ORIGINAL ARTICLE

Psychometric properties of the Oral Mucositis Daily Questionnaire for child self-report and importance of mucositis in children treated with chemotherapy

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Abstract

Purpose The objectives of this study were to examine the psychometric properties of the self-report Oral Mucositis Daily Questionnaire (OMDQ) and to measure the importance of mucositis in children receiving intensive chemotherapy.

Methods Children ≥12 years of age receiving intensive chemotherapy for leukemia/lymphoma or undergoing stem cell transplantation were asked to complete the OMDQ daily for 21 days after chemotherapy. Other measures of mucositis obtained concurrently with OMDQ included the World Health Organization (WHO) mucositis scale, the pain visual analog scale (VAS), and the Functional Assessment of Cancer Therapy Esophageal Cancer Sub-scale (FACT-ECS). The importance of mucositis was estimated using a VAS, time trade-off technique, and willingness to pay to avoid mucositis.

Results Fifteen children participated. Test–retest reliability demonstrated at least moderate correlation for all questions within the OMDQ. Assessment of construct validity of the OMDQ revealed at least moderate correlation with WHO, VAS, and FACT-ECS for questions regarding pain, swallowing, drinking, and eating. Effect on sleeping and talking had lower correlations than that expected a priori. The diarrhea question of the OMDQ did not correlate with other measures of mucositis. Severe mucositis is important to children, while mild mucositis is less important to them. Children were willing to pay moderate amounts of money to prevent mucositis.

Conclusions The OMDQ exhibits test–retest reliability, and most questions show construct validity with the exceptions of the sleep, talking, and diarrhea questions. Therefore, the OMDQ should not be used unmodified as a self-report instrument in children with cancer. Severe mucositis is of importance to these children.

Keywords Mucositis · Pediatrics · Validation studies · Children · Cancer · Psychometric properties

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Introduction

There have been significant improvements in the survival of children diagnosed with cancer over the past three decades [15]. Despite advances in cancer therapy, chemotherapy continues to be associated with clinically significant adverse effects which often limit treatment intensity while causing considerable morbidity. Oral mucositis is a common treatment-related complication which occurs in approximately 40% of patients treated with standard-dose chemotherapy regimens [17]. Children with hematological malignancies receiving more intensive therapies such as those with acute myeloid leukemia (AML), relapsed acute lymphoblastic leukemia (ALL), and advanced lymphoma, as well as those undergoing stem cell transplantation (SCT), are at higher risk for developing mucositis [2, 3, 7, 10]. Lesions can be severe, causing significant pain, dysphagia, alteration in nutritional status, and risk of infection [11].

Structured evaluation of the severity of oral mucositis is useful clinically and is critical for conducting clinical trials

to compare management strategies [24]. It is essential that such instruments report adequate psychometric properties; unfortunately, however, there is a paucity of validated instruments measuring oral mucositis that are suitable for use in children [26]. Patient-reported assessment of mucositis is important for two reasons. First, it is optimal to capture the perspective of patients to ensure that symptoms are meaningful to them. Second, physical examination of the oral cavity is recognized as being problematic in children who are ill and in pain, further heightening the need for measures incorporating patient-reported outcomes [24]. The Oral Mucositis Daily Questionnaire (OMDQ) is a promising instrument based on patient-reported outcomes of mucositis, which is reliable and valid in adults undergoing chemotherapy [22]. The OMDQ was recently modified for use in children; the modified version was understandable and acceptable (Fig. 1) [25]. The parent report of this modified OMDQ was then established as reliable and the questions relating to mouth and throat pain, as well as effect on functioning, displayed construct validity [23]. However, there has been no psychometric evaluation of a child self-report instrument measuring oral mucositis, such as the modified OMDQ, previously reported in the literature.

As it is a transient side effect of therapy, it is also valuable to know how patients prioritize oral mucositis in order to help allocate resources for its prevention or treatment. One way to assign a value to the prevention or treatment of mucositis is to measure utilities for mucositis health states. Utility can be defined as the strength of an individual's preference for a health state measured under conditions of uncertainty [27]. Utilities are an important measure, in part, because of their use in decision and health economic analyses.

The primary objective was to evaluate the psychometric properties of the self-report OMDQ in children receiving intensive chemotherapy for AML, relapsed ALL, advanced lymphoma, and those undergoing SCT. Specifically, we wanted to determine if the child self-report OMDQ demonstrates (1) test–retest reliability and (2) construct validity by hypothesizing a priori that OMDQ would have at least moderate correlation with other measures of oral mucositis. The secondary objective was to assess the importance of oral mucositis to children undergoing cancer therapy by measuring utilities for mucositis health states.

