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Nursing management of oral mucositis in cancer patients

Key Messages

1. Oral care by nurses can help to reduce patients' mucositis-related symptoms arising from stomatotoxic chemotherapy.
2. Further education and reinforcement of the importance of oral care is crucial to increase the 'dose' of oral care received by patients undergoing chemotherapy.
3. Additional research is needed to develop measurements that can distinguish mucositis-related symptoms and functions, determine necessary interventions based on the underlying causes, and stratify patients according to key risk factors.

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Introduction

Reducing the development of oral mucositis by promoting patient compliance with oral care regimens[1,2] can be achieved by teaching patients meticulous oral care during chemotherapy, reinforcement of these instructions as well as regular nursing assessment of the oral cavity. While such care has been reported to produce positive oral mucosal outcomes in patients undergoing chemotherapy[3,4] some researchers found no significant improvement.[2,5] Thus the evidence supporting the effectiveness of oral care is minimal with studies limited by the use of small and heterogeneous samples, and the use of different assessment tools. Although the effectiveness of oral care protocols is inconclusive, there are certain universally accepted indications for oral care interventions, which include: regular oral assessment, patient education, teeth brushing, frequent rinsing of the mouth, and other comfort measures. The oral care guidelines to be tested in this study were based on available evidence and supplemented by expert clinical opinion.[6] However, many nurses often lack the knowledge and skill to prevent oral mucositis.

Aims and objectives

The aim of this two-phase study was to firstly determine the current nursing oral care practice and mucositis-related outcomes for patients undergoing chemotherapy. The second phase of the study aimed to provide nurses with education on oral care to prevent mucositis and then to compare patient outcomes for those receiving chemotherapy. The oral care protocol emphasised regular oral assessment and frequent mouth rinsing using normal saline or water. The main outcomes of mucositis prevalence and mucositis-related symptoms were measured at baseline (day 1), day 8 and day 16 post-commencement of chemotherapy.

Methods

This study was conducted from May 2002 to October 2004. All eligible adult patients receiving stomatotoxic chemotherapy were asked to participate. In phase I subjects undergoing any cycle of their chemotherapy were included, while in phase II only those receiving their first chemotherapy cycle were included. The phase II study used a quasi-experimental design to compare the level of mucositis between experimental patient group (cared for by specially educated nurses) and control patients. It also assessed the knowledge of the nurses and the extent of oral care they provided throughout the study.

Results entailing categorical and continuous variables were analysed by analysis of covariance (ANCOVA), Chi squared, and *t*-tests as appropriate.

Results

Ninety-three phase I subjects completed all episodes of data collection while in phase II 128 subjects completed all data collection. Phase I subjects had a significantly ($P<0.05$) higher prevalence of mucositis (grade ≥1), level of baseline oral symptoms, and longer duration of cancer compared to phase II patients.

Phase II experimental and control group subjects were homogeneous for

Table 1. Comparison of phase II experimental and control group patients' sample characteristics (n=128)

	Experimental group (n=64) No. (%)	Control group (n=64) No. (%)	Independence (Chi squared)
Gender			
Female	22 (34.4)	20 (31.3)	0.14*
Male	42 (65.6)	44 (68.8)	
Education level			
Nil	4 (6.3)	8 (12.5)	1.72*
Primary	17 (26.6)	18 (28.1)	
Secondary	37 (57.8)	32 (50.0)	
Postgraduate	6 (9.4)	6 (9.4)	
Married	58 (90.6)	60 (93.8)	0.43*
Has a religion	29 (45.3)	22 (34.4)	1.60*
Metastases present	11 (17.2)	30 (46.9)	12.95†
Received 5-fluorouracil chemotherapy	58 (90.6)	33 (51.6)	23.76†
Prevalence of mucositis (grade ≥1)	2 (3.1)	4 (6.3)	0.70*
Prevalence of mucositis (grade ≥2)	2 (3.1)	2 (3.1)	0.00*

* Not significant
† P<0.001

Table 2. Comparison of phase II nurses' adherence to oral care guidelines

	Experimental group (n=64) Mean (SD)	Control group (n=64) Mean (SD)	*t*-test
Total assessment and oral care score	15.2 (4.1)	12.1 (5.0)	3.87*
Oral assessment score	1.1 (1.7)	0.2 (0.8)	3.83*
Oral care score	14.1 (3.4)	11.9 (4.8)	2.98†

