Acute oral pain and mucositis in bone marrow transplant and leukemia patients: Data from a pilot study

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Abstract:

The purposes of this prospective, repeated-measures descriptive pilot study were to describe patterns of acute oral pain and mucositis in patients receiving a bone marrow transplant or high-dose chemotherapy for leukemia, and to test procedures and instruments before initiating a larger intervention study. A nonprobability, purposive selection process was used to enroll 18 patients admitted to two acute care inpatient hospital units for bone marrow transplantation or leukemia therapy at a university health sciences center in the southeastern United States. Data were collected at baseline, then daily through patient interviews, oral examination, and chart review for at least 3 weeks or until discharge. Research variables were pain intensity, intolerable pain, verbal descriptors of pain, pain relief, and use of pain relief strategies (Pain Assessment Form), mucositis (erythema and ulceration) in eight anatomic locations of the oral cavity (Oral Mucositis Index), voice/talking (Oral Assessment Guide), and mood states (11-item Brief Profile of Mood States). Mild to moderate pain occurred in nearly 70% of patients and was described as "tender," "irritating," and "sore." Patients used pain medicines, mouth care, and mental and physical activities to relieve pain, and reported partial overall relief of pain. Mucositis was mild, with the tongue and buccal and labial mucosa most commonly affected with erythema and the buccal mucosa with ulceration. Voice/talking were only mildly impaired, and mood disturbance was mild. Patterns of pain, mucositis, and mood disturbance were consistent with each other and followed the trajectory described in previous research. Results suggest that nurses should continue to assess these symptoms vigorously and assist patients in selecting multiple management strategies. Research using repeated-measures designs in this acutely ill inpatient population is challenging and needs careful attention by researchers. The results have been used to improve the ongoing larger intervention study.

Article:

Pain in individuals diagnosed with cancer is a significant and challenging clinical problem. It is multidimensional in nature (1,2) and requires an interdisciplinary approach as well as multimodal interventions for successful management (3). Acute oral pain caused by mucositis from intensive cancer chemotherapy affects more than 75% of patients (4-6). This pain can be

severe, inhibit nutritional intake, restrict communication with others, cause psychosocial distress, contribute to infections, and even cause premature withdrawal from therapy (7-9). Despite effective state-of-the-art pain management, including behavioral therapy (7,9,10), there is evidence that patients still do not achieve complete relief of pain caused by mucositis (4,11).

Nurses who care for patients with acute oral pain and mucositis often assume a major role in assessment and management of these treatment side effects, using a variety of pharmacologic, physical, nonpharmacologic, and educational strategies (12). Few studies have investigated the effects of systematic nurse-implemented multimodal interventions for acute oral pain or mucositis on such patient outcomes as decreased duration or severity of symptoms or psychosocial distress. A pilot study was conducted within the context of a large funded intervention project aimed at improving these outcomes. The purposes of the pilot study were two: (a) describe patterns of acute oral pain and mucositis in patients undergoing bone marrow transplantation (BMT) or high-dose chemotherapy for leukemia, and (b) test procedures and instruments before initiating the larger study. This article addresses only the first purpose by presenting descriptive data on pain and mucositis.

REVIEW OF LITERATURE

Acute Oral Pain

Cancer-related pain has multiple causes: the disease itself and a plethora of diagnostic, treatment, and complication factors (8,13,14). Common among syndromes of treatment-related pain is the acute oral pain secondary both to intensive cytoreductive conditioning regimens for BMT (high-dose chemotherapy and sometimes total body irradiation) and to intensive induction regimens used to treat leukemia (8). Both treatment approaches have evolved into highly sophisticated treatment modalities accompanied by numerous side effects (15,16). Miser and colleagues (17), in a prevalence survey of pediatric and young adult cancer patients, reported that 40% had treatment-related pain, including 27% with acute oral pain due to mucositis. Kolbinson et al. (18), studying oral changes after transplantation, noted that 70% of BMT patients required intravenous opioids for pain management. Chapko and colleagues (19) described the time course and variations in acute oral pain after BMT, but did not give incidence or prevalence data.

