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Reliability and construct validity of the oral mucositis daily questionnaire in children with cancer

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ABSTRACT

Background: The objective of this study was to examine the test–retest reliability and construct validity of parent-reported Oral Mucositis Daily Questionnaire (OMDQ) in children receiving intensive chemotherapy.

Methods: Parents of children with cancer receiving intensive chemotherapy for leukaemia/lymphoma or undergoing stem cell transplantation (SCT) were asked to complete OMDQ daily for 21 d after chemotherapy. Other measures of mucositis obtained concurrently with OMDQ included the World Health Organization (WHO) Mucositis Scale, pain Visual Analogue Scale (VAS) and the Functional Assessment of Cancer Therapy Esophageal Cancer Sub-scale (FACT-ECS).

Results: Parents of 59 children (median age = 5.62) provided complete OMDQ data for inclusion in analysis. The majority of children (73%) received SCT. Test–retest reliability of OMDQ exceeded the expected moderate reliability threshold established *a priori* and in particular, was good to excellent when mucositis was expected. In general, items of OMDQ that relate to pain, swallowing, drinking, eating and talking demonstrated moderate correlations with WHO, VAS and FACT-ECS indices with correlation coefficients $\geqslant 0.5$.

Conclusions: Parent-report of a modified version of OMDQ is reliable and the questions relating to mouth and throat pain, as well as effect on function display construct validity for this population of children receiving intensive chemotherapy.

1. Introduction

Oral mucositis is a common consequence of chemotherapy, occurring in about 40% of chemotherapy regimens.[1] Children with haematological malignancies receiving more intensive therapies such as those with acute myeloid leukaemia (AML), relapsed acute lymphoblastic leukaemia (ALL) and advanced lymphoma, as well as those receiving stem cell transplantation (SCT) are at higher risk for mucositis.[2–5] Mucositis is important because it is painful, affects quality of life, may lead to hospitalisation for hydration or pain control and provides a portal of entry for oral microflora. In addition, oral mucositis has become a major dose-limiting toxicity.[6]

Many trials are targeted at preventing or treating oral mucositis. In order to judge efficacy of these therapies, much effort has been invested in developing reliable and valid assessments of oral mucositis. There are few instruments that are suitable for use in children and even less that are

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suitable in patient or proxy reported outcomes.[7] "Patient reported outcomes (PROs)" in clinical trials are essential to ensure that effective interventions improve symptoms in a way that is meaningful to patients and their families.

A promising PRO for mucositis is termed the Oral Mucositis Daily Questionnaire (OMDQ).[8] The OMDQ was developed through multiple focus groups and one-on-one interviews with cancer patients.[9] The psychometric properties of the OMDQ were examined in adults 18 years of age and older undergoing SCT for a haematological malignancy. The OMDQ was found to be feasible, reliable and valid in this patient population.[8] However, this measure has not been assessed in paediatrics, either as a self-report measure for older children or as proxy-report measure for younger children. We modified the OMDQ for use in children and previously confirmed the understandability and acceptability of the modified instrument (Fig. 1).[10] However, the psychometric properties of this modified instrument remained uncertain.

Consequently, the objectives of this current study were to determine in children receiving intensive chemotherapy for AML, relapsed ALL, advanced lymphoma and those undergoing SCT, if parent-reported OMDQ demonstrates: (1) test–retest reliability and (2) construct validity by hypothesising that OMDQ would have at least moderate correlations with other measures of oral mucositis.

2. Patients and methods

2.1. Participants

Parents of children ages $\geqslant 1$ and <12 years receiving induction or consolidation chemotherapy for AML, relapsed ALL, advanced lymphoma and those receiving myeloablative SCT for any indication at The Hospital for Sick Children in Toronto, Ontario, Canada were eligible. The respondent had to be able to read English. There were no other eligibility criteria. Because this report focuses on parent proxy report and children $\geqslant 12$ years of age should be able to self-report, this analysis was restricted to parents of children <12 years of age.

2.2. Study design

The study was approved by the Research Ethics Board of The Hospital for Sick Children. Written informed consent was obtained prior to enrollment. Respondents completed a daily mucositis diary that started 1 d following the last dose of chemotherapy or stem cell infusion. The diary was continued daily for 21 d or until the initiation of the next cycle of chemotherapy, whichever occurred first. Respondents were asked to consider symptoms related to mucositis for the 24 h period prior to each daily diary completion.

