Assessment of minimal clinically important improvement by using Oral Health Impact Profile-14 in Behçet's disease

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ABSTRACT

Objectives. *The aim of this prospective study was to detect minimal clinically important improvement (MCII) of oral health impact profile-14 (OHIP-14) for assessing the effect of treatments for oral ulcers in Behçet's disease (BD).*

Methods. *BD patients with active oral ulcers (F/M:36/22) were selected. Baseline and follow-up data were collected by clinical examinations and questionnaires. Patients rated their global impression of change (PGIC) measured by a transitional question. MCII was defined as the difference in mean change from baseline in OHIP-14 between patients with no response to therapy and patients with next higher level of response.*

Results. *Approximately one third (29.3 %) of the patients expressed an improvement during control examinations. A significant correlation was observed between raw change in OHIP-14 score and change in number of oral ulcers (r=0.69 p=0.017). Inactive patients increased from 44.1% in baseline to 58.8% in follow-up examination. A trend towards decreased number of oral ulcers was observed in follow-up (0.64±0.93) compared to baseline (1.44±1.92) in the improved group (p=0.096). According to regression analysis, PGIC was a significant predictor of change in raw OHIP-14 score. The threshold levels generated from the ROC analyses in OHIP-14 score best associated with clinically important improvement were -3.5 points (sensitivity: 80%, specificity: 88.6%) and -38.1% (sensitivity: 86.7%, specificity: 97.1%) respectively.*

Conclusion. *Changes in OHIP-14 scores seem to be a sensitive and valuable tool for the determination of MCII during follow-up of Behçet's disease patients for oral disease assessment.*

Introduction

Behcet's disease (BD) is chronic and relapsing multi-systemic inflammatory disorder (1-5). Oral ulcer is the most common clinical manifestation of BD and is associated with a poor oral health (2, 4-6) and quality of life (2, 7-9).

Although clinician-based objective outcome measures are preferred traditionally, the importance of patients' point of view on their oral health status and treatments is also widely accepted in dentistry and medicine. The Oral Health Impact Profile-14 (OHIP-14) as an oral health related quality of life (OHRQoL) questionnaire is amongst the most widely used instruments in clinical studies evaluating oral health and quality of life in dentistry. The OHIP-14 is based on a conceptual model of oral health that uses the World Health Organization International Classification of Impairments, Disabilities and Handicaps framework (10, 11).

Presence of oral ulcers cause poor OHRQoL when evaluated by OHIP with 14 items (OHIP-14) in patients with BD. Having active oral ulcers, being female and treatment with colchicine are found to be risk factors for impaired OHRQoL in BD patients (7, 8). OHRQoL status is also found to be similar in different countries when studied in patients from UK and Turkey. Poor OHRQoL is related with the healing time of oral ulcers in UK and the number of oral ulcers in Turkey (9). The close association between the presence of oral ulcer and OHRQoL status in BD may be a part of the decision-making process of treatment modalities in BD.

Treatment options of BD patients vary from colchicine and antibiotics (12-13) to high dose immunosupppressives (IS)(1-4). Colchicine is usually the first option for patients with mucocutaneous involvement, whereas ISs are used for major organ involvement (1-4,14). Although elimination of infection foci from the oral environment may be an adjunctive treatment to standard agents to control flare-ups of oral ulcers (2, 3, 6, 14), the most effective medication is still unclear for patients with mucocutaneous

involvement. Topical medications and oral hygiene are the first line of treatment of oral ulcerations in BD (14).

Minimal clinically important difference (MCID) and minimal clinically important improvement (MCII) are instruments to evaluate and interpret the treatment modalities for clinicians. MCID is defined as the smallest change in score of outcome measure perceived by patients as improvement or worsening (15). It helps to assess the patient's status compared to the previous visit. A transition question, "patient's global impression of change (PGIC)" is used for the determination of MCID. One unit difference of PGIC (slightly better or slightly worse) defines MCID. The term minimal clinically important improvement (MCII) addresses only the direction of improvement but not worsening (16, 17), so it is more useful for the evaluation of improvement in clinical practice and preferred in recent studies (17).

The aim of this prospective study was to evaluate MCII of OHIP-14 by using PGIC, for assessing the effect of treatments for oral ulcers in patients with BD.