Three studies have reported incidence data. McGuire et al. (4) documented an incidence rate of 86% in 47 patients undergoing allogeneic and autologous BMT and found that patients most commonly used pain descriptors such as "tender," "aching," and "sharp." Gaston-Johansson and her research group (5) reported that all 17 (100%) of the autologous BMT patients in their study reported acute oral pain, most often described as "sore," "burning," "dull," and "aching." Finally, Waterman and colleagues (6) noted an incidence rate of 89% in 100 patients undergoing BMT. In these three studies, patients' pain peaked about 7 to 8 days after transplantation, resolved by day 21, and had mild to moderate intensity. It is important to note that because patients in these studies were receiving preparative regimens with varying oral toxicities, those with severe acute oral pain and mucositis may have been underrepresented.

Few data on the incidence and severity of acute oral pain and mucositis in nontransplant leukemia therapy are available, but clinical experience with treatment regimens that cause mucositis suggests that these problems are common. Only one study (5) explored psychologic aspects of acute oral pain and mucositis, revealing that anxiety and depression were higher than

normal during treatment. Although pain is distressing for some patients, others may interpret it as meaning that their cytoreductive therapy is working. Because this pain is short-lived, these individuals may be able to benefit from nurse-administered, multimodal interventions once a clearer picture of specific patterns of pain, mucositis, and emotional distress emerges to help develop such interventions.

Mucositis Secondary to Cancer Treatment

Chemotherapy, BMT conditioning-associated therapy, or both can produce serious direct and indirect stomatotoxic alterations in oral mucosa (4,20,21). Such alterations can be associated with a wide range of mucosal changes, including infection, bleeding, and pain (22). By comparison, an intact oral mucosal barrier serves a variety of host defense functions (23).

Mucositis occurs in an estimated 40% of individuals receiving intensive cytoreductive therapy, and can exceed 75% in BMT cohorts (4-6,24). The lesions typically manifest with mucosal burning and erythema approximately 10 days after initiation of therapy, and may progress to diffuse, extensive, painful oral ulcerations (24). These ulcerations often persist for 2 weeks after their onset, with resolution based on cessation of the cytotoxic agents and return of blood cell counts to normal ranges (24).

Mucositis and the pain that may result interfere with adequate oral intake, predispose patients to infections, may cause bleeding, interfere with social interaction, and cause psychosocial distress (5). Patients undergoing BMT, and their nurses as well, have cited acute oral pain, mucositis, and inability to eat as major sources of distress (25). In some cases, exceedingly severe mucositis might result in life-threatening situations or cause patients to withdraw from treatment (7,9). Infections that originate in the oral cavity are also a major concern because they may progress to systemic infections in the myelosuppressed patient (26).

Significance

The significance of this research relates to several specific areas. As noted earlier, acute oral pain and mucositis are prevalent in patients undergoing BMT or intensive cytoreductive therapy, yet are extremely variable in incidence and severity according to preparative regimen. These two symptoms, cited as important clinical research priorities in oncology nursing for many years (27-29), have been the subject of NIH Consensus Conferences (30,31) and clinical practice guidelines (3). This research provides a better understanding of the multidimensional experience of acute oral pain (2). Finally, the researchers conducted this pilot study to identify clinical and methodologic issues as a preliminary step to implementing the larger intervention study.

Conceptual Framework

The conceptual framework for this study describes cancer-related pain as a multidimensional experience consisting of physiologic, sensory, affective, cognitive, behavioral, and sociocultural dimensions (1,2). This framework views pain as a subjective phenomenon best described by the individual who has it, and offers a comprehensive way to consider an individual's experience of pain and to select interventions. Based on the Gate Control Theory of Pain (32), this framework was initially proposed and confirmed with five dimensions by Ahles and colleagues (1), who studied patients with cancer-related pain and measured components of each dimension. In a similar study, McGuire (33) found support for these five dimensions and, as a result of subjects'

reports of pain interference with daily activities, social relationships, and role performance, added a sixth dimension-the sociocultural dimension.

