5 weeks of data collection. Patients were classified in the ATC group if they took 80% or more of their prescribed ATC dose of opioid analgesic medications for each week of the 5 weeks. Patients were classified in the PRN group if they had an opioid analgesic ordered on a PRN basis for the 5 weeks of data collection and did not take the analgesics on a routine schedule. This information for the PRN group was verified through an inspection of each of the patients' pain medication diaries.

To account for the prescription and administration of all non-opioid, opioid, and adjuvant analgesic medications, a Medication Quantification Scale (MQS) score was calculated using the method described by Steedman and colleagues (1992). The MQS provides a method for quantifying analgesic medication prescription and use by calculating scores for each analgesic medication based on weights assigned by medication class (e.g., aspirin or acetaminophen = 1, strong narcotics = 6) and dosage level. These individual scores are summed to yield a total score of analgesic medication prescription and usage suitable for statistical analyses. MQS scores for analgesic medications that were prescribed and taken on an ATC basis as well as on a PRN basis were calculated daily. Daily scores were averaged to provide a weekly MQS score.

Independent Student's t-tests or Chi-square analyses were done to determine differences in patient characteristics, differences in KPS scores, differences in baseline pain scores, and differences in scores on the interference items.

Separate two-way, repeated measures analyses of variance (RM-ANOVA) with one between subjects factor (i.e., group with two levels [ATC vs PRN]) and one within subjects factor (i.e. time with five levels) were done to examine each of the following outcome variables: pain intensity, pain duration, prescribed opioid dose, taken opioid dose, prescribed MQS score, and taken MQS score. This RM-ANOVA design allows for testing the main effect of group, the main effect of time, and the group by time interaction. If the Mauchly criterion indicated that the within subject's assumption of sphericity was not met, Greenhouse-Geiseer corrected p-values are reported. If the group by time interaction was significant, simple main effect tests were examined to help describe the nature of the interaction. For all tests, a p-value of less than 0.05 was considered statistically significant.

Results

Sample demographics

A total of 88 oncology outpatients participated in this study. There were 32 patients in the ATC group and 56 patients in the PRN group. Of those 32 patients in the ATC group, 25 (78.1%) were prescribed opioids on an ATC and PRN basis and seven (21.9%) were prescribed opioids on an ATC basis only. The demographic characteristics of the patients in the ATC and PRN groups are listed in Table 1. No significant differences were found in age, education level, gender, marital status, ethnicity, employment status, and living arrangements between the two groups. Patients in the PRN

group reported a significantly higher KPS score (73.9, t= -3.4, p= .002) than patients in the ATC group (65.0).

The diagnosis and treatment related characteristics of the two groups are listed in Table 2. No significant differences were found between the ATC and PRN groups on any of the disease or treatment characteristics except in the proportion of patients who were not receiving any current cancer therapy. A significantly larger percentage of patients in the ATC group were not receiving cancer therapy at the time of the study ($\chi^2 = 13.3$, p= .0003).

Baseline characteristics of the pain problem

All of the oncology outpatients were experiencing moderate to severe pain from bone metastasis that lasted almost half the day. Table 3 provides data on the pain characteristics of the two groups of patients at the time of enrollment into the study. Patients in the ATC group reported significantly higher worst pain scores at baseline (7.8; t = 2.6, p = .01) than patients in the PRN group (6.5).

Several significant differences were found between the two groups in the patients' ratings of how much pain interfered with activities (See Table 4). Patients in the ATC group compared to patients in the PRN group reported significantly higher pain interference scores associated with general activities (t= 2.1, p= .04), mood (t= 3.0, p= .004), walking ability (t= 2.0, p= .05), relations with other people (t= 3.5, p= .001), and enjoyment of life (t= 2.6, p= .01). Overall, patients in the ATC group reported a significantly higher total interference score (t = 3.1, p = .003) than patients in the PRN group.

Pain intensity and duration over time

Least, average, and worst pain scores, as well as the number of hours per day in pain over the 5 weeks of data collection for patients in the ATC and PRN groups are illustrated in Figure 1. Four separate two-way RM-ANOVAs found no significant group by time interaction between the two groups of patients in average, least, or worst pain intensity scores or in the number of hours per day that the patients experienced significant pain. No significant differences were found in the main effect of group or time for average, least, or worst pain intensity scores or in the number of hours per day that the patients experienced significant pain.

