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A microcosting analysis of zoledronic acid and pamidronate therapy in patients with metastatic bone disease

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Abstract Our goal was to calculate resource use associated with administration of zoledronic acid, compared with pamidronate, as palliative care for patients with metastatic bone lesions. We conducted a time-and-motion study of therapy administration at each of three outpatient chemotherapy infusion sites participating in clinical trials of zoledronic acid and pamidronate. We developed a data-collection instrument to record all staff effort and patient resource use in drug administration. The main outcome measures were (a) direct costs of therapy administration per patient and (b) opportunity benefits expressed as the availability of resources gained per year. The average visit time for patients receiving the study dose of zoledronic acid, 4 mg, was 1 h, 6 min, compared to 2 h, 52 min for patients receiving a 90-mg dose of pamidronate. Infusion time accounted for much of the difference. In the base-case analysis, total direct costs per patient were $728 for zoledronic acid and $776 for pamidronate. The opportunity benefit for infusion of zoledronic acid vs pamidronate in the base case was 1.8 chairs per day, or 426 chairs per 240-workday year. Results were sensitive to changes in infusion facility size, days of operation, and average number of patients treated. Shorter infusion time associated with the administration of zoledronic acid, compared with pamidronate, yields substantial time savings for patients, as well as opportunity benefits for outpatient oncology facilities.

Keywords Costs and cost analysis · Palliative care · Time and motion studies · Zoledronic acid · Pamidronate

Introduction

Over the past decade, intravenous bisphosphonates have emerged as an important tool in palliative care for patients with metastatic bone disease. Pamidronate currently constitutes the standard of care for prevention of skeletal-related events in patients with bone metastases secondary to breast cancer and multiple myeloma. A new third-generation bisphosphonate, zoledronic acid, has a reported potency at least 100 times greater than that of pamidronate and potential activity in metastatic disease associated with a greater range of primary tumors [1]. In addition to greater potential potency, recommended zoledronic acid infusion time is considerably shorter than that for pamidronate.

Traditionally, microcosting studies in health care have been developed to assess resource use associated with specific activities when data regarding the resources re-

quired for treatment are not adequately captured in administrative data sets or through accounting systems. These studies allow the quantification of costs that are difficult to assess and often higher than anticipated. Such detailed assessments of the resources used in providing a service can more accurately reflect practice expense components than resource-based relative value units [2] or other measures. Microcosting methods have been used to compare treatment costs and length of stay in an inpatient setting [3]; these methods may offer increased accuracy in assessing labor costs associated with drug infusion in the outpatient setting, especially since there currently are no detailed databases that collect information on staff effort and supply costs for individual patients in community oncology practices. However, microcosting methods in the outpatient setting may substantially underestimate the benefits offered by more efficient infusion services from the perspective of patients.

In this study, we applied standard microcosting methodologies to assess resource use associated with administration of zoledronic acid compared with pamidronate as palliative care for patients with metastatic bone disease. In addition, we evaluated the benefits associated with use of the less time-consuming therapy. Reduced infusion time has the potential to provide direct benefits to patients, in the form of shorter visit duration, and to the practice, in terms of additional availability of fixed and often scarce resources (termed its "opportunity benefit" in this paper). From the practice's perspective, the additional availability of resources provides the opportunity to divert these resources toward other pressing needs of the facility, such as increased chemotherapy administration or additional supportive care visits.

Patients and methods

Microcosting model

The model used to assess variable and fixed costs was designed to account for the range of variable and fixed costs involved in administration of bisphosphonate therapy in an outpatient oncology practice. Although a wide range of infusion-setting characteristics exists, results reported from this microcosting analysis were obtained using a base case derived from the average of observed characteristics at three sites.

Data collection

A data-collection instrument based on existing microcosting methods was developed to record all staff effort and patient resource use during drug administration at three outpatient chemotherapy infusion sites participating in ongoing clinical trials of the investigational drug zoledronic acid (ZOL 010, ZOL 011, Novartis Pharmaceuticals, East Hanover, N.J.), one each in Florida, Oregon, and Indiana. The objective of protocol 010 is to study the efficacy of zoledronic acid compared with pamidronate in preventing skeleton-related events in patients with osteolytic bone disease associated with multiple myeloma and breast cancer. Protocol 011 compares the efficacy of zoledronic acid with that of placebo in prevention of skeleton-related events in patients with osteolytic bone disease associated with lung cancer and with solid cancers other than lung, breast, and prostate.