2.3. Outcome measures

The respondents for all outcome measures were parents. All outcome measures were collected on the daily mucositis diary that began 1 d following the last dose of chemotherapy or stem cell infusion and continued for 21 d. The OMDQ results in scores for six questions which were scored separately since an aggregate score has not been examined or validated. The six questions include measurement of: (1) amount of mouth and throat pain (MT1), (2) affect of pain on sleeping (MT2), (3) affect on swallowing (MT3), (4) affect on drinking (MT4), (5) affect on eating (MT5) and (6) affect on talking (MT6). A seventh item measured amount of diarrhoea (see Fig. 1).

The other measures of oral mucositis were the World Health Organization (WHO) mucositis score,[11] a mucositis pain Visual Analogue Scale (VAS) and the oral component of the Functional Assessment of Cancer Therapy Esophageal Cancer Sub-scale (FACT-ECS). The WHO mucositis scale is based upon the ability to eat and drink. The possible WHO mucositis scores are 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) and 4 (oral alimentation impossible). The pain VAS was 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 paediatric populations.[12,13] For the WHO and VAS, higher scores reflect worse mucositis. The FACT-ECS scale is a validated measure of quality of life for patients with oesophageal cancer and we chose to include this instrument because of previously demonstrated excellent psychometric properties in a condition which has substantial overlap with chemotherapy induced oral mucositis.[14] We used the oral questions from this scale which resulted in a total score, swallowing index and eating index. In the FACT-ECS indices, higher scores reflect less mucositis.

2.4. Statistical methods

In order to examine test–retest reliability, we compared the OMDQ when measured 24 h apart with two separate evaluations on days 0–1 and 14–15 using the Spearman correlation coefficient and anticipated at least moderate correlation for each item at both time points.

The second objective was to describe the construct validity of the OMDQ. We hypothesised that the OMDQ would be at least moderately correlated with other measures of oral mucositis, namely WHO, VAS and the FACT-ECS sub-scales. We used Spearman correlations to evaluate 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.[15] However, because each child had several assessments (and we considered it unlikely that these assessment could be considered statistically independent), we obtained the P values using a generalized mixed model, assuming that the OMDQ scores followed a Poisson distribution. All analyses were conducted with SAS software (version 9.2; SAS Institute Inc., Cary, NC).

3. Results

Between July 2007 and August 2009, 90 potentially eligible participants were approached. Twenty-one were excluded for the following reasons: does not read English ($n = 7$), parent not present ($n = 1$) and declined study participation ($n = 13$), thus

