Time spent on treatment (TSOT). An independent assessment of disease severity in atopic dermatitis

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ABSTRACT

Introduction: Time spent on treatment (TSOT) appears to reflect disease severity in pediatric patients with atopic dermatitis (AD). Our purpose was to examine the relationship between time spent on treatment and parental psychological parameters such as anxiety and depression.

Methods: TSOT was studied in a group of parents of patients with AD participating in an eczema school. TSOT included all types of topical treatment. In addition, dermatological life quality (the IDLQI questionnaire), depression (the MDI questionnaire), and anxiety (the STAI questionnaire) were assessed as well as the self-reported (by parent) disease severity, treatment effect, and confidence in treatment (VAS scales) using descriptive statistics, multiple linear regression, and rank correlations (Kendall's tau).

Results: TSOT was found to be significantly associated with parental age (older parents report lower TSOT) and IDLQI (low quality of life with high TSOT), whereas all the other parameters appeared redundant. Sex of the parent showed no effect on TSOT.

Conclusion: Our data suggest that TSOT is not correlated with anxiety or depression. A positive independent correlation was found with general quality of life, offering mutual validation of the measures. The observations suggest that further investigation of TSOT as a surrogate measure of morbidity in AD may be of practical interest in order to develop an internationally comparable morbidity measure in AD.

KEY WORDS

time, spent on treatment, quality of life, assessment, atopic dermatitis, children

Introduction

An accurate, reproducible and valid measure of disease severity is a prerequisite for pathogenetic, epidemiological, and therapeutic studies of any disease. Sometimes these measures are simple physical measures; at other times composite or surrogate measures are the best option (1).

Time is a universal human condition. In contrast to many other common human conditions, the allocation and use of time can to some degree be controlled by the individual. We have therefore suggested that time spent on treatment (TSOT) may be an appropriate surrogate measure of morbidity in patients with non-lethal

chronic recurrent diseases such as skin diseases. For atopic dermatitis (AD) we have found support for this suggestion in a positive correlation between disease severity and TSOT (2).

Skin diseases are most often treated with topical therapy. For the patient this involves time-consuming applications of either drugs or emollients. Treatment such as UV therapy are also time-consuming for patients, and systemic therapy requires follow-up visits, blood tests, and a continued need for adjuvant therapy with emollients. If the treatment is effective over time, the time spent will gradually decrease as disease intensity decreases and the treatment routine of the patient increases.

When the patient chooses to spend a lot of time on treatment, this is furthermore not only a measure of the amount of disease present, but also of the importance the patient or the patient's caregiver attaches to the disease. It is unlikely that anyone will spend much time on something he or she does not expect any benefit from. Time may therefore also be an overall measure of disease impact for non-lethal diseases.

We have previously shown that TSOT correlates with objective SCORAD as a measure of morbidity in children with AD (2). Psychological factors may, however, be assumed to influence the time devoted to maintaining good skin health in children; for example, care, compassion, and a sense of responsibility for the next generation. It may therefore be a reflection not only of disease severity but also of general life quality, anxiety, and depression. To examine these aspects further we analyzed 10 self-reported factors that were thought to represent different aspects of morbidity; for example, TSOT and other measures of disease severity, anxiety, and depression in a larger group of parents of AD patients.

Methods

Participants were recruited from January 2002 to May 2004 in connection with the establishment of an Eczema School at Roskilde Hospital, Denmark, which serves as a secondary referral center. This means the test persons were recruited among highly motivated families actively seeking knowledge. Using questionnaires, the participants were asked to provide information about the following aspects of their disease:

1. TSOT (2, 3). How much time did they spend on different activities as a consequence of their disease during routine visits? This included time directly spent in self-care: "How much time do you spend daily on?" 1) Application of ointments. 2) Application of topical medicine. 3) Time spent at the pharmacy. 4) Time spent at the doctor(s). TSOT in this study represented only positive actions such as treatment and not negative impacts such as loss of sleep. Time spent on treatment (TSOT) was calculated as the total amount of time spent daily on treatment (min./day). TSOT has a theoretical maximum of 1,440 min.