* P<0.001
† P<0.01

Table 3. Nurses' knowledge of oral care

	Experimental group		Control group	
	No.	Mean (SD)	No.	Mean (SD)
Baseline test score	21	11.9 (3.6)	29	16.5 (2.6)
1st Repeated test score	19	16.7 (3.2)	18	17.7 (3.7)
2nd Repeated test score (6 months)	12	16.3 (2.4)	27	17.0 (2.0)

most demographic and baseline variables while there were significantly more controls with metastases (P<0.001) and significantly more in the experimental group who received 5-fluorouracil (5FU) within their chemotherapy regimen (P<0.001) [Table 1]. Control group patients had significantly (P>0.01) greater baseline total mucositis-related symptoms and longer duration of cancer.

In phase I, nurses' adherence to oral care principles for patients undergoing chemotherapy was relatively low; mean (and standard deviation [SD]) assessment and care scores were 11.2/24 (SD, 4.5). The prevalence of mucositis (grade ≥1) was 58% at day 8 and dropped to 43% by day 16.

In phase II, the nurses' adherence to oral care principles was significantly higher than that in phase I and for the experimental group it was significantly higher than that for controls (Table 2).

The baseline scores of knowledge of oral care in the experimental group of nurses were lower than those in the controls. However the experimental group of nurses had significantly greater improvement in knowledge (difference between pre and first repeated test scores) than the control group (P<0.01) and their knowledge gain was maintained for 6 months (Table 3).

Comparison of mucositis in patients of experimental and control groups (phase II)

There were no significant differences between the phase II experimental and control groups in the overall prevalence of mucositis (grade ≥1). This similarity continued when separate analyses were performed according to whether 5FU chemotherapy had been used (Table 4). The prevalence of oral mucositis (grade ≥2) was significantly (χ^2=5.49) lower in patients of the control group (9.4%) than of the experimental group (25.0%). However, no significant differences were found in separate analyses according to use of 5FU chemotherapy (Table 4).

The mean grade of mucositis for the experimental group at day 8 was 0.9 (SD, 0.9) and for day 16 was 0.4 (SD, 0.7), and for the control group at day 8 was 0.5 (SD, 0.7) and for day 16 was 0.4 (SD, 0.8). No significant differences between the experimental and control groups were found when 5FU chemotherapy was controlled for.

Comparison of experimental and control groups' oral symptoms (phase II)

Patients of the experimental group had higher levels of oral symptoms at day 8 than those of the controls. However using ANCOVA to account for the higher levels of 5FU received by the experimental group, oral discomfort was the only symptom with significantly higher scores (F=5.59, P<0.05). At day 16 all the symptom scores were lower for the experimental group with only oral dryness being significantly lower (F=10.10, P<0.01). Overall there were

Table 4. Comparison of phase II prevalence of mucositis with 5-fluorouracil (5FU) as covariate

Level of mucositis	Experimental group		Control group		Independence (Chi squared)
	No 5FU chemotherapy (n=6) No. (%)	5FU chemotherapy (n=58) No. (%)	No 5FU chemotherapy (n=31) No. (%)	5FU chemotherapy (n=33) No. (%)	
Mucositis grade ≥1					
Day 8	2 (33.3)	35 (60.3)	11 (35.5)	16 (48.5)	5.79*
Day 16	1 (16.7)	18 (31.0)	11 (35.5)	6 (18.2)	3.08*
Mucositis grade ≥2					
Day 8	1 (16.7)	15 (25.9)	3 (9.7)	3 (9.1)	5.82*
Day 16	1 (16.7)	8 (13.8)	5 (16.1)	3 (9.1)	0.79*

* Not significant

no significant differences between the groups with respect to total symptom score.

Resolution of oral symptoms from day 8 to day 16

There were significant differences between experimental and control groups (ANCOVA) using the covariate of 5FU chemotherapy. The experimental group of patients had greater resolution from day 8 to 16 for the mucositis symptoms of: oral dryness, oral discomfort, difficulty in speaking, difficulty in chewing/eating, oral pain, and for total symptom score. However there were no statistically significant differences in the level of resolution or reduction of difficulty in swallowing (Table 5).