The three oncology practices were representative of practice sites in a major physician practice management company. Two patients were observed at each site, one patient with an infusion of either pamidronate or placebo and one patient with an infusion of either zoledronic acid or placebo. The data-collection instrument was pilot-tested at one infusion site not included in the study. A structural assessment of fixed and variable resources that comprise the practice infrastructure was also developed. Trained research analysts observed and recorded the preparation, infusion, and follow-up time involved in therapy administration, as well as the personnel involved with each phase of the treatment. Finally, all supplies used in therapy preparation and administration, including both disposable and durable medical equipment, were recorded.

Valuation of variable costs

Variable costs were calculated by summing values for total labor costs, total supply resource costs, and total drug costs for each patient. Time intervals for drug administration were recorded for each patient and were averaged across the three sites for each of the two clinical trial protocols.

Labor costs

Total labor costs were obtained by summing the labor costs for each procedure performed during the patient visit using the procedure's average time. Each procedure's labor cost was calculated as the product of the time measured for each step in the process and the hourly wage rate of the personnel performing the labor. Hourly wages for each personnel type (e.g., physician, laboratory technician) were determined using 1999 national average wages for the position. Fringe benefits were calculated as a percentage of the annual wage (based on prorated university fringe benefit rates current as of 12 July 2000 at the Department of Medicine, Duke University Medical Center). Annual salaries were converted to hourly wages by dividing the average annual salary, with fringe benefits added, by 1920 h (8 h per day, 240 workdays per year).

Supply costs

Total supply resource costs were calculated by adding the total costs of all disposable supply resources used during each patient visit. Unit costs were obtained for each product from ordering schedules at the data-collection sites. Quantities of each resource used were recorded during direct observations, and these amounts were multiplied by unit costs for each resource to obtain total resource costs for each item.

Drug costs

Total drug costs were calculated using the assumption of one drug unit per patient visit. A cost of $565.71 for a 90-mg dose of pamidronate was calculated by deducting an estimated standard 16.6% from the 2000 average wholesale price ($678.31) [4]. Because zoledronic acid had not yet been assigned a price at the time of study, a 4-mg dose of zoledronic acid was assigned the same price and unit cost as that of pamidronate. This assumption was made to remove the effect of drug price from the analysis. Drug price is, however, included in this analysis and in the interactive version of this model to accommodate future pricing.

Valuation of fixed costs

Fixed costs were calculated for each patient by summing the values for utilities, rent, maintenance, capital, administration and staffing, and durable medical equipment. Costs were obtained by querying administrators at each site about their expenditures for these items.

Utilities, rent, maintenance, and capital costs

Utilities, rent, maintenance, and capital costs were obtained by multiplying the total area of the drug infusion facility in square feet by $25, an estimated average industry cost for leasing class A medical office space. This annualized amount was converted to a per-patient cost by dividing it by the total number of patients treated in 1 year (calculated by multiplying the average number of patients per day by the total number of days of operation per year).

Administration and staffing costs

Administration and staffing costs were estimated on an annual basis as 5% of total revenues, comprised of drug and procedure reimbursement revenues according to payer mix (C.H. Weaver, personal communication, 1996). This annual amount was divided by the total annual number of bisphosphonate patient visits to obtain administration and staffing costs for each patient. Procedure reimbursement costs were calculated based on resource-based relative value units and *Current Procedural Terminology* codes for laboratory complete blood count, office or outpatient visit, intravenous infusion for therapy or diagnosis of up to 1 h, and intravenous infusion for each additional hour. Procedure reimbursement amounts were calculated using nonfacility reimbursement indices to reflect the community outpatient setting and geographic practice cost index values to account for geographic variation in reimbursement schedules from Medicare. Drug reimbursement was calculated based on reimbursement rates for these Medicare patients as a percentage of the average wholesale price (Medicare 95%), current as of 1999.