Patients and methods

Participants

Children ≥12 and <18 years of age undergoing induction or consolidation chemotherapy for AML, relapsed ALL, or

advanced lymphoma or receiving myeloablative SCT for any indication at The Hospital for Sick Children in Toronto, Ontario, Canada were eligible. The children were the respondents and they were required to be able to read English.

Study design

The study was approved by the Research Ethics Board of The Hospital for Sick Children. This report is a sub-analysis of a larger study designed to assess the psychometric properties of the parent-reported OMDQ [23]. Written informed consent was obtained prior to enrollment. Respondents completed a daily mucositis diary beginning 1 day following the last dose of chemotherapy or stem cell infusion. This diary was completed daily for 21 days or until the initiation of the next cycle of chemotherapy, whichever occurred first. The questions involved symptoms related to mucositis for each preceding 24-h period. The respondents for all outcome measures were children themselves. The importance of mucositis was determined in a face-to-face interview conducted with each child participant by a trained research assistant using standardized scripts and visual aids. The interview occurred prior to initiation of the diary.

Outcome measures

OMDQ psychometric evaluation Psychometric evaluation of the OMDQ was conducted using the daily mucositis diary.

OMDQ The OMDQ (Fig. 1) scores six questions separately since an aggregate score has not been examined or validated. The six questions measure: (1) amount of mouth and throat pain (MT1), (2) effect of pain on sleeping (MT2), (3) effect on swallowing (MT3), (4) effect on drinking (MT4), (5) effect on eating (MT5), and (6) effect on talking (MT6). A seventh item measures amount of diarrhea. If the response to MT1 is 0, then questions MT2 to MT6 are not completed, and thus, the sample size changes for different components of the OMDQ.

Other measures of oral mucositis The World Health Organization (WHO) mucositis score [28], a mucositis pain visual analog scale (VAS), and the oral component of the Functional Assessment of Cancer Therapy Esophageal Cancer Sub-scale (FACT-ECS) [5] were used in all children to measure oral mucositis. The WHO mucositis scale, based upon the ability to eat and drink, involves the assignment of a score of 0 (no symptoms), 1 (oral soreness and erythema—no change in oral intake), 2 (oral erythema and ulcers, solid diet tolerated—soft foods only), 3 (oral ulcers, liquid diet only), or 4 (oral alimentation impossible). The mucositis pain VAS consisted

Fig. 1 Pediatric OMDQ: child version (adapted from Stiff and colleagues [22])

1. During the PAST 24 HOURS, how much **MOUTH AND THROAT SORENESS** did the patient have? (*Circle one face*)

No soreness ....

> If this face is circled please skip to question 3

A little soreness ....

Moderate soreness ....

Quite a lot of soreness ....

Extreme soreness ....

2. During the PAST 24 HOURS, how much did **MOUTH AND THROAT SORENESS** limit the patient in each of the following activities? (*Circle one face on each line*)

	Not Limited	Limited a Little	Limited Some	Limited a Lot	Unable to Do
a. Sleeping					
b. Swallowing					
c. Drinking					
d. Eating					
e. Talking					

3. During the PAST 24 HOURS, how much **DIARRHEA** did the patient have? (*Circle one face*)

No diarrhea

A little diarrhea

Moderate diarrhea

Quite a lot of diarrhea

Severe diarrhea

Table 1 Demographics of children

Characteristic	Value, $N=15$
Male (%)	8 (53.3)
Median age (IQR) in years	16.7 (14.6, 16.8)
Diagnosis (%)	
Leukemia/lymphoma	13 (86.7)
Solid tumor	1 (6.7)
Brain tumor	1 (6.7)
Metastatic disease (%)	2 (13.3)
Treatment at OMDQ assessment (%)	
Chemotherapy	8 (53.3)
SCT	7 (46.7)
Median years since diagnosis (IQR)	0.2 (0.1, 0.4)
Median days since last chemotherapy (IQR)	0.0 (0.0, 6.0)
Prior history of mucositis (%)	4 (26.7)

OMDQ Oral Mucositis Daily Questionnaire, *IQR* interquartile range

of a horizontal 10-cm scale anchored at 0 (no symptoms) and 10 (worst symptoms possible). This type of VAS has previously been used to measure pain in pediatric populations [14, 18]. The FACT-ECS scale, a validated measure of quality of life for patients with esophageal cancer, was included because of previously demonstrated excellent psychometric properties in a condition which has substantial overlap with chemotherapy-related oral mucositis [5]. The oral questions from this scale were utilized, resulting in a swallowing index, eating index, and total score. While higher WHO mucositis scores and pain VAS scores reflect worse mucositis, higher FACT-ECS scores reflect milder mucositis.