Table 5. Resolution of mucositis symptoms from day 8 to day 16

	Experimental group (n=64) Mean (SD)	Control group (n=64) Mean (SD)	F (ANCOVA)
Oral dryness	23.2 (32.1)	2.1 (21.2)	16.12*
Oral discomfort	29.7 (30.5)	6.4 (28.8)	14.73*
Difficulty in speaking	11.8 (21.7)	1.1 (18.1)	6.46†
Difficulty in chewing/eating	13.3 (22.3)	0.2 (21.9)	6.21†
Difficulty in swallowing	12.4 (22.9)	1.1 (21.9)	3.63‡
Oral pain	15.4 (23.9)	1.6 (22.8)	4.11§
Total symptom score	105.7 (114.3)	12.5 (95.7)	15.85*

* P<0.001
† P<0.01
‡ Not significant
§ P<0.05

Discussion

Oral mucositis

While the prevalence of mucositis at day 8 in the phase II study was greater for the experimental group receiving the oral care protocol, the difference was not statistically significant when adjusted for 5FU chemotherapy, as more of the corresponding patients received such treatment. At day 16 there was no significant difference between patients of the experimental and control groups with respect to prevalence of mucositis after accounting for 5FU therapy. Another factor influencing the findings of this study was the overall low level of mucositis. Moreover, as the assessment of mucositis occurred at fixed days post commencement of chemotherapy, there was no assessment of the pre-treatment levels of mucositis.

The use of trend analysis as in studies by Dodd et al[2] and Graham et al[7] indicate a non-significant lower level of day 8 mucositis in phase II than for phase I studies but for phase II a significantly lower level of day 16 mucositis. This may have been influenced by the differences in the number of chemotherapy cycles.

Dodd et al[8] point out the limitations in past studies of effectiveness of oral care in preventing mucositis as: small sample sizes, the extent to which oral care regimens were implemented, and the variety of chemotherapeutic agents used. The current study attempted to overcome these limitations by increasing the sample size, providing education on the oral care protocol, using a tool to appraise the extent of oral care practice and accounting for the more toxic chemotherapy in the data analysis. Post-hoc power analysis for the comparison of the prevalence of mucositis indicates that a bigger sample of 160 per group is needed to detect a 15% difference between the experimental and control groups.

The Oral Nursing Care Monitor developed for this study indicated an improvement in the level of oral care from phase I to phase II and a significantly higher level of oral care provided by the experimental group nurses in phase II. However as the maximum possible score was 24, the mean of 15.2 shows the need for further improvement in oral care as well as the education and follow-up of nurses in the implementation of oral care for patients receiving chemotherapy. While only patients receiving stomatotoxic chemotherapy were included in the study and the data analysis took account of the influence of the more toxic drug 5FU in determining the level of mucositis—no significant differences were found—further study is needed to determine whether this type of oral care intervention is beneficial for those not receiving 5FU chemotherapy regimens, as the patient numbers in the latter group was very small. Barasch and Peterson[9] in their review of the prevention and treatment of mucositis point to the need for the use of stratification and a clearer identification of risk factors for future effectiveness studies.

Oral symptoms

At day 8, symptoms for patients in the experimental group

were greater than those in the control group, although only oral discomfort was significantly greater when 5FU was used as a covariate. At day 16 there was a significantly lower level of oral dryness for the patients in the experimental group. There were no significant differences between the patients in the experimental and control groups in terms of total symptom score at day 8 or day 16. However post-hoc power analysis indicates that a larger sample would be needed to verify these findings. The mean scores presented in Table 5 indicate the actual level of mucositis appears much greater at day 8 but considerably less at day 16.

However the amount of mucositis resolution, calculated by subtracting day 16 symptom scores from those of day 8 in patients cared for by the nurses suggests that the intervention had some impact. Determining the level of resolution at fixed time points was possible as the measurement of the main mucositis outcomes and related symptoms occurred on set days following commencement of chemotherapy. Other approaches to study resolution as an outcome have measured mucositis more frequently[8,10] and have thus reported the rate of resolution. Such an approach could be used in future studies where the rate of resolution is required.