Pain medication data

Opioid dose.

Figure 2A illustrates the total opioid dose prescribed (in morphine equivalents) over the 5 weeks of data collection for patients in the ATC and PRN groups. A two-way RM-ANOVA showed a significant group by time interaction in total dose of prescribed opioid ($F(4,336) = 18.4$; $p<.00001$). Simple main effects indicated a significant increasing linear trend for the ATC group ($F(4,336) = 30.5$; $p<.00001$). There was no significant change over time in the average total opioid dose prescribed in the PRN group. A significant main effect of group indicated that the average total opioid dose prescribed was always significantly greater for the ATC group than for the PRN group ($F(1,84) = 46.6$; $p<.00001$).

Figure 2B illustrates the total opioid dose taken (in morphine equivalents), over the 5 weeks of data collection. A two-way RM-ANOVA showed a significant group by time interaction in total opioid dose taken for patients in the ATC and PRN groups

(F(4,336) = 17.3; p<.00001). Simple main effects indicated a significant increasing linear trend for the ATC group (F(4,336) = 28.2; p<.00001). There was no significant change over time in the total opioid dose taken in the PRN group. A significant main effect of group indicated that the average total opioid dose taken was always significantly greater for the ATC group than for the PRN group (F(1,84) = 40.4; p<.00001).

MQS scores.

Figure 3A illustrates the total MQS scores prescribed over the 5 weeks of data collection for patients in the ATC and PRN groups. A two-way RM-ANOVA found a significant group by time interaction in the MQS scores for prescribed analgesics (F(4,344) = 12.9; p<.0001). Simple main effects indicated a significant increasing linear trend for the ATC group (F(4,344) = 26.9; p<.00001). There was no significant change over time in the average MQS score for prescribed analgesics of patients in the PRN group. A significant main effect of group indicated that the average MQS score for prescribed analgesics of patients in the ATC group was always significantly greater than that of the PRN group (F(1,86) = 51.2; p<.00001).

Figure 3B illustrates the total MQS scores taken over the 5 weeks of data collection for patients in the ATC and PRN groups. A two-way RM-ANOVA found a significant group by time interaction in the MQS scores for analgesics taken by patients (F(4,336) = 12.7; p<.0001). Simple main effects indicated a significant increasing linear trend for the ATC group (F(4,336) = 24.5; p<.00001). There was no significant change over time in the average MQS score for analgesics taken by patients in the PRN group. A significant main effect of group indicated that the average MQS score for analgesics

taken by patients in the ATC group was always significantly greater than that taken by patients in the PRN group ($F(1,84) = 51.2$; $p<.00001$).

Discussion

This study is the first to follow the natural history of routine prescription and administration of analgesic medication and its effect on cancer pain intensity in oncology outpatients who were experiencing pain from bone metastasis. In theory, patients who were prescribed and who took pain medications on an ATC basis should have reported better levels of pain control than a similar group of patients who were prescribed and who took analgesic medications on a PRN basis. The findings contradict the established credo that ATC administration of analgesic medications compared to PRN administration should provide optimal pain management for patients with chronic cancer-related pain. Several factors need to be considered as one attempts to explain these surprising results.

One possible explanation for the lack of differences in pain intensity scores over time is that the pain medication regimens that the patients were on in this study were not effective treatments for bone metastasis. The majority of the patients in the ATC group were prescribed and were taking a sustained/controlled release opioid analgesic or were wearing a transdermal fentanyl patch. The majority of the patients in the PRN group were prescribed and were taking a combination opioid nonopioid preparation (e.g., codeine and acetaminophen, hydrocodone and acetaminophen). In addition, less than 20% of the patients in both groups received radiation therapy (RT) during the study and only one-third of the patients received pamidronate during the study. However, no differences were found between the ATC and PRN groups in the percentage of patients who were receiving RT or pamidronate. The optimal treatment regimen for patients who are

experiencing pain from bone metastasis warrants additional investigation because in the ATC group 93.4% of the patients told us that their pain returned in less than 8 hours from the time that they took their pain medication. In the PRN group, 84.9% of the patients reported similar data.