Importance of mucositis Hypothetical scenarios of mild (National Cancer Institute Common Toxicity Criteria for Adverse Events (CTCAE) v.3.0 grade 1 or 2) and severe (CTCAE grade 3 or 4) oral mucositis were created and described to the patient. In addition to using an importance VAS, elicited time trade-off (TTO) utilities and willingness-to-pay (WTP) questions were utilized to determine the importance of mucositis to the patient. While there are several approaches to determining preferences for health states, WTP and TTO are considered standard methods and

are used widely in health care [9]. Since TTO and WTP represent the amount of time or money the respondent is willing to give up to prevent mucositis, they provide a measure of how important mucositis is to the respondent. The TTO method is well accepted in adults and consistent with economic theory [8, 12]; WTP, however, has since been shown to be a more sensitive measure of change in health status [21]. It is generally accepted that TTO and WTP questions pose similar complexity to standard gamble surveys [19] which are reliable in children above the age of 12 [16]. Both of these methods have been shown previously to be feasible in adolescent patients [1, 29].

VAS The children were asked to rate the importance of mild and severe oral mucositis on 100-mm lines anchored at one end by "least important" and the other end by "most important."

TTO This method requires respondents to compare different combinations of quantity and quality of life and can be used to estimate utility. The children were asked for the smallest number of weeks in perfect health that they would give up in order to prevent mild and severe mucositis after one cycle of chemotherapy or SCT. To facilitate understanding of this concept, a visual-aid board was used and patients were asked to imagine that a treatment existed to prevent mucositis, but that a side effect of this treatment would shorten the child's life span. With the visual-aid board, two options were presented— either to accept mucositis and to live for an additional 50 years or to accept the imaginary treatment that would prevent mucositis but also reduce length of life. The first option, acceptance of mucositis, was represented by a horizontally long and vertically short white rectangle with tick marks that ranged from 0 to 50 years. The second option, acceptance of the imaginary treatment, was represented by the same size rectangle in which the left side was white and the right side was black with the amount of black representing the decrease in life expectancy. For example, a life expectancy of an additional 40 years was represented by 40/50 years being white (left side) and 10/50 being black (right). The reduction in survival time associated with elimination of mucositis was systematically altered using a ping-pong and then a titration approach until the patient was indifferent to the choice. This

Table 2 Test–retest reliability of OMDQ between days 14 and 15

	Number[a]	Spearman correlation coefficient	*P* value
MT1—amount of mouth and throat pain	13	0.88	<0.0001
MT2—effect of pain on sleeping	5	0.92	0.029
MT3—effect on swallowing	5	0.89	0.042
MT4—effect on drinking	4	0.82	0.184
MT5—effect on eating	4	1.00	<0.0001
MT6—effect on talking	5	0.92	0.028
Amount of diarrhea	13	0.73	0.005

[a] If MT1 is answered as 0, then MT2–MT6 are not completed; thus, the number is much smaller for these questions since MT1 must be ≥1 on both days 13 and 14 in order to calculate a Spearman correlation coefficient

Table 3 Construct validation of OMDQ

	Pain	Sleep	Swallow	Drink	Eat	Talk	Diarrhea
WHO mucositis	0.90 (<0.0001)	0.35 (<0.0001)	0.65 (<0.0001)	0.73 (<0.0001)	0.83 (<0.0001)	0.41 (<0.0001)	0.16 (0.009)
VAS mucositis	0.81 (<0.0001)	0.51 (<0.0001)	0.67 (<0.0001)	0.57 (<0.0001)	0.47 (<0.0001)	0.59 (<0.0001)	0.08 (0.192)
FACT-ECS swallow index	−0.77 (<0.0001)	−0.40 (<0.0001)	−0.67 (<0.0001)	−0.77 (<0.0001)	−0.84 (<0.0001)	−0.46 (<0.0001)	−0.09 (0.134)
FACT-ECS eat index	−0.62 (<0.0001)	−0.35 (0.0001)	−0.60 (<0.0001)	−0.65 (<0.0001)	−0.82 (<0.0001)	−0.35 (0.0001)	−0.04 (0.573)
FACT-ECS total index	−0.71 (<0.0001)	−0.59 (<0.0001)	−0.71 (<0.0001)	−0.74 (<0.0001)	−0.85 (<0.0001)	−0.53 (<0.0001)	−0.14 (0.030)