Material and methods

In this prospective study, 58 BD patients (F/M:36/22, mean age: 39.2±11.9 yrs) classified according to the International Study Group (ISG) criteria (18) and were selected from the Behcet's disease outpatient clinic of Marmara University Hospital. BD patients were under treatment with colchicine (1.5 mg/day, n=38) or immunosuppresives (IS, n=20) within the last year. The main clinical manifestation for patient selection was persistent oral ulcers within a 12-month period and consecutive patients who had active ulcers in the previous three months and used medication regularly were included in the study. Patients who were incompliant to visits and medications were excluded.

No major organ involvement was observed in most of the patients (n=45, 77.6%). As oral ulcers can persist under both colchicine and ISs, patients were not categorized according to treatment modality. Thirteen patients with BD had major organ involvement among patients treated with ISs (n=20), others (n=7) used ISs to eliminate resistant oral ulcers. Disease duration was 9.9±7.1 years in patients with BD. If disease duration was over 5 years and no major organ involvement was present currently or in past history, routine follow-up was performed in every 6-monthly periods. Therefore, the follow-up period was 6 months for the majority of the group (n=49) and 4 months for the others (n=9) according to the clinical course. Treatment modalities were not changed during the study. The criteria for exclusion were pregnancy, chronic diseases, psychiatric disorders, cancer and other oral mucosal disorders and lack of compliance.

Baseline and follow-up data were collected by the investigators. After the approval of the Marmara University Local Ethics Committee and having the written informed consent of the patients, clinical examinations were done by the investigators and two questionnaires were filled. First questionnaire included questions regarding demographic characteristics, symptoms and oral ulcer pattern of the patients and filled by the researchers during face-to-face interviews. Second questionnaire was "oral health impact profile-14 (OHIP-14)", which consisted of 14 questions for measuring self reported oral health quality of life (OHQoL). The questionnaire developed by Slade (10) was translated into Turkish and validated in our previous study (8). Subjects self-completed OHIP-14 two times, one at baseline and the other during the follow-up visit. Responses to each item of OHIP-14 were scored on five categories (0 = never, 1 = hardly ever, 2 = occasionally, 3 = fairly often, 4 = very often). Consequently, total score could be ranged from 0 to 56 with a high score indicating poor OHRQoL status (10). All physical examinations were repeated during the follow-up visit and OHIP-14 was re-filled. Reference period was the duration in between 2 visits for OHIP-14, the number of oral ulcers and personal oral health perception. The mean duration between visits was 6.1±3.1 months in BD.

In addition, PGIC was measured by a transition question during the follow-up which was: "How do you feel today as compared to your last visit as far as your oral health is concerned?". Responses were recorded as "worse", "slightly worse", "no change", "slightly better", or "better". The concept of "transition" method was originally developed by Jaeschke *et al*. (16) and since applied in different rheumatological settings (16, 19). This question was needed for the evaluation of minimal clinically important improvement (MCII). Among different methods used for measuring MCII, the most widely used methodology is to use an external anchoring question to identify the cut-off points for MCII, in other words, a question that asks the patient about perceived improvement (20, 21).

Statistical analysis was performed by using SPSS 11.5. Patients were stratified according to their PGIC category, and the mean OHIP-14 raw and percent change scores [(raw change/baseline) x 100], and also the mean change in the number of oral ulcers were calculated for each level of the PGIC category. MCII was defined as the difference in mean change from baseline (mean baseline score - mean follow-up score) in OHIP-14 between patients with no or negative response to therapy ("no change", "slightly worse" and "worse") and patients with next higher level of response ("slightly better"). Mean changes in OHIP-14 scores and number of oral ulcers were compared by Student's t test and analysis of variance (ANOVA). Pearson correlation test was used in the evaluation of the relationship between OHIP-14 and the number of oral ulcer. Predictors of OHQoL were analyzed by multiple linear regression. Receiver operating characteristic (ROC) curve method was used to determine the sensitivity and specificity of OHIP-14 score changes. The criteria for ROC analysis was PGIC which was categorized into two groups for making the variable dichotomous: non-improved ("worse", "slightly worse", and "no change") and improved group ("slightly better"). The area under the ROC curve ranged from 0.8 to 1.0 and discriminated improved patients from non-improved with high accuracy.