Another potential explanation for the lack of difference in the pain intensity measures of the ATC and PRN groups is that patients in both groups were tolerant to the effects of the analgesic medications. While information on the exact length of time patients in both groups were taking analgesic medications is not available, differences in tolerance between the two groups is not likely for several reasons. No differences were found in the length of time that patients in both groups were in pain. In fact, over 50% of the patients in both groups were in pain greater than 6 months. In addition, no differences were found in the percent of pain relief or in the amount of satisfaction with pain relief that these two groups of patients reported.

Another reason why differences in pain measures were not observed between patients in the ATC group and PRN group may be that the use of pain intensity measures may not be the most appropriate method for evaluating the effectiveness of analgesic medications. This explanation seems unlikely because numeric rating scales and visual analogue scales have been shown to be valid and reliable measures to evaluate the effectiveness of analgesic medications in a variety of analgesic studies (Broomhead et al., 1997; Bruera et al., 1999; Citron et al., 1998; Gourlay et al., 1997; Hagen & Babul, 1997; Peat et al., 1999; Grond et al., 1999; Reuben et al., 1999; Salzman et al., 1999; and Wong et al., 1997). However, this hypothesis warrants further investigation because most analgesic trials published to date were evaluating novel analgesic regimens or comparing

different routes of administration. The use of a novel analgesic regimen may have effected the patient's ratings of pain intensity. In our study, patient's prescriptions were not changed at the time of enrollment. Our patients were asked to record their pain intensity scores in "the context" of their routine analgesic administration. Perhaps an evaluation, over time, of patients' perceptions of pain relief would be a more appropriate outcome measure to evaluate the effectiveness of analgesic medications used in routine clinical care.

The most likely explanation for the surprising findings is that patients were not having their analgesic regimen titrated to effect or intolerable side effects. The titration of analgesics for oncology patients with a chronic pain problem like bone metastasis is a basic principle of effective pain control (World Health Organization, 1996; Jacox et al., 1994). While patients in the ATC group had significant increases in their analgesic regimen prescribed over time and these patients did increase their analgesic consumption over time; these increases were not sufficient to decrease their pain intensity scores. Patients in the PRN group did not have their analgesic prescriptions increased over time nor did they increase the consumption of their analgesic medications. The failure to titrate analgesic medications to effect or intolerable side effects appears to be a significant barrier to effective pain control in this population of oncology outpatients who are experiencing pain from bone metastasis.

It is not readily apparent why patients in the ATC group were prescribed seven times more opioid analgesics and were taking twenty-one times more analgesic medications (based on MQS scores) than patients in the PRN group. No correlations were found in either group between any of the pain intensity measures or hours per day in pain

and analgesic medication dose prescribed or taken. In fact, no information is available on how clinicians perform pain assessments or make decisions about which analgesic medication and which dose of medication to prescribe to oncology outpatients with chronic pain problems.

Several limitations of this study are worth noting. The length of time that patients were taking analgesic medications and the length of time on a particular regimen is not known in these two groups of patients. The sample was primarily of Caucasian origin that limits the generalizability of the study findings. The pain problem was limited to one cause, therefore these findings may not apply to oncology outpatients with other types of chronic pain problems.

The results of this study challenge an accepted principle of effective cancer pain management (i.e., that analgesics should be given to patients on an ATC basis rather than on a PRN basis to achieve optimal pain control). While this principle is sound based on pharmacokinetic considerations and we agree that patients with chronic cancer pain should be given analgesics on an ATC basis with a PRN order for breakthrough pain, an equally important principle for effective cancer pain management is to titrate to effect or intolerable side effects. It appears that this second principle is not being followed in routine care of oncology outpatients who are experiencing pain from bone metastasis.

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Table 1

Comparison of the demographic characteristics of the patients

Characteristics of patients		Mean (SD) ATC Group (n=32)	Mean (SD) PRN Group (n=56)	Statistic, significance
Age (years)		56.5 (12.6)	59.6 (12.3)	NS
Education (years)		14.2 (3.1)	13.9 (3.1)	NS
Karnofsky		65.0 (12.5)	73.9 (8.6)	t = -3.4, p= .002
Gender (%)	Male	38.7	29.1	NS
	Female	61.3	70.9	
Lives Alone (%)	Yes	30.0	40.0	NS
	No	70.0	60.0	
Marital Status (%)	Married	64.5	45.5	NS
	Other	35.5	54.5	
Ethnicity (%)	Caucasian	83.9	81.8	NS
	Other	16.1	18.2	
Employment Status (%)	Working Full-time or Part-time	13.3	18.2	NS
	Disability	40.0	29.1	
	Retired	26.7	38.2	
	Other	20.0	14.5	