This table represents the Spearman correlation coefficients with *P* values derived from a generalized linear mixed model with repeated measures in parentheses. OMDQ is comprised of seven components: (1) MT1—amount of mouth and throat pain; (2) MT2—effect of pain on sleeping; (3) MT3—effect of pain on swallowing; (4) MT4—effect on drinking; (5) MT5—effect on eating; (6) MT6 —effect on talking; (7) Amount of diarrhea (Fig. 1)

FACT-ECS Functional Assessment of Cancer Therapy Esophageal Cancer Sub-scale, *WHO* World Health Organization mucositis scale, *VAS* pain visual analog scale

exercise was performed for both mild and severe mucositis. TTO was the point of indifference, presented as the number of weeks of life that the patient would give up to avoid mild or severe mucositis.

WTP To determine the monetary value of a health state using contingent valuation, researchers have directly elicited respondents' WTP to prevent a poor health outcome [13]. This can provide a holistic monetary value of the health benefit associated with the prevention of mucositis, where health benefit is defined by a number of quality of life years or nonhealth characteristics [6]. In this task, we asked patients whether they would pay a specified bid amount for an imaginary treatment that would prevent mild and severe oral mucositis with a cycle of chemotherapy or SCT. Patients were instructed to imagine that the cost of this treatment was not covered by insurance or the Ontario Health Insurance Plan and that the family would be responsible for paying for these costs out-of-pocket. The starting bid amount each respondent faced was $0; if raters responded with "yes," the bid was set to $100,000. Intermediate bid amounts below $100,000 were determined using a ping-pong and then a titration approach. If patients replied with "no" to the initial bid of $0, the answer was treated as a protest response and thus excluded from the analysis [20]. For amounts >$100,000, respondents were asked to state their maximum WTP. Respondents' understanding of the task was facilitated using a WTP visual-aid board, which was anchored with a $0 amount at one end and $100,000 at the other.

Statistical methods

Test–retest reliability was examined by comparing two consecutive OMDQ scores in the same patient, 24 h apart on days 14 and 15, when we would expect a peak in mucositis. We anticipated at least moderate correlation between the two time points for each item. In order to describe the construct validity of the OMDQ, we hypothesized a priori that the OMDQ would be at least moderately correlated with other measures of oral mucositis, namely, WHO, mucositis pain VAS, and FACT-ECS. Spearman correlation coefficients were used to evaluate reliability and the association between measures. Correlation coefficients were defined as follows: 0–0.25, negligible or not correlated; 0.25–0.50, fair correlation; 0.50–0.75, moderate to good correlation; and >0.75, very good to excellent correlation [4]. However, because each child had several assessments which were considered unlikely to be statistically independent, we obtained the *P* values using a generalized mixed model, assuming that the OMDQ scores followed a Poisson distribution. Because of the small sample size, we focused

Table 4 Mucositis importance and TTO utilities for mild and severe mucositis

	Mild mucositis	Severe mucositis
Median importance VAS (IQR) ($N=12$)	2.4 (1.6, 3.4)	7.0 (6.4, 9.1)
Median reduction in survival time with TTO in weeks (IQR) ($N=12$)	0.0 (0.0, 1.0)	0.9 (0.0, 3.0)
Median willingness to pay (IQR) ($N=11$)	$500.00 ($75.00, $775.00)	$1,250.00 ($550.00, $2,050.00)

IQR interquartile range

more on the value of the correlation coefficients rather than the *P* values.

In order to describe the importance of mucositis from the perspective of children, the analysis was descriptive. All analyses were conducted with the SAS software (version 9.2; SAS Institute Inc., Cary, NC, USA).

Results

Between July 2007 and August 2009, 28 potentially eligible children were approached for participation in this study. Thirteen children declined and thus 15 children were enrolled.

Table 1 illustrates the demographics of the patient sample. The median age of patients was 16.7 years. A little more than half of the patients were being treated with chemotherapy, while the remainder was undergoing SCT. Most patients had been diagnosed within the previous 5 months, and 27% had previous experience with mucositis.