The oral rinse agent (normal saline or water) used in this study appears to have ameliorated related symptoms rather than preventing or reducing mucositis, which is in contrast to the findings of the systematic review by Clarkson et al[11] who described the effectiveness of ice chips in preventing mucositis. Their review also reported that there was no evidence for the effectiveness of chlorhexidine, prostaglandin, glutamine or sucralfate. Studies subsequent to that review continued to demonstrate inconsistent findings on the prevention and treatment of mucositis.

Limitations

The main limitations of this study were: insufficient sample size to determine the significance of difference in mucositis prevalence, the moderate extent of oral care provision, the highly variable chemotherapy the patients received, and the number of times main outcomes were measured. A sample size of about 160 per group would be needed to determine a 15% significant difference in prevalence of mucositis. As the extent of oral care provided was still far from ideal, education and reinforcement of oral care by nurses needs to be improved. A similar study with a 'higher dose' of the intervention (oral care) could provide more rigorous testing of the effectiveness. Further studies should stratify patients according to the type of chemotherapy received while ensuring sufficient sample numbers at each stratum. Due to individual differences in responses to chemotherapy, more regular measurement of the level of mucositis and related symptoms than the three set times could be beneficial. The continual increase in the number of patients receiving chemotherapy as out-patients means that new approaches for oral assessment will be needed to capture daily measurements.

Conclusion

The findings of this study led to improvement in the experimental nurses' knowledge of oral care for patients receiving chemotherapy and thereby to a greater better oral care practice. While not improving the level of mucositis, this intervention did lead to greater resolution of mucositis-related symptoms between day 8 and 16. Such findings provide guidance for nurses in the provision of care to ameliorate the oral mucosal impact of stomatoxic chemotherapy. Furthermore the correlation of Oral Nursing Care Monitor for measuring patients' perceptions of the amount of oral care for mucositis provided nurses with a means for determining the extensiveness of their intervention. Future research could be enhanced by the daily use of a standardised mucositis assessment tool, distinguishing mucositis measurements from mucositis-related symptoms and functions, determining interventions based on the underlying causes, and stratifying patients according to key risk factors.

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References

1. Dose AM. The symptom experience of mucositis, stomatitis, and xerostomia. Semin Oncol Nurs 1995;11:248-55.
2. Dodd MJ, Larson PJ, Dibble SL, et al. Randomized clinical trial of chlorhexidine versus placebo for prevention of oral mucositis in patients receiving chemotherapy. Oncol Nurs Forum 1996;23:921-7.
3. Beck S. Impact of a systematic oral care protocol on stomatitis after chemotherapy. Cancer Nurs 1979;2:185-99.
4. Hickey AJ, Toth BB, Lindquist SB. Effect of intravenous hyperalimentation and oral care on the development of oral stomatitis during cancer chemotherapy. J Prosthet Dent 1982;47:188-93.
5. Kenny SA. Effect of two oral care protocols on the incidence of stomatitis in hematology patients. Cancer Nurs 1990;13:345-53.
6. The Joanna Briggs Institute for Evidence Based Nursing and Midwifery. The prevention and treatment of oral mucositis in cancer patients. Best Practice 1998;2:1-6.
7. Graham KM, Pecoraro DA, Ventura M, Meyer CC. Reducing the incidence of stomatitis using a quality assessment and improvement approach. Cancer Nurs 1993;16:117-22.
8. Dodd MJ, Dibble SL, Miaskowski C, et al. Randomized clinical trial of the effectiveness of 3 commonly used mouthwashes to treat chemotherapy-induced mucositis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2000;90:39-47.
9. Barasch A, Peterson DE. Risk factors for ulcerative oral mucositis in caner patients: unanswered questions. Oral Oncol 2003;39:91-100.
10. Hejna M, Kostler WJ, Raderer M, et al. Decrease of duration and symptoms in chemotherapy-induced oral mucositis by topical GM-CSF: results of a prospective randomised trial. Eur J Cancer 2001;37:1994-2002.
11. Clarkson JE, Worthington HV, Eden OB. Interventions for preventing oral mucositis or oral candidiasis for patients with cancer receiving chemotherapy (excluding head and neck cancer). Cochrane Review. In: The Cochrane Library, 2003, Oxford: Update Software.