Table 2

Disease related characteristics of patients in the around-the-clock (ATC) group and patients in the as-needed (PRN) group

	Percentage (%)		
Characteristics of patients	ATC Group (n=32)	PRN Group (n=56)	Statistic, significance
Cancer Diagnosis			
Breast	40.6	55.4	NS
Prostate	12.5	12.5	NS
Lung	21.9	8.9	NS
Other	25.0	23.2	NS
Current Treatment			
Radiation	15.6	20.0	NS
Chemotherapy	37.5	50.9	NS
Biotherapy	3.1	1.8	NS
Hormonal Therapy	25.0	40.0	NS
No Therapy	31.3	1.8	$\chi^2 = 13.3$, p=.0003
Therapy received since the beginning of study			
Radiation	12.5	16.4	NS
Pamidronate	28.1	34.5	NS
Strontium-89	0.0	1.8	NS

Table 3

Baseline pain characteristics of patients in the around-the-clock (ATC) group and patients in the as-needed (PRN) group

Characteristic of patients	Mean (SD)		Statistic, significance
	ATC Group (n=32)	PRN Group (n=56)	
Pain right now	4.1 (2.5)	3.7 (2.1)	NS
Average daily pain	4.7 (1.7)	4.1 (1.8)	NS
Worst pain	7.8 (2.0)	6.5 (2.2)	t = 2.6, p = 0.01
Least pain	2.3 (2.1)	1.9 (1.4)	NS
Days pain interferes	4.9 (2.3)	5.1 (2.4)	NS
Hours per day that pain lasts	12.1 (7.5)	10.0 (8.0)	NS
Pain relief (%) last week [1]	69.4 (20.2)	69.0 (22.1)	NS
Satisfaction with pain relief [2]	7.0 (2.5)	6.6 (2.8)	NS
Length of time in pain (%) [3]			
Less than one week	3.2	5.6	NS
1 to 2 weeks	3.2	1.9	
About 1 month	3.2	3.7	
2 to 6 months	32.3	35.2	
7 months to 1 year	16.1	22.2	
More than 1 year	41.9	31.5	

Pain limits work activities (%)[4]			
Yes	54.8	59.6	NS
No	0.0	9.6	
Not employed	45.2	30.8	
Hours before pain returns (%)[5]			
Medications do not help	0.0	5.7	NS
1 hour	10.0	11.3	
2 hours	10.0	9.4	
3 hours	30.0	15.1	
4 hours	16.7	20.8	
5 to 8 hours	26.7	22.6	
9 to 12 hours	3.3	7.5	
More than 12 hours	3.3	1.9	
Do not take medications	0.0	5.7	

[1] In the last week, how much relief have you gotten from your pain medicine?
[2] How satisfied are you with the amount of pain relief you are experiencing?
[3] How long have you been in pain?
[4] Has your cancer pain forced you to limit your work activities?
[5] When you take your pain medicine, how many hours does it take before the pain returns?

Table 4

Pain Interference with Activities [from the Patient Outcomes Questionnaire]

Activity	Mean (SD)		Statistics, significance
	ATC Group (n=32)	PRN Group (n=56)	
General activity	6.2 (2.5)	5.0 (2.6)	t= 2.1, p= .04
Mood	5.7 (2.8)	4.0 (2.5)	t= 3.0, p= .004
Walking ability	6.3 (2.7)	5.0 (3.1)	t= 2.0, p= .05
Normal work	6.8 (2.7)	5.6 (3.0)	NS
Relations with other people	4.8 (2.7)	2.8 (2.5)	t= 3.5, p= .001
Sleep	4.8 (2.8)	4.3 (2.7)	NS
Enjoyment of life	6.0 (2.6)	4.4 (2.9)	t= 2.6, p= .01
Sexual activity	6.6 (3.8)	5.0 (4.2)	NS
Total interference score (Range from 0 to 80)	47.1 (16.6)	35.8 (16.5)	t = 3.1; p = .003

Figure 2B

The total opioid dose taken (in morphine equivalents) over the 5 weeks of data collection for oncology outpatients in the around-the-clock (ATC, n = 32) and as needed (PRN, n = 56) groups. Values are plotted as means $\pm$ standard errors of the mean.