Durable medical equipment costs

Durable medical equipment costs were obtained by estimating an annual cost for these resources based on their original unit costs [5]. Each equipment item was assumed to have a lifespan of 7 years, after which it would be replaced and have no salvage value. Based on both the number of infusion chairs at a facility and the chair time associated with either pamidronate or zoledronic acid therapy, a percentage of annual chair use was calculated for each treatment. This percentage was used to calculate annual costs for the use of durable medical equipment for the therapies as part of their respective fixed cost estimates.

Data analysis

We created a decision model to generate the direct costs and opportunity costs and benefits associated with zoledronic acid and pamidronate therapy based on our data-collection efforts. We used the following assumptions for the base-case analysis: medium-sized facility (6–12 infusion chairs) in Ft Lauderdale, Fla; 10 available infusion chairs; facility size of 5300 sq ft; average of 8 patients per day receiving bisphosphonate therapy; Medicare as primary insurance; 1920 personnel hours per year (8 h per day, 240 workdays per year); personnel fringe benefits at 23% of base salary; administration and staffing costs at 5% of total revenue; wholesale acquisition price of $565.71 per dose of pamidronate or zoledronic acid; and a 7-year lifespan for durable medical equipment.

Time

Patient benefit was reported as treatment time saved per visit and was calculated using the decision model, substituting the infusion time of a bisphosphonate practice based on pamidronate for that of a bisphosphonate practice based on zoledronic acid.

Annual direct costs

Total costs were calculated by summing variable costs and fixed costs based on an estimate of bisphosphonate patient volume. The annual cost difference was calculated by substituting the total costs of a bisphosphonate practice using pamidronate for the costs of a bisphosphonate practice using zoledronic acid.

Annual opportunity benefits

Opportunity benefits were expressed as the number of additional chairs made available each day through the use of the more efficient treatment. Number of chairs made available was calculated by subtracting the chairs required per day for zoledronic acid administration from those required for pamidronate administration. Calculations for chairs required per day involved multiplying total infusion chair time per patient visit by the average number of patient visits per day to produce total number of chair hours required per day for patients receiving bisphosphonate therapy. This amount was then divided by the daily hours of operation to yield chairs required per day. Number of additional chairs available each year is the product of the daily additional chairs and the number of days of operation per year.

Sensitivity analyses

Using the decision model, we conducted a sensitivity analysis using the base-case scenario. The following inputs were varied: infusion facility size, number of infusion chairs, workdays per year, and average number of patients per day receiving bisphosphonate therapy. Outcome measures were total costs, chairs freed per day, and chairs freed per year.

Results

Time

Average total time required to administer the study dose of zoledronic acid was 1 h, 6 min (standard deviation [SD] 27 min), compared to 2 h, 52 min for a 90 mg dose of pamidronate (SD 16 min). This amounts to a patient benefit of 1 h, 46 min per visit. Average total times for pre-infusion preparation, drug preparation, and follow-up were similar for both treatments; however, average times for drug infusion alone (Table 1) were 25 min for zoledronic acid (SD 6 min) and 2 h, 10 min for pamidronate (SD 6 min).

Table 1 Mean time for drug administration by therapy

Procedure	Pamidronate (h:min:s)	Zoledronic acid (h:min:s)	Personnel
Pre-infusion			
Pre-infusion vitals	0:03:02	0:02:34	Lab technician
Phlebotomy	0:04:30	0:02:19	Lab technician
Physical exam	0:08:21	0:11:07	Physician
Total	0:15:53	0:16:00	
Drug preparation/set-up			
Preparation	0:02:38	0:03:41	Pharmacy technician
Reconstitution	0:01:27	0:00:43	Pharmacy technician
Dilution	0:00:44	0:01:18	Pharmacy technician
Total	0:04:50	0:05:42	
Administration/infusion			
Prepare/insert IV	0:02:21	0:04:29	Nurse
Prepare/hang drug	0:02:15	0:01:31	Nurse
Attach/connect tubing	0:02:03	0:02:11	Nurse
Saline infusion	0:03:53	0:02:59	Nurse
Drug infusion	2:10:02	0:24:48	Nurse
Saline flush	0:07:33	0:04:25	Nurse
Total	2:28:07	0:40:21	
Follow-up			
Remove/discard IV	0:01:13	0:01:30	Nurse
Bandage/discharge	0:02:23	0:02:24	Nurse