The physiologic dimension involves the etiology of pain (e.g., cancer treatment modalities and their direct sequelae such as mucositis), physical and tissue-damaging aspects of pain (e.g., erythema and ulceration) and specific pain syndromes, duration of pain (acute vs. chronic), temporal patterns of pain (continuous, intermittent), and biologic markers of pain. The sensory dimension encompasses characteristics that contribute to how pain actually feels: location, intensity, and quality of pain (34). The affective dimension describes a range of emotional and affective responses to pain such as depression, anxiety, and alterations in mood. The cognitive dimension consists of an individual's thought processes related to pain, perceptions of pain, meaning of pain, attitudes and beliefs about pain and pain treatments, coping strategies, factors influencing pain, relief of pain, and mental status. The behavioral dimension includes observable behaviors either undertaken to alleviate pain (e.g., positioning, massage, use of medications) or manifested as indicators of pain's presence (e.g., facial grimacing, vocalization) (35,36). The sociocultural dimension of pain refers to a plethora of demographic, ethnic, spiritual, social, cultural, and related factors influencing both perception of and responses to pain (37). Support for this multidimensional conceptualization of pain is strong in cancer and other types of pain (2,38).

METHODS

The component of the pilot study reported in this article was achieved by use of a prospective, repeated-measures, descriptive approach embedded within a larger randomized clinical trial with patients assigned to either an intervention or control group. Since the purpose of this article is to present patterns of acute oral pain and mucositis, data were aggregated across intervention and control groups and analyzed descriptively. Because the second component of the pilot study-testing procedures and instruments-was performed on a small sample (n = 18), analyses comparing outcomes in the intervention and control groups were not planned or used on any data from the overall pilot study.

The setting for the study was the leukemia and bone marrow transplantation inpatient nursing units at a university health sciences center hospital located in the southeastern United States. A primary nursing model of care was in place on the units at the time of the study.

The nonprobability sample consisted of 18 patients admitted to the nursing units to receive therapy for hematologic malignancies or solid tumors. Because treatment regimens produce variable rates and severity of acute oral pain and mucositis, the sample was purposively selected to include patients receiving autologous BMT for breast and other cancers, allogeneic BMT, matched unrelated donor BMT, and non-BMT leukemia therapy. Patients eligible for the study were (a) scheduled for admission to the nursing units for intensive cytoreductive therapy, (b) 18 years of age or older, (c) able to read and comprehend English, (d) without acute oral pain, (e) without active oral or systemic infection, (f) without preceding oral pathology, and (g) not receiving radiation therapy to the head or neck region.

All patients on the study units received the same prophylactic antimicrobial, antiviral, and antifungal agents; the same oral care regimen (39); and the same pain management algorithm

(40). The oral care regimen consisted of three patient-performed steps: (a) brushing with a supersoft toothbrush, (b) swishing and spitting with Biotene mouthwash (Laclede, Gardena, CA), and (c) applying a moisturizer to lips or oral cavity as needed after meals, at bedtime, and at least once during the night. Additionally, nurses assessed and documented patients' oral status and pain regularly. Frequency of mouth care was increased to every 2 hours if severity of oral complications intensified. Demographic and clinical characteristics are shown in Table 1. Not shown, but of note, is that 61.1% of the patients smoked or had smoked cigarettes, pipes, or cigars, but only 16.7% had ever chewed tobacco. A variety of chemotherapy drugs was used in treatment regimens, some of them commonly associated with development of mucositis (e.g., etoposide, methotrexate). Approximately one-third of the patients received growth factors during their chemotherapy, and one-half after chemotherapy.

Gender		Age		Marital status	
Male	8 (44.4%)	Mean = 44 Years		Married	13 (72%)
Female	10 (55.6%)	*SD* = 13.4		Single	4 (22%)
		Range = 21–67		Divorced	1 (6%)
Race				Education	
African American	4 (22%)			High school	3 (16.7%)
Euro-American	14 (78%)			College 2 years	5 (27.8%)
				College 4 years	3 (16.7%)
				Graduate school	7 (38.8%)
Disease				Group assignment	
Acute myelogenous leukemia		4 (22%)		Control group	9 (50%)
Breast cancer		4 (22%)		Experimental group	9 (50%)
Chronic myelogenous leukemia		3 (17%)			
Hodgkin's disease		2 (11%)		Treatment plan	
Acute lymphocytic leukemia		1 (6%)		Bone marrow transplant	14 (78%)
Non-Hodgkin's lymphona		1 (6%)		Leukemia therapy	4 (22%)
Other		3 (17%)			
				Drugs used in treatment regimen	
Type of transplant (n = 14)[a]				Cytoxan	15 (83.3%)
Autologous–marrow		5 (36%)		Busulfan	10 (55.5%)
Allogeneic–matched		4 (29%)		Cytosine arabinoside	8 (44.4%)
Autologous–stem cell		3 (21%)		Etoposide	7 (38.8%)
Allogeneic–matched unrelated		1 (7%)		Thiotepa	5 (27.7%)
Syngeneic		1 (7%)		Methotrexate	2 (11.1%)
Use of growth factors (n = 14)				(*Note:* 5 patients received methotrexate	
During chemotherapy		6 (42.9%)		for prophylaxis of graft-vs-host disease)	
Postchemotherapy		9 (50.0%)			