2. MDI (Major Depression Index). The MDI items cover the ICD-10 symptoms of depression (4). These symptoms also include the DSM-IV major depression symptoms; although in the DSM-IV "low self-esteem" is incorporated within the item of guilt. The score is:

- Mild depression: A score of 4 or 5 in two of the first three items + a score of at least 3 on two or three of the last seven items.
- Moderate depression: A score of 4 or 5 in two of the first two items + a score of at least 3 on four of the last seven items.
- Severe depression: A score of 4 or 5 in all of the first three items + a score of at least 3 on five or more of the last seven items.

The total score was used in the calculations.

3. STAI (5) (Spielberger's State Anxiety Index) questionnaires. This is a self-administered standard, validated tool for the assessment of anxiety. It is designed to measure anxiety proneness and current level of tension and may be used in the general population. It has been used in numerous studies, and been shown relevant to the specific study of AD (6). It consists of 40 items in a Likert scale format and has a range of 20 to 80, with higher scores indicating higher levels of anxiety.

4. Quality of life was assessed by the Infant Dermatology Life Quality Index (IDLQI, for infants under 4 years of age) or Dermatology Life Quality Index (DLQI, for older children). They are self explanatory, and are usually completed in 2 minutes. For the IDLQI and DLQI, the general scoring guidelines provided by Finlay and Lewis-Jones were used (7, 8). Only the total score was used. The scores were pooled in order to compare the different age groups directly. No data exist to support this at present, but the two questionnaires have a very similar structure and deal with the same domains. The scores are also in the same range. In the calculation of further results from the two questionnaires, they were therefore thought to be directly comparable. The maximum score for both questionnaires is 30, and a higher score indicates diminished life quality.

5. VAS Scores. All participants were asked to indicate: Overall morbidity, confidence with coping, adherence to therapy, and effect of current therapy on a Visual Analogue Scale (VAS: 0–100). Because of the overall nature of the question, no additional attempts were made to verify the validity of the VAS scores. Questionnaires were assessed as directed by acknowledged guidelines and overall scores noted. VAS scores and sick-leave data were noted as whole numbers.

The factors analyzed were: age, sex, self reported overall morbidity (SROM), self-reported treatment effect (SRTE), confidence (CONF), adherence to therapy (ADTH), anxiety (STAI), depression (MDI), TSOT, and IDLQI/DLQI.

Table 1. Parameters studied.

	Mean	95% CI
Age*	13 years	9–17 years
Severity†	3.9 cm	3.3–4.5 cm
TSOT	17 min/day	1.3–20 min/day
Confidence†	5.6 cm	5.0–6.2 cm
Adherence†	7.8 cm	7.3 –8.0 cm
Treatment effect†	6.0 cm	5.4–6.6 cm
IDLQI	6	5–7
MDI	11	9–13
STAI	36	33–39

A total of 86 patients participated, but only 82 patients' complete datasets were analyzed. *Patient age. The parents answered the questions for patients that were children. †Self reported aspect on VAS.

Statistical methods

The aim of the statistical analysis is to determine the correlation of TSOT with other variables and to establish that TSOT holds unique information.

Data were not found to be normally distributed (Lilliefors Test) (9), and rank correlation (Kendall's tau) (10) was therefore used for initial analysis.

To determine whether TSOT holds unique information, variables having significant correlations ($p < 0.05$) with TSOT were combined in a linear regression model attempting to predict TSOT. We do this by performing stepwise regression using a standard function in MatLab (11). We then investigate the correlation between the resulting model and TSOT using Kendall's tau.

Results

A total of 86 patients participated. Four patients did not provide complete datasets and were therefore excluded from further analysis. A complete matrix was available for analysis for 82 patients. For children up to 16 years of age the parents completed the questionnaires. Using the correlation and significance matrices shown in Table 1, it is shown that there is no difference in TSOT related to sex. Furthermore, it is seen that only age, SROM, MDI and IDQLI/DLQI have a significant correlation with TSOT, with $p = 0.007$, $p = 0.009$ $p = 0.0003$, and $p =$

Table 2a. Correlation between the parameters studied, Kendall's tau.