Table 2 Variable costs per patient visit[a]

Variable costs	Pamidronate	Zoledronic acid
Total labor costs ($)	93	47
Total supply resource costs ($)	8	8
Total drug costs ($)	566	566
Total variable costs ($)	667	621

[a] Assumes fringe benefits of 23% of annual salary and hourly wages of relevant personnel based on 1,920 h per year (8 h per day, 240 workdays per year).

Annual direct costs

All costs are based on our base-case scenario and are expressed in 1999 US dollars. Total variable costs per patient visit were $621 for patients receiving zoledronic acid and $667 for patients receiving pamidronate (Table 2). This difference derives entirely from the differential in labor costs associated with the additional time required for drug infusion ($47 for zoledronic acid vs $93 for pamidronate). Table 3 shows the wage calculations associated with labor costs for the average infusion times observed. Costs for the use of disposable medical equipment were assumed to be identical ($8.31) in both arms of the study (Table 4).

Table 3 Wage calculations by treatment

Personnel	Annual salary ($)	Fringe benefits ($)	Total time (h:min:s)	Hourly wage ($)	Personnel costs ($)
Pamidronate					
Physician	192,055	44,173	0:08:21	123.04	17.12
Nurse	44,458	10,225	2:31:44	28.48	72.02
Lab technician	31,775	7,308	0:07:32	20.36	2.55
Pharmacy technician	24,040	5,529	0:04:50	15.40	1.24
Zoledronic acid					
Physician	192,055	44,173	0:11:07	123.04	22.81
Nurse	44,458	10,225	0:44:15	28.48	21.01
Lab technician	31,775	7,308	0:04:53	20.36	1.65
Pharmacy technician	24,040	5,529	0:05:42	15.40	1.46

Table 4 Resource costs for disposable medical equipment[a]

Item	Quantity	Unit cost ($)	Total cost ($)
Primary tubing	1	1.80	1.80
Secondary tubing	1	0.97	0.97
Needles	2	0.06	0.12
Gauze	2	0.01	0.02
Thermometer cover	1	0.07	0.07
Alcohol swab	2	0.01	0.02
Syringe	2	0.10	0.20
Set of gloves	3	0.11	0.33
Medical tape	1	0.71	0.71
Saline bag	2	0.66	1.32
Test tubes	2	0.07	0.14
Disposable IV	1	2.06	2.06
Piggyback connector	1	0.55	0.55
Total	–	–	8.31

[a] Use of disposable medical equipment is identical for pamidronate and zoledronic acid therapies. The costing model allows for addition of other disposable items.

Table 5 Fixed costs by treatment

Item	Pamidronate	Zoledronic acid
Fixed annual costs		
Utilities, rent, maintenance, capital ($)	132,500	132,500
Administration and staffing ($)	75,698	73,535
Durable medical equipment		
Infusion pump ($)	254	97
IV pole ($)	1	<1
Electronic blood pressure machine ($)	2	1
Complete blood count machine ($)	86	33
Infusion chair ($)	4	2
Electronic thermometer ($)	25	10
Scale ($)	8	3
Total durable medical equipment ($)	380	145
Total fixed annual costs ($)	208,578	206,181

Table 6 Sensitivity analysis: costs and opportunity benefits by treatment

Input	Costs per patient visit ($)		Cost savings ($)	Opportunity benefits	
	Pamidronate	Zoledronic acid		Chairs/day	Chairs/year
Base case	776	728	47	1.8	426.0
Infusion facility size (sq ft)					
4,300	763	715	47	1.8	426.0
4,800	769	722	47	1.8	426.0
5,300	776	728	47	1.8	426.0
5,800	782	735	47	1.8	426.0
Days of operation per year					
160	810	763	47	1.8	284.0
200	790	742	47	1.8	355.0
240	776	728	47	1.8	426.0
280	766	719	47	1.8	497.0
320	758	711	47	1.8	568.0
Average number of patients per day					
4	845	797	47	0.9	213.0
8	776	728	47	1.8	426.0
12	753	705	47	2.7	639.0
16	741	694	47	3.6	852.0
20	734	687	47	4.4	1065.0

Total annual fixed costs were slightly higher for pamidronate therapy ($208,578 vs $206,181 for zoledronic acid), driven by the higher annual usage costs of durable medical equipment for patients in the pamidronate arm ($380 vs $145 for zoledronic acid) (Table 5).