[a]Four of the pilot sample were not transplanted.

TABLE 1. Demographic and clinical characteristics of patients (n = 18)

The research variables in this pilot study represented salient components belonging to the multidimensional experience of acute oral pain caused by mucositis secondary to intensive cytoreductive therapy. Table 2 depicts the multidimensional conceptual framework with these variables categorized by dimension of pain and accompanied by the specific instrument(s) used to measure them.

Physiologic	Sensory	Affective	Cognitive	Behavioral	Sociocultural
Mucositis Oral mucositis index (45.7–46.9%)[b]	Pain intensity Graphic rating scale on the pain assessment form (4.1%)[c] Intolerable pain intensity rating Graphic rating scale on the pain assessment form (6.8%)[c] Quality of pain Verbal descriptors (35.5%)	Mood states Brief profile of mood states (50.9%)	Pain relief Ordinal adjectival scale on the pain assessment form (8.2%)[c]. Pain relief strategies on the pain assessment form	Pain relief strategies Pain assessment form	Voice/talking Oral assessment guide (13.9%)

[a]Numbers in parentheses indicate rate of missing data before data were collapsed into time periods and means calculated; absence of numbers in parentheses indicates that rate of missing data was not calculated.
[b]A range is reported because individual items (anatomic locations) on Index were analyzed separately.
[c]Number in parentheses indicates rate of missing data for patients who filled out the Patient Data Form *and* reported oral pain.

TABLE 2. Conceptual framework: Dimensions of pain, study variables, and instruments[a]

Several instruments were used in this study. The Patient Data Form (PDF), developed for previous studies (2,33), was adapted and used to collect demographic and clinical information on patients. Content validity of the adapted tool was determined by an expert group of oncology nurses and physicians.

For patients reporting pain on any given day, the following two pain-related instruments were used: (a) The Pain Assessment Form (PAF), which was developed by the investigators and includes reliable and valid indicators of pain (41) such as graphic rating scales for pain intensity and intolerable pain ranging from 0 (no pain) to 10 (pain as bad as it could possibly be), a five-item pain relief scale with a range of 5 (no relief) to 1 (complete relief), and an item asking about use and helpfulness of pain-relieving strategies. (b) The Verbal Descriptor Scale (VDS), which is a list of verbal descriptors for acute oral pain (e.g., "tender," "sore") compiled by the researchers from previous research in cancer patients with oral complications (4,5) (J. Clark, unpublished data, 1994). Patients completed the PAF and VDS through interview with the study nurse.

Mucositis was measured with the clinically oriented Oral Assessment Guide (OAG) and the research-oriented Oral Mucositis Index (OMI). The OAG (42) is an instrument that assesses functional impairment caused by mucositis (e.g., problems with swallowing, voice, and talking) and changes on four anatomic structures. It consists of 8 assessment categories (voice, swallow, lips, tongue, saliva, mucous membranes, gingiva, and teeth/dentures), each rated as 1 (normal), 2 (mildly altered), or 3 (definitely compromised). Categories can be summed for a total score (possible range = 8 to 24), or they can be used alone as subscales. Content validity was supported by an expert panel, an interrater reliability of $r = 0.912$ with pairs of nurses, and observed percentages of agreement ranging from 70% to 100% across all eight subscales (42). Used by investigators studying the effects of oral care protocols (43,44), the OAG was included in this study because it was in use on the study units (45) and provided information on variables that were not included on the OMI, specifically voice and talking. Nurses completed the OAG in conjunction with patient input.