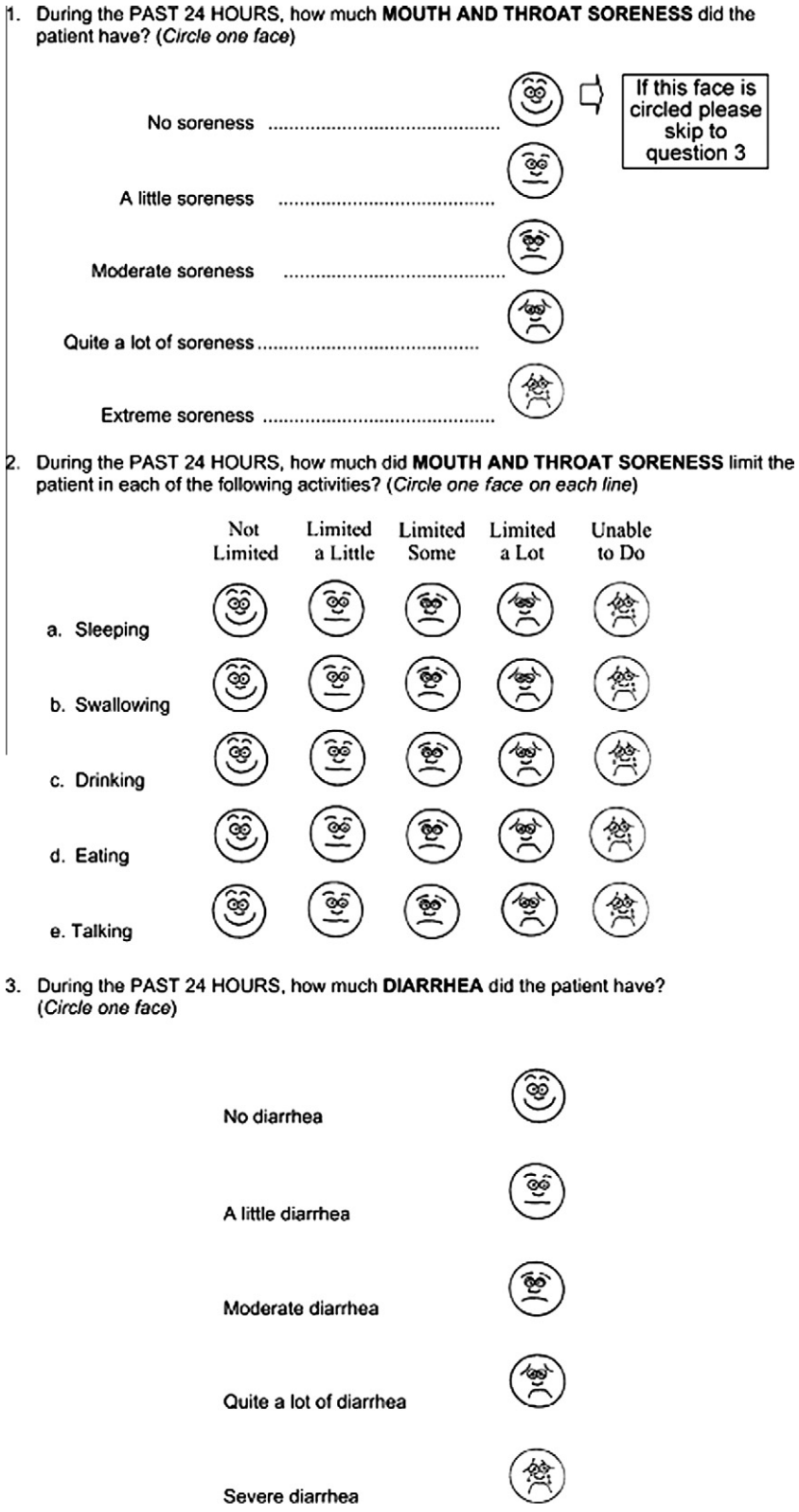

Fig. 1 – Modified OMDQ for use in children.

leaving 69 parent proxy-respondents who consented to the study. One parent withdrew consent prior to the start of the study. Nine parents did not complete the diary (due to child death in 2 cases) and therefore 59 parents provided complete OMDQ data.

The parent and child demographics are shown in Table 1. Mothers were more likely to be the respondent. Most respondents were 30–50 years of age, married and had at least a college level education. The majority of children were undergoing SCT and most had been diagnosed within the previous

Table 1 – Demographics of parents.

Characteristic	Value N = 59
Parent characteristics	
Male (%)	15 (25.4)
Age group (%)	
<30 years	6 (10.2)
30–<50 years	53 (89.8)
⩾50 years	0 (0.0)
At least college education (%)	41 (69.5)
Married (%)	53 (89.8)
Father work full time (%)	45 (76.3)
Mother work full time (%)	31 (52.5)
Supplemental insurance (%)	45 (76.3)
Child characteristics	
Male (%)	40 (67.8)
Median age (IQR) in years	5.62 (2.64, 9.83)
Diagnosis (%)	
Leukaemia/lymphoma	26 (44.1)
Solid tumour	9 (15.3)
Brain tumour	7 (11.9)
Other[a]	17 (28.8)
Metastatic disease (%)	18 (30.5)
Treatment at OMDQ assessment (%)	
Chemotherapy	16 (27.1)
Stem cell transplantation	43 (72.9)
Median years since diagnosis (IQR)	0.35 (0.18, 0.62)
Median days since last chemotherapy (IQR)	6.00 (0.00, 15.00)
Prior history of mucositis (%)	26 (44.1)

OMDQ – Oral Mucositis Daily Questionnaire.