Table 2 illustrates the test–retest reliability of the OMDQ when measured 24 h apart on days 14 and 15. The moderate correlation threshold (>0.50), established a priori, was exceeded for all questions within the OMDQ. In fact, all questions exhibited very good to excellent correlation with the exception of the diarrhea question.

Assessment of construct validity is demonstrated in Table 3. We anticipated that the OMDQ would have at least moderate correlation (>0.5) with the WHO, mucositis pain VAS, and FACT-ECS indices. In general, we established at least moderate correlation with the pain (MT1), swallow (MT3), drink (MT4), and eat (MT5) questions of the OMDQ. However, we found that correlations with the sleep (MT2) and talk (MT6) questions were lower when compared against the WHO and some of the FACT-ECS indices. Of note, the diarrhea question of the OMDQ performed very poorly, with correlations ranging from 0.04 to 0.16.

Table 4 illustrates how children reported the importance of mucositis using the VAS, TTO, and WTP utility assessments. According to the VAS results, children did not report mild mucositis as being of particular importance to them, reflected by a median score of 2.4. However, severe mucositis was identified as being of greater importance to them with a median score of 7.0. There was a general lack of willingness to trade any significant survival time to

prevent mucositis. However, patients were willing to pay moderate amounts of money to prevent mucositis, with an increased willingness to pay to prevent severe mucositis (median $1,250.00).

Discussion

To our knowledge, this is the first study to describe the psychometric properties of a child self-report instrument in pediatric mucositis. While the OMDQ has been shown to be reliable and valid in adults undergoing chemotherapy, only the modified OMDQ relying on parent report has been studied previously for reliability and validity. Our report is important because obtaining self-report estimates of mucositis from the patients themselves is optimal, although this may not always be possible if the child lacks the cognitive ability to report mucositis or if the child is too ill or unwilling to respond on their own behalf. We found that children ≥12 years of age can self-report mucositis scores without a problem.

This study suggests that the child self-report OMDQ is reliable and that questions of the OMDQ which relate to pain, swallowing, drinking, and eating are valid assessments of mucositis. While the sleeping and talking components exhibited fair correlation with other mucositis measurement tools, they did not meet the a priori defined threshold for construct validity. The diarrhea question performed very poorly with negligible correlation with other measures, and thus, this study suggests that this item should be excluded from the measurement of oral mucositis in children. Furthermore, the sleeping and talking questions should be used cautiously.

We also found that children do not consider mild mucositis very important but do ascribe more importance to severe mucositis as evidenced by their VAS and WTP scores. Utilities have never before been directly elicited from adolescents for oral mucositis as an endpoint and are difficult to obtain because of the short-term nature of mucositis. However, these measures do provide insight into attitudes toward mucositis and may be used in economic analyses.

Limitations of this study may include a lack of generalizability as subjects were recruited from a single Canadian center and, given the intensity of therapy, were more likely to

be inpatients at the time of the study. The small sample size is another important limitation of our study; although for inferences, we focused primarily on correlation coefficients rather than P values. Thirteen out of the 28 patients approached declined participation in our study, which may have also resulted in bias. The completion of the diary on a daily basis may have allowed a respondent's answers to be influenced by those provided on the previous day, thereby falsely elevating test–retest reliability. Furthermore, given that only four patients had a prior history of mucositis, this lack of experience may have affected their WTP and TTO utility assessments. Finally, while most adolescents are generally sophisticated enough to use these valuation methods, their health state values may differ significantly from those elicited from adults [19] because of differences in their attitudes toward risk, quantity and quality of life, and monetary value of a health state.

In conclusion, the child self-reported OMDQ is reliable and the questions related to mouth and throat pain, swallowing, drinking, and eating display construct validity. The diarrhea question should be removed from future studies that include the OMDQ for child self-report of mucositis. This study demonstrated that severe mucositis is important to adolescents themselves; this approach to measuring health preferences can potentially be applied to other complications of cancer therapy within this population, yielding important results for use in decision and health economic analyses. Methods that seek to enable young people to self-report their symptoms and experiences should be a priority in clinical care and future research. Future work should focus on identifying better measures of child self-report of mucositis, identifying how self-reported mucositis can be measured in younger children, and gaining further insight into how children and their parents prioritize the prevention or treatment of mucositis.

Conflict of interest statement None to declare.

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