The OMI evolved from a lengthy instrument used in Kolbinson et al.'s (18) early work on oral complications to its present form as a specific index for assessing acute oral mucositis after BMT (46). It consists of 30 items (divided into anatomic regions of the oral cavity) for assessing

atrophy, erythema, edema, and pseudomembrane/ulceration. The OMI is internally consistent (Cronbach's alpha = 0.90-0.94); demonstrates test-retest reliability ($r = 0.31$-0.73, $p < 0.0001$), content validity, and construct validity; and is useful in assessing effects of oral care protocols on mucositis (46). It was selected because it represents the most complete and sensitive research tool currently available and provides precise and quantifiable data that are amenable to statistical analysis. The study nurse completed the OMI as she performed oral examinations.

Finally, emotional distress was measured using the 11-item Brief Profile of Mood States (BPOMS) adapted from the original 65-item Profile of Mood States (POMS) by Cella and colleagues (47). Respondents record self-ratings of different mood states (e.g., miserable, uneasy) on a five-point scale of 0 (not at all) to 4 (extremely). In studies of patients with cancer, the authors reported excellent internal consistency (Cronbach's alpha = 0.92) and strong correlations between this version and the original scale ($r = 0.93$, $p < 0.001$). The BPOMS was selected because it had been used successfully in a previous study of pain in BMT (48). Patients either completed it themselves or told the study nurse what their ratings were so she could complete it for them.

The study was approved by the institutional review board before its initiation. The study nurse identified potentially eligible patients through admissions coordinators. After confirming their eligibility, she explained the study and obtained their written informed consent. At the baseline point in time, she administered the PDF, OMI, and BPOMS. Each day thereafter for 21 days or until discharge, she visited patients, performed oral examinations, and completed the OMI, BPOMS, and, for patients reporting pain, the PAF and VDS. Day 21 was selected as the end point in the pilot study for feasibility reasons.

The OAG was completed by staff nurses trained to use it in a standard manner (45), who then recorded the scores on the patients' hospital flow sheets. The study nurse reviewed medical records and patient flowsheets on an ongoing basis to abstract information such as OAG scores, pain medicines, and laboratory data. She received extensive training by the principal investigator and dental coinvestigator in using a standard method to approach patients, perform oral examinations, and collect data.

With the daily data collection schedule, there were numerous occasions when patients were unavailable or unwilling to complete interviews or oral examinations because they were too sedated, too ill, or too uncomfortable. Some instruments required more cognitive effort for patients (e.g., BPOMS) and were therefore more burdensome when patients were experiencing the sedative effects of antiemetics or other drugs. The completion rate of the various instruments is shown in Table 2. In all instances when a tool was not completed for these reasons, an "unable to assess" code was used to denote missing data.

After data were reviewed and edited, they were double-entered using the SPSS Data Entry Module, then analyzed with SPSS for Windows Version 7.0. Because of missing data (see Table 2) and the variability in the oral toxicity of the chemotherapy regimens, repeated measures across the entire study period were collapsed into four time intervals within which means were calculated for each patient. These intervals were constructed to adjust for the anticipated time

frame between administration of drugs and resultant mucositis and pain, taking into account individual chemotherapy regimens. The intervals were defined as follows:

1. Baseline: a single day of data collected before the onset of chemotherapy
2. Chemotherapy Interval: period during which the patient was undergoing chemotherapy (ranging from 2 to 10 days)
3. Postchemotherapy Interval One: the 7-day interval after cessation of chemotherapy
4. Postchemotherapy Interval Two: the period of time after the first week postchemotherapy to end of study (ranging from 10 to 18 days).

To control for the variable number of measurement days in the Chemotherapy Interval and Postchemotherapy Interval Two and to retain as much data as possible for analysis, the investigators decided to compute mean scores for each patient within these time intervals. A mean was computed on tools with continuous data, even if there was only one observation in a time interval. Patients were considered to have missing data only if there were no observations in a given interval. Items asking about presence of pain and use of pain relief strategies had dichotomous responses (yes/no), which are reported in the following section.