One patient who had responded "better" to the transition question was ex-

cluded from the analysis during logistic regression and ROC curve analysis. The response was above the threshold of MCII that was minimum or the lowest degree of improvement. Wilcoxon rank test was used in the evaluation the number of oral ulcers in between baseline and follow-up examinations in both improved and non-improved groups due to non-normal distribution of data and the number of patients in the analysis.

Results

In the prospective study, mean change was 1.83±1.89 for OHIP-14 score, and -0.11±0.41 for the number of oral lesions in patients with BD (n=58). The change in OHIP-14 scores measured during the follow-up visit was not associated with the change in the number of oral lesions (r=0.033, p=0.808). Mean change in OHIP-14 scores and number of oral lesions according to various variables are presented in Table I. As seen in the Table, mean changes in OHIP-14 score and number of lesions were similar according to the gender, treatment modality and duration of the follow-ups in the prospective study (p>0.05).

According to PGIC categories, the proportion of the patients who expressed improvement during control examinations was 29.3% (n=17) in the study. Majority of the study group (n=34, 58.6%) expressed no change and 12.1% (n=7) expressed worsening during follow-up. Mean change in the number of oral lesions was not different by PGIC categories, however the mean change in OHIP-14 score was significantly different for each category of PGIC (p<0.001). Similar results were obtained when the data was analyzed by multivariate method, multiple linear regression and presented in Table II. According to the multiple regression analysis, PGIC was the only significant predictor of change in raw OHIP-14 score, while the patients' age, sex, number of oral lesions and duration of follow-up were not associated. When patients expressed improvement during control examination (n=17) were re-evaluated, the percentages of being inactive were 44.1% (n=7) in baseline and 58.8% (n=10) in follow-up examination. Although a trend towards decreased number of oral ulcers was observed in follow-up (0.64±0.93) compared to baseline (1.44±1.92), no statistically significant difference was present (p=0.096). Yet, OHIP-14 score was significantly lower in follow-up examination (6.23±10.18) than baseline examination (17.17±15.41) (p=0.011). In addition, a significant correlation was also observed between raw change in OHIP-14 score and change in number of oral ulcers (r=0.69 p=0.017). These findings could explain the relationship between oral ulcer patterns as an objec-

Table I. Mean change in OHIP-14 score and number of oral lesions in BD patients according to various variables.

	Change in OHIP-14 Score (Baseline- Follow-up) Mean ± SE	Change in Number of lesions (Baseline- Follow-up) Mean ± SE
Gender		
Male (n=22)	1.04 ± 2.05	-0.44 ± 0.63
Female (n=36)	2.30 ± 2.79	0.09 ± 0.54
	t=0.32 p=0.75	t=0.62 p=0.53
Treatment modalities		
Colchicine (n=38)	2.02 ± 2.28	0.29 ± 0.51
Immunosupressive (n=20)	1.45 ± 3.45	-0.88 ± 0.65
	t=0.14 p=0.88	t=1.38 p=0.17
Duration for follow-up:		
<3 months(n=18)	2.61 ± 4.45	0.84 ± 0.77
3-6 months (n=17)	1.17 ± 2.51	-1.17 ± 0.78
7-12 months (n=23)	1.69 ± 2.82	-0.07 ± 0.57
	F=0.04 p=0.58	F=1.89 p=0.16
PGIC categories:		
Worse (n=1)	-20.00	-6.00
Slightly worse (n=6)	-14.00 ± 7.89	0.29 ± 2.88
No change (n=34)	0.70 ± 0.99	-0.46 ± 2.41
Slightly better (n=16)	10.37 ± 4.72	0.90 ± 0.48
Better (n=1)	20.00	-1.00
	F=5.60 p<0.001	F=1.31 p=0.21
Total group (n=58)	1.82 ± 1.89	-0.11 ± 0.41

Table II. Predictors of change in OHIP-14 score by linear regression analysis.