Opportunity benefits

The opportunity benefits for a given facility were measured in number of infusion chairs made available through the use of the more efficient treatment. When the average number of bisphosphonate patients treated per day was set at 8 in the base case, use of zoledronic acid compared with pamidronate was estimated to free 1.8 additional chairs per day, or 426.0 additional chairs per 240-workday year.

Sensitivity analysis

Results for total costs per patient visit were sensitive to changes in infusion facility size, days of operation, and

average number of patients treated, while results for opportunity benefits were sensitive to days of operation per year and average number of bisphosphonate patients treated per day (Table 6).

Discussion

Both cost consequences and patient expectation of benefit depend on how intravenous bisphosphonates are delivered [6]. Compared with an oral route of administration, infusion therapies are associated with substantial patient burden and higher costs [7]. Patient burden from the longer infusion time required for pamidronate therapy has been cited as an important consideration in assessing the benefits of this therapy [8]. In outpatient community oncology practices offering palliative treatment for patients with metastatic cancer, finite practice resources can be allocated based on practice expenses associated with the different therapies. Thus, therapies that provide at least equivalent benefits and reduced infusion time have the potential to offer direct benefits to patients and an opportunity to use fixed practice resources to treat additional patients. While efficacy data comparing pamidronate and zoledronic acid are forthcoming, in this study, shorter infusion time resulted in a substantial reduction in patient visit time and in nurse labor costs at the practice level. In addition, shorter infusion times for bisphosphonate therapy resulted in substantial opportunity gain to practices by making available additional fixed assets (infusion chairs).

Microcosting studies generally are reserved for settings in which other means of obtaining data on practice efficiency are not available. In economic analysis, microcosting studies are rarely used due to their expense and to the limited types of questions they address. Because of the limited number of patients monitored in each treatment arm, there is a possibility of measurement error in the times recorded (with ranges represented as standard deviations). However, microcosting methods were useful in this setting because there was no other means of assessing resource use associated with bisphosphonate infusion therapy. Through intensive, direct observation of tasks associated with pamidronate and zoledronic acid infusion, the time-and-motion data-collection strategy offers a more accurate assessment of labor and nonlabor resources expended than other data-collection methods [9].

We faced several challenges in conducting this assessment. First, medical practice is not standardized across practice sites. Thus, even though we developed our data-collection instrument based on a single practice setting, we found differences in actual procedures across practice sites. We made adjustments for these differences to report an average practice cost across the three sites, but applicability of the results to any individual practice site will be based on actual practices at that site. In addition, opportunity gain to practices using zoledronic acid would be realized differently depending on how practices use additional freed chair time; alternative uses of infusion chair time would be associated with varying patient benefit, overhead, and profit.

Since zoledronic acid therapy had not been approved by the Food and Drug Administration in the United States during the period of this analysis, this microcosting study was developed in the setting of a clinical trial of zoledronic acid therapy and a comparative trial of zoledronic acid therapy vs pamidronate therapy. While the clinical trial protocols may not dictate infusion practices that are different from those in the usual practice setting, our observed infusion times did differ from those dictated by the protocols. At the same time, our nurse-to-patient ratio of 1:1 during the infusion may have been more reflective of the research setting we observed. The value of economic analysis lies in the model that is developed. Based on data observed at three oncology practices, the present model fulfills this need for information useful in assessing true costs of therapy both in the trial and practice settings.

Conclusions

We successfully conducted a microcosting study in three community oncology practices to determine the benefit of shorter infusion time for patients and for clinical practices. In this assessment, shorter infusion time required for zoledronic acid was associated with substantial patient benefit, as well as opportunity benefits for the practices.

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