RESULTS

The number of patients reporting pain changed across the study period (Table 3). At baseline, 11% reported pain, but this increased over time to 67%. Patients' ratings of pain intensity increased over the study period, but when averaged across all patients at each time interval, they never exceeded a moderate (5.5) rating (see Table 3). Ratings of pain perceived as intolerable, however, reached a level that could be construed as severe. When asked to select verbal descriptors of pain, the words most commonly chosen were "tender," "sore," and "irritating," each mentioned nearly 40 times over the entire study period. The number of times these and other words were chosen increased during the third and fourth time intervals, when pain was worse.

Time interval pain and relief variables	Baseline	Chemotherapy interval	Postchemotherapy interval one	Postchemotherapy interval two
Patients reporting presence of pain	2 (11%)	6 (33%)	11 (61%)	12 (67%)
Mean rating of pain intensity 0 (no pain) to 10 (pain as bad as it could possibly be)	3.5 (n = 2) (range = 1–6)	4.5 (n = 6) (range = 1–8)	5.5 (n = 10) (range = 3.5–8)	5.5 (n = 12) (range = 2.5–8.5)
Mean rating of intolerable pain 0 (no pain) to 10 (pain as bad as it could possibly be)	8.0 (n = 2) (range = 7–9)	8.6 (n = 6) (range = 7–10)	8.6 (n = 10) (range = 6–10)	8.6 (n = 12) (range = 6–10)
Percent reporting use of strategies helpful for mouth pain				
Medicines	0	0	44.4	55.6
Mouthcare	5.6	33.3	55.6	66.7
Mental activities	5.6	33.3	55.6	44.4
Physical activities	0	22.2	22.2	50.0
Mean rating of overall pain relief 1 (complete relief) to 5 (no relief)	3.0 (n = 2) (range = 2–4)	2.7 (n = 6) (range = 2–3)	2.9 (n = 10) (range = 2–4)	2.7 (n = 11[b]) (range = 1–4)

[a]At each time interval, the sample size varies because data were provided only by patients who reported having mouth pain, and because of missing data.
[b]One patient was unable to complete this scale because of cognitive impairment.

TABLE 3. Patterns of pain and pain relief in patients reporting pain at each time interval[a]

When asked to indicate which pain-relieving strategies decreased their mouth pain, patients indicated that they used pain medicines, mouth care, and a variety of mental (e.g., thinking about something else) and physical (e.g., walking) activities (Table 3). As pain worsened over time, the percentage of patients reporting use of these strategies increased, with mouth care being mentioned more frequently than medicines. Patients' reports of overall pain relief across the study period suggested that their pain was only partially relieved.

The data on mucositis in the sample were challenging to analyze and interpret. The missing OMI ratings in various anatomic locations of the oral cavity (Table 2) precluded calculation of total OMI scores. Thus, each anatomic location was examined individually for hall-marks of mucositis: erythema and ulceration (pseudo-membrane). The use of mean scores within the time intervals as described earlier helped to minimize the effects of missing data. For example, the number of patients with valid erythema and/or ulceration ratings for commonly affected sites such as the labial or buccal mucosa ranged from 16 to 18. Table 4 shows only those areas most affected with mucositis-lateral tongue, buccal and labial mucosa for erythema, and buccal mucosa for ulceration. This data indicates that, as anticipated, mucositis worsened during the third and fourth time intervals.

	Baseline	Chemotherapy interval	Postchemotherapy interval one	Postchemotherapy interval two
Mean rating of erythema (possible range 0–3)				
Lateral tongue	0	0.13	0.49	0.55
Right buccal mucosa	0.11	0.16	0.74	0.66
Left buccal mucosa	0	0.14	0.70	0.73
Lower labial mucosa	0.06	0.20	0.66	0.59
Upper labial mucosa	0.06	0.14	0.67	0.44
Mean rating of ulceration (possible range 0–3)				
Right buccal mucosa	0	0.03	0.34	0.14
Left buccal mucosa	0	0.04	0.34	0.30

TABLE 4. Patterns of mucositis in anatomic areas most affected (n = 18)

With respect to mood disturbance, patients' average total scores on the BPOMS during the study period were 5.8, 5.8, 8.2, and 8.1, respectively, across the four time intervals described earlier. Because the possible total score on the BPOMS ranges from 0 (none) to 44 (worst), these scores were relatively low. Patients' average voice/talking scores on the OAG were 1.0 at baseline and 1.05, 1.43, and 1.48, respectively, during the remaining time intervals. These scores suggested that talking itself was not a problem for the patients in this sample, although communication in general was more difficult because of sedating medications and other factors.