[a] Other diagnoses include: aplastic anaemia ($n = 7$), adrenoleukodystrophy ($n = 2$), hemophagocytic lymphohistiocytosis ($n = 2$), post-transplant lymphoproliferative disorder ($n = 2$), chronic granulomatous disease ($n = 1$), Langerhans cell histiocytosis ($n = 1$), Hurler's syndrome ($n = 1$), and Fanconi's anaemia ($n = 1$).

6 months. Approximately half of the children had previous experience with oral mucositis.

Table 2 illustrates test–retest reliability when measured 24 h apart on days 0–1 and days 14–15. All assessments exceeded the expected moderate reliability threshold established *a priori*. In fact, on days 14–15,[16] when we would have expected mucositis to be present, correlations were good to excellent.

Table 3 illustrates the examination of construct validity. We anticipated that OMDQ would have at least moderate correlation with WHO, VAS and FACT-ECS indices. For the OMDQ questions that relate to pain, swallowing, drinking, eating and talking, almost all correlations coefficients were ⩾0.5. Conversely, correlation coefficients related to the effect on sleeping OMDQ question were generally lower and were <0.5 when examined against the WHO scale and the FACT-ECS eating index. The correlation coefficients with the diarrhoea OMDQ question also were lower and ranged from 0.24 to 0.32.

4. Discussion

This study suggests that the parent-report modified OMDQ is reliable and that questions of OMDQ which relate to pain, swallowing, drinking, eating and talking are valid assessments of mucositis. In contrast, the sleeping and diarrhoea questions did not meet the *a priori* defined threshold for construct validation and thus, this study suggests that these items should be excluded from the measurement of oral mucositis in children.

Whilst a great deal of research has focused on the development and evaluation of oral mucositis scales in adult cancer and SCT patients, very little work has focused on children. Modified instruments have been used in research involving paediatric cancer patients.[17,18] However, a recent systematic review of oral assessment instruments for use with children cited only 3 articles published up to 2008 that reported on the reliability or validity of oral assessment instrument use in children and young people with cancer.[19] One study evaluated the psychometric properties of the Oral Mucositis Assessment Scale (OMAS)[20] and the remaining two studies reported on the use of the Oral Assessment Guide (OAG).[21,22]

The OMAS was evaluated by Sung and colleagues for construct validity in children at least 6 years of age.[20] The OMAS was assessed by a trained evaluator and was measured in 16 children during 45 cycles of chemotherapy for a total of 156 assessments. Convergent construct validity was demonstrated by correlation between OMAS and WHO scores ($r = 0.56$; $P = .0006$), pain VAS scores ($r = 0.37$; $P = .002$), number of doses of topical analgesia ($r = 0.43$; $P = .001$) and cumulative dose of opioid analgesia ($r = 0.38$; $P = .003$).[20] Although correlation was exhibited, the instrument lacked feasibility given difficulty with oral examination in young children.

Chen and colleagues used the OAG to evaluate efficacy of an oral hygiene care regimen in children.[22] Early experience with the OAG revealed confusion with scoring related to the teeth category in babies without teeth along with other measurement issues.[23] Subsequently, a modified OAG was established to score 'no teeth' as normal for that particular child, the gag reflex test was omitted, signs and symptoms of teething were included, descriptive pain assessment was

Table 2 – Test–retest reliability of Oral Mucositis Daily Questionnaire.[a,b]

	Pain	Sleep	Swallow	Drink	Eat	Talk	Diarrhoea
Days 1 and 2	0.676 (<.0001)	0.642 (0.0625)	0.933 (0.0002)	0.511 (0.1594)	0.539 (0.1341)	0.837 (0.0096)	0.700 (<.0001)
Days 14 and 15	0.889 (<.0001)	0.958 (0.0002)	1.000 (<.0001)	0.990 (<.0001)	1.000 (<.0001)	0.844 (0.0083)	0.783 (<.0001)

[a] Table represents Spearman correlation coefficients with P values in parentheses for components of OMDQ measured on two consecutive days, namely days 1 and 2 and on days 14 an 15.

[b] OMDQ comprised seven components: (1) MT1 – amount of mouth and throat pain; (2) MT2 – affect of pain on sleeping; (3) MT3 – affect on swallowing; (4) MT4 – affect on drinking; (5) MT5 – affect on eating; (6) MT6 – affect on talking; and (7) amount of diarrhoea (see Fig. 1).