Variables	B	Std error	p	Beta (standardized coefficient)
Age	-0.133	0.160	0.408	-0.106
Gender	3.159	3.813	0.411	0.107
Treatment modality	-1.628	3.615	0.654	-0.054
Duration of follow-up	0.047	0.580	0.935	0.010
PGIC	11.266	2.448	0.000*	0.550
Change in no. of oral lesions	-0.531	0.578	0.362	-0.115
Constant	-31.99	12.540	0.014	0.282

* Statistically significant
no. 58, R=0.560, R^2=0.313, Adjusted R^2=0.232.

Table III. The threshold levels generated from the ROC analyses for both raw and percent change in OHIP-14 score best associated with clinically important improvement (slightly better).

OHIP-14 score:	Area under the curve ±SEM (95%CI)	Change (optimal cut-off points)	Sensitivity (%)	Specificity (%)
Raw change	0.843±0.074 (0.698-0.988)	-3.5	80.0	88.6
Percent change	0.893±0.072 (0.753-1.034)	-38.1	86.7	97.1

tive measurement and OHIP-14 score in patients expressing improvement during control examinations according to PGIC. In contrast, patients in the non-improved group (n=41) were active at baseline examination and a patient was inactive and others were active at the follow-up examination of the non-improved group. The number of oral ulcer and OHIP-14 score were almost same at baseline (2.55±2.98 and 20.65±15.87, respectively) and at follow-up examinations (3.04±3.42 and 22.60±15.16, respectively) (p=0.289 and p=0.973, respectively).

ROC curve analysis results of the data are presented in Tables III and Figure 1. Raw and percent changes in OHIP-14 scores were used during this analysis. The threshold levels generated from the ROC analysis for both raw and percent change in OHIP-14 score best associated with clinically important improvement were -3.5 points (sensitivity: 80%, specificity: 88.6%) and -38.1% (sensitivity: 86.7%, specificity: 97.1%) respectively (Table III). Area under the curve was 0.843 for raw OHIP-14 change and 0.893 for percent change, which means that a decrease of 3.5 points in raw OHIP-14 score can correctly identify 84.3% of improved patients from non-improved, while 38.1% decrease in baseline percentage of OHIP-14 score can identify 89.3% of the improved from non-improved.

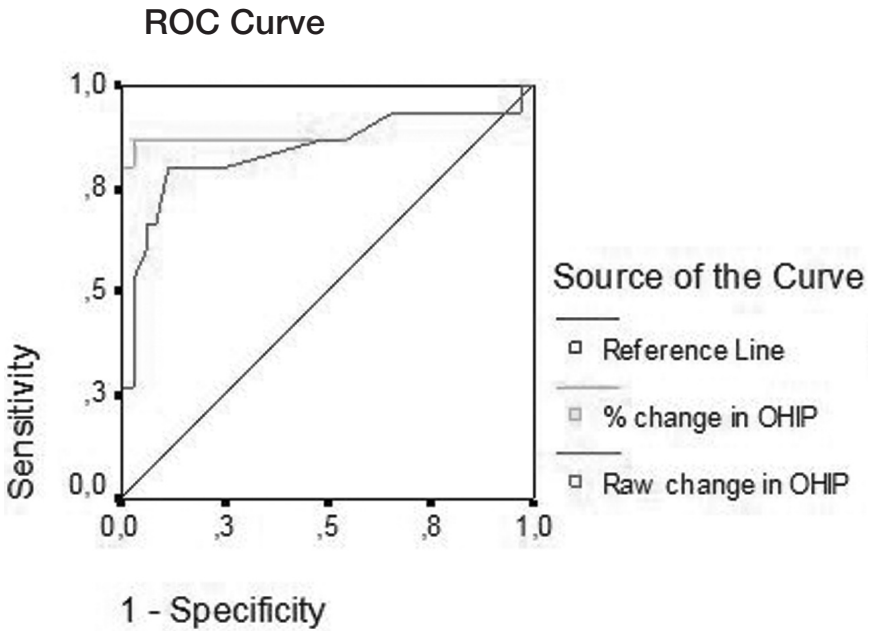

Fig. 1. ROC curve for MCII. Diagonal segments are produced by ties.