DISCUSSION

The data obtained in this pilot study suggested that the dimensions of the conceptual framework were supported in the sample, since the variables representing each dimension appeared to be relevant to patients. As noted earlier, this multidimensional conceptualization of cancer pain provides a template not only for assessment of pain, but also for interdisciplinary, multimodal management of pain.

The results indicate that pain is a problem for approximately two-thirds of patients during the third and fourth time intervals, the time during the treatment trajectory when pain is commonly experienced by this population. The mean pain intensity ratings are similar to those reported by

McGuire et al. (4), whose patients had a mean of 56 on a 0-100 scale and a mean of 2.62 on a 0-5 scale. In both samples, the reported pain intensity was mild to moderate. The selection of the pain descriptor "tender" in this study also confirmed earlier work (4), but "irritating" and "sore" as descriptors of acute oral pain were not reported previously. The fact that patients reported only partial relief of pain overall suggests that their pain was incompletely relieved, despite use of a standard pain management algorithm on the study units. Others have noted that even when drugs and technologic devices are available and used, pain relief is still incomplete (4,19). Overall, these findings are commensurate with previous research and serve to verify both the presence of pain and the challenge of managing it successfully.

Mucositis appeared relatively mild in this sample. This finding may be due to (a) the makeup of the sample with patients selected from treatment regimens of varying oral toxicity, (b) the use of growth factors either during or after chemotherapy, and (c) the high proportion of missing data. The observation that erythema was most prominent on the tongue and buccal mucosa confirms previous research (4). However, the observation that the upper and lower labial mucosa were also affected is unique. The reasons for this difference are unclear, but may be due to specific characteristics of the sample such as treatment regimens or general oral hygiene.

This study had several limitations. First, because it was a pilot study, it had a small nonprobability sample purposively selected to conform to specific strata and criteria. The effect this sampling strategy had on the variability and severity of acute oral pain, mucositis, mood disturbance, and voice/talking is unknown. Because patients were on at least five different treatment regimens, their incidence and severity of pain and mucositis were variable. Although some patients received drugs known to produce severe mucositis (e.g., etoposide or methotrexate) (Table 1), sample size precluded any substantive analysis of relationships between severity of mucositis and specific drugs. The inclusion of eight patients receiving autologous BMT, who experienced lower rates and severity of pain and mucositis, may have skewed the data toward an underestimation of the magnitude of mucositis and pain. Second, as evidenced by the missing data discussed earlier, it is clear that the study of these patients was difficult in the hospital environment. They experienced many distressing symptoms and side effects and received numerous sedating medications, which contributed to missing data. In addition, some data were missed because the data collection schedule did not include weekend days. Finally, the strategy devised to handle missing data-calculating mean scores within time intervals-may have smoothed out large differences that might have been detected with shorter time intervals between data collections. As a result of these limitations, the findings should not be generalized beyond the immediate sample, although they may be helpful to nurses faced with similar patient populations.

The methodologic issues encountered in this study have been used by the investigators to modify the larger intervention study. For example, the data collection schedule was reduced in frequency to decrease the burden for patients and minimize missing data. This correction has also alleviated pressures on the data management system. Specific methodologic issues and challenges that arose in the conduct of this pilot are presented elsewhere (49).

Implications of this study for clinical nursing are tentative because of the study's limitations. It is clear from the data, however, that pain and mucositis continue to be a clinical problem in this

type of patient population. The lack of complete relief despite implementation of a pain algorithm suggests an ongoing need for vigilant and thorough nursing assessment and management. Patients' use of multiple strategies for relieving pain suggests that nurses need to continue helping them identify and use a variety of methods to reduce pain. The intervention study, as well as other research, will serve to develop and test multimodal interventions in a systematic way and ultimately decrease the distress caused by acute oral pain and mucositis.

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