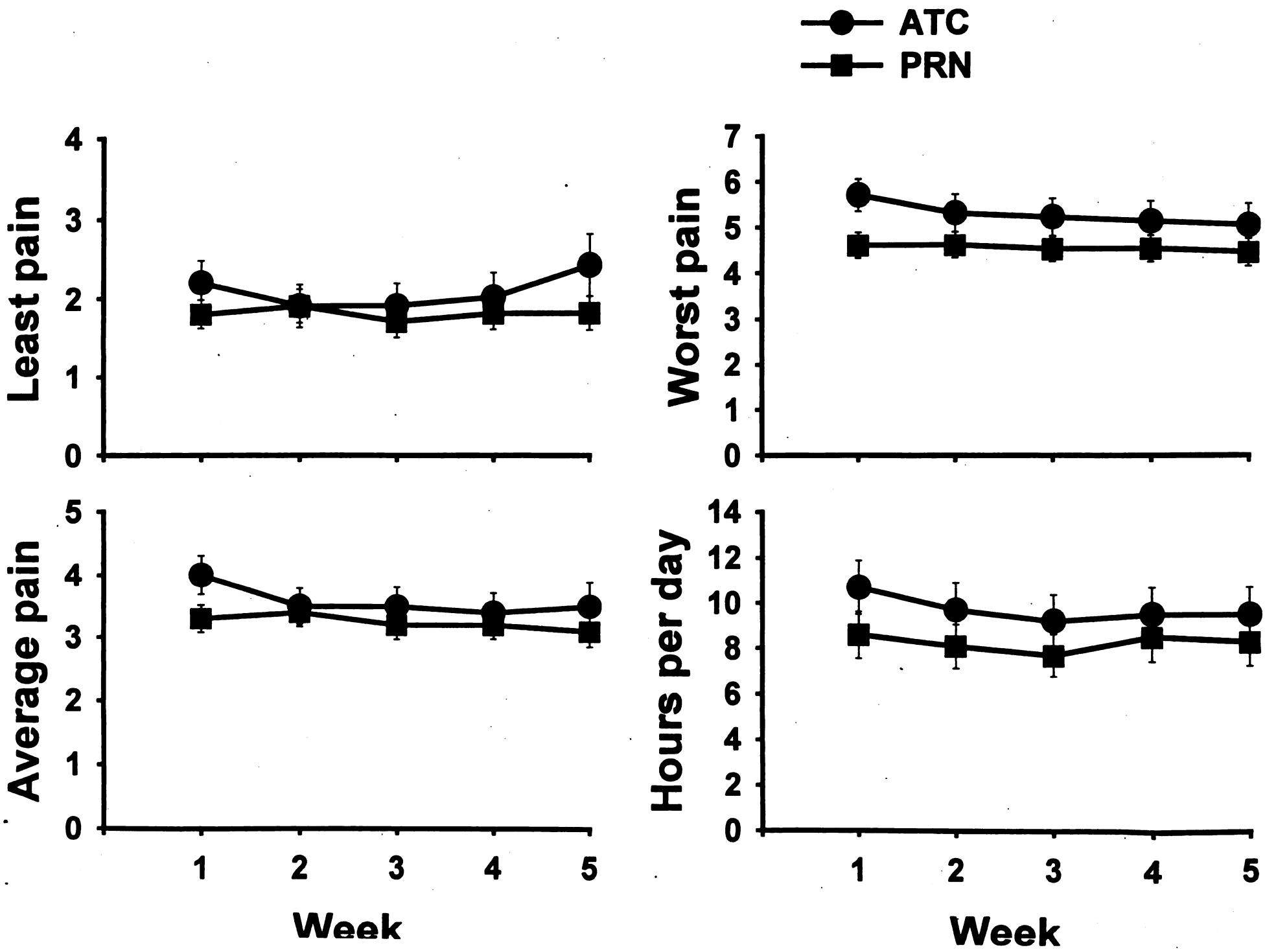
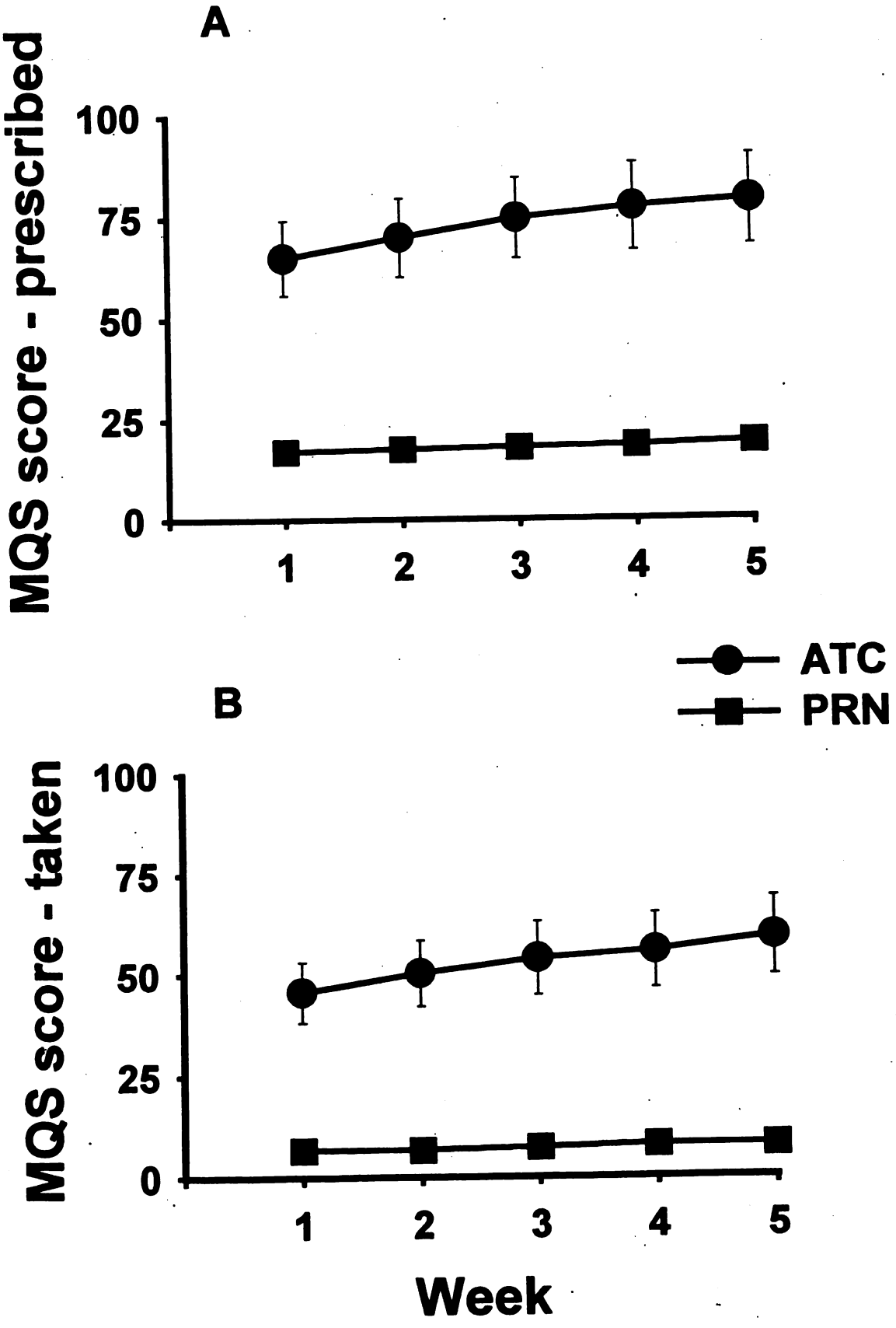

ATC
PRN
Least pain
Worst pain
Average pain
Hours per day
Week
Week
0
1
2
3
4
5
6
7
8
10
12
14

Figure 2A

Least, average, and worst pain intensity scores and average number of hours per day in pain over the 5 weeks of data collection for oncology outpatients in the around-the-clock (ATC, n = 32) and as-needed (PRN, n = 56) groups. Values are plotted as means $\pm$ standard errors of the mean.

Figure 3B

The total medication quantification scale (MQS) score for analgesic medications taken over the 5 weeks of data collection for oncology outpatients in the around-the-clock (ATC, n = 32) and as-needed (PRN, n = 56) groups. Values are plotted as means + standard errors of the mean.


A
MQS score - prescribed
100
75
50
25
0
1
2
3
4
5
ATC
PRN
B
MQS score - taken
100
75
50
25
0
1
2
3
4
5
Week