Table 3 – Construct validation of Oral Mucositis Daily Questionnaire.[a,b]

	Pain	Sleep	Swallow	Drink	Eat	Talk	Diarrhoea
WHO mucositis	0.88 (<.0001)	0.44 (<.0001)	0.69 (<.0001)	0.72 (<.0001)	0.72 (<.0001)	0.68 (<.0001)	0.24 (0.0492)
VAS mucositis	0.82 (<.0001)	0.58 (<.0001)	0.77 (<.0001)	0.77 (<.0001)	0.77 (<.0001)	0.73 (<.0001)	0.24 (0.013)
FACT-ECS Swallow Index	–0.63 (<.0001)	–0.51 (<.0001)	–0.84 (<.0001)	–0.85 (<.0001)	–0.85 (<.0001)	–0.79 (<.0001)	–0.29 (0.143)
FACT-ECS Eat Index	–0.46 (<.0001)	–0.33 (<.0001)	–0.67 (<.0001)	–0.71 (<.0001)	–0.73 (<.0001)	–0.67 (0.005)	–0.29 (0.086)
FACT-ECS Total Index	–0.55 (<.0001)	–0.55 (<.0001)	–0.83 (<.0001)	–0.82 (<.0001)	–0.83 (<.0001)	–0.83 (<.0001)	–0.32 (0.410)

Abbreviations: FACT-ECS – Functional Assessment of Cancer Therapy Esophageal Cancer Sub-scale; WHO – World Health Organization mucositis scale; VAS – pain visual analogue scale.

[a] Table represents Spearman correlation coefficients with *P* values derived from a generalized linear mixed model with repeated measures in parentheses.

[b] OMDQ comprised seven components: (1) MT1 – amount of mouth and throat pain; (2) MT2 – affect of pain on sleeping; (3) MT3 – affect on swallowing; (4) MT4 – affect on drinking; (5) MT5 – affect on eating; (6) MT6 – affect on talking; and (7) amount of diarrhoea (see Fig. 1).

added and the instrument was reworded to make it more understandable to scorers.[23] Gibson and colleagues established content validity of the modified OAG instrument by using a judgmental quantification process that included the opinions of 19 experts.[21]

There are very few oral mucositis instruments that report entirely patient-generated scores.[19] Three such instruments have been identified by Gibson and colleagues, namely the OMDQ,[8] an instrument by Kushner and colleagues[24] and an instrument created by Ohrn and colleagues.[25] These instruments use VAS to ask patients about mouth pain and the effect of mucositis on function. Although these have not previously been used in a paediatric population, clinical studies that have assessed oral mucositis in children with cancer have relied mainly on observational reports by trained observers or health care professionals.[7,18,22] Consequently, our study is important as it is the first report to describe the psychometric properties of a PRO in paediatric mucositis.

Limitations to this study may be a lack of generalizability since participants were recruited from a single Canadian centre. Also, we report only parent-proxy assessments of mucositis. A future goal will be to examine the psychometric properties of oral mucositis measures including PROs from children themselves. Nonetheless, although self-report may be preferable, parental report of oral mucositis may frequently be the only source of repeated information in children who are too young or too ill to self-report. In addition, parent report also provides an important perspective in the child's health.[26,27]

Whilst we have shown that the OMDQ is reliable and that the questions relating to mouth and throat pain and effect on function are valid, nonetheless, there are limitations to the OMDQ. First, the instrument currently contains questions related to sleeping and diarrhoea. Deletion of these questions may be appropriate for future studies. Second, the OMDQ does not address other items that are considered important in mucositis such as the presence of ulcers and the requirement for pain medications. Consequently, further improvement in mucositis instrumentation and PROs in children have also commenced to address these deficiencies.[28–30]

In conclusion the parent-reported OMDQ is reliable and the questions relating to mouth and throat pain and effect on function display construct validity. Future work should include evaluation in a wider population and wider age range of children with cancer. Further research also should focus on self-report mucositis evaluation for children and continuing to improve mucositis instrumentation in paediatric cancer.

Conflict of interest statement

None declared.

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