	Age	Sex	SROM	CONF	ADTH	SRTE	IDLQI/DLQI	MDI	STAI	TSOT
Age	1.00									
Sex	0.27	1.00								
SROM	0.11	0.04	1.00							
CONF	−0.07	−0.12	−0.14	1.00						
ADTH	−0.18	0.06	−0.04	0.25	1.00					
SRTE	−0.11	0.04	−0.19	0.46	0.32	1.00				
IDLQI/DLQI	0.14	−0.06	0.48	−0.10	0.02	−0.18	1.00			
MDI	0.08	0.12	0.22	−0.16	−0.07	−0.12	0.37	1.00		
STAI	0.23	0.00	0.12	−0.24	−0.14	−0.17	0.30	0.57	1.00	
TSOT	−0.22	0.00	0.21	−0.02	0.14	0.04	0.31	0.24	0.11	1.00

Kendall's tau reflects the strength of the association.

Table 2b. Correlation between the parameters studied, *p*-values.

	Age	Sex	SROM	CONF	ADTH	SRTE	IDLQI/DLQI	MDI	STAI	TSOT
Age	0.00									
Sex	0.004	0.00								
SROM	0.20	0.70	0.00							
CONF	0.40	0.20	0.08	0.00						
ADTH	**0.03**	0.50	0.60	**0.003**	0.00					
SRTE	0.2	0.70	**0.02**	**0.0000**	**0.0000**	0.00				
IDLQI/DLQI	**0.08**	0.60	**0.0000**	0.20	0.80	**0.02**	0.00			
MDI	0.3	0.20	**0.005**	**0.05**	0.40	0.10	**0.0000**	0.00		
STAI	**0.006**	1.00	0.10	**0.002**	0.08	**0.03**	**0.0002**	**0.0000**	0.00	
TSOT	**0.007**	1.00	**0.009**	0.80	0.09	0.60	**0.0003**	**0.005**	0.20	0.00

The p-values reflect the statistical significance of the mathematical correlations described in Table 2a. Significant correlations are highlighted in bold.

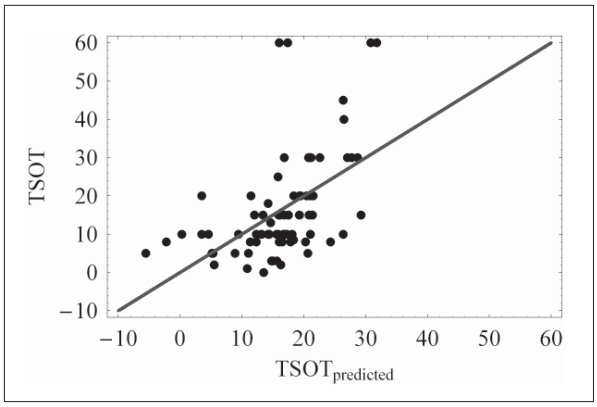

Figure 1. Test of the model. The mathematical model can be tested by plotting predicted values against actual values. For each patient the predicted time spent on treatment ($TSOT_{predicted}$) is plotted versus the actual reported value. Well-predicted values will be on the line $TSOT_{predicted}$ = TSOT.

0.0045, respectively. Age has a low negative correlation (ρ = -0.22) with TSOT, indicating a small tendency to spend less time the older the patient is, whereas morbidity shows a small positive correlation (ρ = 0.21), supporting the intuitive argument that time consumption tends to increase with the perception of severity. IDLQI/DLQI and MDI both have a small positive correlation with TSOT of ρ = 0.31 and ρ = 0.24, respectively. This shows that TSOT has a small tendency to increase if the either dermatological life quality is perceived to be poor (IDLQI/DLQI) or if depression is high (MDI).

From the low correlation values we conclude that TSOT cannot be predicted from one of the other variables. However, the question remains whether the TSOT variable may be predicted from a combination of these four variables or if it holds unique information. To explore this further we built a linear regression model, based on the four variables with significant correlation, using stepwise regression. The best linear regression model is $TSOT_{predicted}$ = 12.61 ” 0.2867 × Age + 1.242 × × IDLQI/DLQI.