Discussion

Patient-reported outcomes provide the patient's perspective on health outcome and help to understand treatment effects on medical conditions (22, 23). Traditionally, clinicians diagnose and treat oral diseases regarding caries, periodontal health problems and oral mucosal diseases by using clinician-based objective outcome measures in dentistry (24). In contrast, OHRQoL reflects subjectively perceived oral functions, psychological and social impacts and pain experience in relation to oral health problems in clinical practice (24, 25). The combined clinical indicators and subjective instruments give important information to evaluate individual well-being. In this respect, it is necessary to evaluate "responsiveness" for understanding of health outcomes, such as patients' reports about their health conditions as improving, worsening, or no change. Although changing pattern of some indicators could be statistically significant or not, correct interpretation of the results by clinicians is the most important issue. A specific guidance produced for this purpose may solve these problems more effectively (23, 26).

In the present study, changing OHIP-14 scores was different according to PGIC categories whereas it was not related to disease-related conditions regarding gender, treatment modality and follow-up periods. There was also no significant correlation between the change in OHIP-14 score and change in the number of oral lesions. The relationship between changing pattern of OHIP-14 that converts subjective findings to objective criteria and PGIC categories is an important issue for clinical evaluation and our results may indicate that patient's perception of oral health may not be in concordance with the number of oral ulcers in Behçet's disease as a global assessment. However, our analysis changed to explain the level of improvement. When oral ulcer pattern was compared to baseline and follow-up examinations in patients expressing improvement according to PGIC categories, an increase in being inactive and a decrease in the number of oral ulcers in active patients were found to be important factors. Moreover, change in OHIP-14 score and oral ulcers were significantly correlated parameters in this group. Therefore, these finding may suggest that a change in oral ulcer pattern could be related with expressed improvement and OHIP-14.

OHIP-14 for measuring OHRQoL was used to describe the patient's perspective and ROC approach in finding the MCII. MCII for OHIP-14 as an objective criteria was determined as -3.5 points and -38.1% in the study. Sensitivities and specificities were equal and over 80% for both conditions. OHIP-14 measures the negative impact of problems. Higher scores indicate greater negative impact, reflecting a poorer OHRQoL whereas a decrease in score could be explained by improving of OHRQoL (7). Clinicians can easily and objectively evaluate the effects of treatment on patient's well-being by using these cut-off values for OHIP-14. Scores below these cut-offs in OHIP-14 may be detectable but will be clinically not meaningful.

The ROC approach is more suitable for data that is not normally distributed, and can describe the magnitude of change by means of sensitivity, specifi-

city, and area under the curve, assuming that the PGIC represents a criterion standard of change and quantifies the validity of the chosen MCII (27). The MCID and MCII are widely used concepts for defining the smallest change in an outcome measure perceived as beneficial by patients or physicians, which is needed for decisions in the patient's management. Recently, there is an increased emphasis on identifying whose perspective the minimally important difference is based on and a substitution of "MID" for MCID is suggested. For patient-reported health-related quality-of-life measures, the MID describes the patient's perspective. However, disease activity indices also rely on clinicians' judgment and, thus, the MID may also present the clinicians' perspective (28).

MCID has not been evaluated in oral quality of life questionnaires in Behçet's disease so far. However, it is commonly used in the evaluation of treatment and patients' conditions for different questionnaires in literature. Range of MCID is from 1.6–7.0 for SF-36 Physical Component Score and 2.3–8.7 for mental component score in Crohn's disease (29). MCID for dermatology quality life index range from 2.24–3.10 for patients with chronic idiopathic urticaria (30). Two important studies assessing this concept in dentistry were published recently. Minimal importance difference for OHIP-20 was evaluated in patients with removable partial dentures and it was found that new dentures had a positive impact in the majority of subjects by using this method as a guideline (31). The other study was carried out by using OHIP-49 in prostodontic interventions. Minimal important difference was found to be 6 OHIP units (95% confidence interval: 2 to 9) (32).

Main limitation of our study was the restricted number of patients. This could be explained by inclusion criteria that only permitted consecutive patients with active oral ulcer, stable treatment modality and using medication regularly. Yet, changes in the presence of oral ulcers could be easily detected by PGIC in our patient group.

As a conclusion, when clinicians use OHIP-14 score changes in clinical practice by using MCID/MCII, patient's perspective on the clinical condition and treatment strategy will be more easily understood. In addition, these findings are the first results evaluated by MCII in disease assessment of BD and may therefore, help in decision-making process of treatment plans in BD.

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