The fit to the data is not improved by including SROM and MDI in the model, suggesting that these factors do not contribute significantly. TSOT and $TSOT_{predicted}$ have a mutual correlation of 0.4187 with $p = 2.6\times10^{-5}$, which is significantly better than the correlation to any single variable. However, the correlation is still far from 1.0, which is also evident from Figure 1, in which $TSOT_{predicted}$ is plotted versus the actual TSOT values. Based on this analysis we conclude that, even though TSOT exhibits an expected correlation with some of the traditional parameters included in this study, TSOT holds a high degree of unique information.

Analysis of the “leftover variables”

Because only two of the four variables that showed significant correlation with the TSOT variable were needed for explaining the linear relationship, one should expect a high correlation between the two leftover parameters (SROM and MDI) and the other two (AGE and IDLQI/DLQI). Table 2 also shows that there is a very significant correlation (0.37) between MDI and IDLQI/DLQI and a very significant correlation (0.48) between SROM and IDLQI/DLQI. From this analysis we cannot conclude that SROM and MDI are redundant variables in general. However, they are redundant in the prediction of TSOT.

Discussion

The factors underlying patients’ perception of their own disease is of general clinical interest. The analysis suggests that TSOT is an independent factor in the description of disease severity in AD. It appears mainly influenced by the IDLQI/DLQI, age of the patient, assessment of severity/morbidity (SROM), and overall parental depression (MDI), but not by the sex, self-reported confidence in the treatment (CONF), self-reported adherence (ADTH), self-reported treatment effect (SRTE), or anxiety (STAI). The validity of the observations is supported by the significant positive correlation between STAI and MDI and between SRTE and Confidence, which both carry high a priori face validity; that is, worry and depression appear to be naturally associated, as do confidence and self-reported treatment effect. In the analysis of the relative importance of these factors, however, it was found that SROM and MDI were redundant parameters. The main explanatory factors suggested for TSOT were IDLQI/CDLQI and patient age, but these only showed partial correlations, suggesting that TSOT contains unique information not contained in traditional self-reported measures of morbidity.

The negative influence of patient age on TSOT suggests that the measure may reflect parental coping and other qualities of the parent-child relationship. It is hypothesized that older patients with more experienced parents apparently spend less time on treatment than younger patients whose parents are assumed to be less experienced. It is also possible, however, that the lower TSOT reflects a lower coping ability and a relative state of neglect, rather than more experience. The independence of the TSOT and MDI scores does not support this interpretation, however.

The finding that IDLQI influences TSOT contrasts with earlier findings. In a previous study we found no correlation between TSOT, disease duration, and the Dermatology Life Quality Index (DLQI) in a mixed group of adult patients (3). It is speculated that TSOT may be disease-specific and that any correlation is therefore obscured if

multiple diseases are compared. Other sources of error also exist. Recall bias may occur when patients estimate factors retrospectively rather than registering them prospectively. Principally, recall bias can therefore be expected, either due to inaccurate estimates of time or willingness to accommodate the doctor. We did not find that parents had problems answering fixed simple questions in an earlier study in which high test-retest congruence was also found (2). The IDLQI and DLQI were combined in order to compare quality of life in patients of different ages. This was done because the questionnaires are very similar in structure, items/domains, and range of scores.

Suspected sources of error such as parental anxiety and depression, perceived effect of treatment, parental confidence (CONF), and self-reported disease severity did not appear to play a major role in TSOT. The level of treatment may be expected to play a role, but is thought to be in calculated in TSOT (2, 3, 11). This suggests that further studies of TSOT as a generic self-reported measure of disease severity may be relevant. The use of time as a measure may allow easier comparisons internationally, compared to more situational or culturally related value items.

List of abbreviations

AD	Atopic dermatitis
ADTH	Adherence to therapy
CONF	Confidence in the one's own ability to manage the disease
DLQI	Dermatology Life Quality Index
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders
ICD10	International Classification of Diseases
IDLQI	Infant Dermatology Life Quality Index
MDI	Major Depression Index
SROM	Self reported overall morbidity
SRTE	Self-reported treatment effect
STAI	Spielberger's state anxiety index
TSOT	Time spent on treatment
VAS	Visual analogue scale

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