Validation of the Urticaria Control Test (UCT) in Children with Chronic Urticaria

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Abstract

ABSTRACT Background No validated tools exist to evaluate chronic urticaria (CU) control in children. While the Urticaria Control Test (UCT) exhibits favourable clinometric properties in adult CU, it is not yet validated in children. Therefore, we sought to evaluate the validity of the UCT for the assessment of pediatric CU. Methods Children presenting with CU were consecutively recruited. Participants completed both the UCT and the Children's Dermatology Life Quality Index (CDLQI). We assessed the internal consistency, convergent and known-groups validity, and screening accuracy of the UCT at study entry and at follow-up. Results A total of 52 children with CU were recruited. The UCT exhibited respectable internal consistency in the evaluation of CU (Cronbach's α=0.73 [95%CI: 0.62, 0.85]). UCT and CDLQI scores strongly correlated (r=-0.74, P<0.01). The UCT distinguished between different strata of disease severities established by the CDLQI (P<0.01). Screening accuracy of the UCT was excellent in the discrimination of poorly controlled CU (area under the curve=0.82). An optimal cut-off of [?]10 was determined for defining poorly controlled CU (sensitivity=95.5%, specificity=63.3%). Data at follow-up were consistent with data at study entry. Conclusion The UCT is a valid tool for the assessment of pediatric CU and CSU, as evidenced by acceptable internal consistency, convergent and known-groups validity, and screening accuracy at multiple time points.

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ABBREVIATIONS

AUC	Area under the curve
CDLQI	Children's dermatology life quality index
CIndU	Chronic inducible urticaria
CSU	Chronic spontaneous urticaria
CU	Chronic urticaria
DLQI	Dermatology life quality index
IQR	Interquartile range
r	Pearson's correlation coefficient
ROC	Receiver operating characteristic
sgAH	Second-generation antihistamine
UAS7	Urticaria activity score over seven days
UCT	Urticaria control test

KEY MESSAGE

The Urticaria Control Test (UCT) is the guideline-recommended tool to evaluate chronic urticaria (CU) disease control in adults. Our findings demonstrate that the UCT is a valid tool for assessing pediatric CU and its favourable clinometric properties and ease of use further supports its use in children.

KEYWORDS

chronic urticaria; validity; urticaria control test; disease control; pediatric; children's dermatology life quality index; patient reported outcome

ABSTRACT

Background

No validated tools exist to evaluate chronic urticaria (CU) control in children. While the Urticaria Control Test (UCT) exhibits favourable clinometric properties in adult CU, it is not yet validated in children. Therefore, we sought to evaluate the validity of the UCT for the assessment of pediatric CU.

Methods

Children presenting with CU were consecutively recruited. Participants completed both the UCT and the Children's Dermatology Life Quality Index (CDLQI). We assessed the internal consistency, convergent and known-groups validity, and screening accuracy of the UCT at study entry and at follow-up.

Results

A total of 52 children with CU were recruited. The UCT exhibited respectable internal consistency in the evaluation of CU (Cronbach's α=0.73 [95%CI: 0.62, 0.85]). UCT and CDLQI scores strongly correlated (r=-0.74, P<0.01). The UCT distinguished between different strata of disease severities established by the CDLQI (P<0.01). Screening accuracy of the UCT was excellent in the discrimination of poorly controlled CU (area under the curve=0.82). An optimal cut-off of [?]10 was determined for defining poorly controlled CU (sensitivity=95.5%, specificity=63.3%). Data at follow-up were consistent with data at study entry.

Conclusion

The UCT is a valid tool for the assessment of pediatric CU and CSU, as evidenced by acceptable internal consistency, convergent and known-groups validity, and screening accuracy at multiple time points.

INTRODUCTION

Chronic urticaria (CU) is defined by the presence of wheals and/or angioedema for at least six weeks[1]. CU is subtyped into inducible (CIndU) and spontaneous (CSU) forms, based on the existence or absence, respectively, of a specific trigger eliciting symptoms[1]. Several assessment tools are validated for evaluating disease control and severity in adult CU[2]. Although none of these tools have been validated in children with CU, current pediatric guidelines state that the urticaria activity score over seven days (UAS7) may be used to evaluate pediatric CU[3-5].

The Dermatology Life Quality Index (DLQI) is a tool that has been extensively validated for the assessment of dermatologic diseases, including CU, in adults[6,7]. The pediatric version of the DLQI, termed the Children's DLQI (CDLQI), is a ten-item questionnaire assessing the impact of dermatologic diseases on various aspects of life over the past seven days[8]. Each question is assigned scored from zero to three, with higher scores representing greater disease severity[8]. The CDLQI is valid for in children aged 4 to 16 years, and is available in a cartoon version for younger children[9]. Although not specifically validated for use in pediatric CU, the CDLQI has been thoroughly validated to assess various other dermatologic diseases[8,10], and has been used to assess pediatric CU[11-13]. Another assessment tool, the Urticaria Control Test (UCT), is a four-item questionnaire retrospectively querying on CU disease control over the prior four weeks[14]. Each item is assigned a score from zero to four, with higher scores representing improved disease control[14]. A cut-off of [?]11 was determined to optimally indicate poorly-controlled disease in adults[14]. Validation of the UCT for use in CSU and CIndU in adults demonstrated high internal validity, convergent validity, known-groups validity, and accuracy[14]. Current EAACI/GA²LEN/EuroGuiDerm/APAAACI guidelines recommend the use of the UCT in the assessment of CU disease control in adults[15]. Our previous work employing the UCT in children revealed that a UCT score [?]12 at study entry was associated with higher disease resolution in pediatric CIndU patients[16]. However, the UCT remains to be formally validated in children.

We sought to validate the UCT in a cohort of children with CU by assessing the internal consistency, convergent validity with the CDLQI, known-groups validity, and screening accuracy.

METHODS

Study Enrolment and Questionnaires

Our CU registry was approved by the Centre for Applied Ethics from the McGill University Health Centre Research Ethics Board (REB 12-255 GEN, June 3, 2013). From 2013-2021 we consecutively recruited pediatric patients (0-17 years) presenting with CU (defined as urticaria persisting at least 6 weeks) from the allergy clinics at the Montreal Children's Hospital and from the Children's Clinic in Montreal, Canada. Written informed consent was obtained from the patients' parent/guardian, and for patients aged 7 years or older an assent form was obtained. As part of standard of care, at study entry participants were assessed both for CSU and CIndU, based on history and provocation testing.

Standardized questionnaires were administered at study entry by a member of the study team which queried on demographics, comorbidities, and management (*i.e.,* second-generation antihistamines (sgAHs)). All participants completed the UCT and the written version of the CDLQI at study entry. Patients less than 12 years old were permitted to answer the questionnaires with the help of their parent/guardian. Follow-ups were conducted over the phone and queried on the management and resolution of CU (defined as one year without symptoms and treatment), as well as the UCT and CDLQI. In case of loss of follow-up, patients were contacted at least five times at multiple times of day.

Statistical Analyses

Statistical analyses were performed with R software (2020, version 4.0.0, R Core Team, Vienna, Austria). Data on patient demographics, comorbidities, and management were presented with proportions for categorical data and medians with an interquartile range (IQR) for continuous data. Subgroup analyses were performed for patients presenting with only CSU and patients presenting with CIndU (regardless of co-existing CSU). To ensure the validity of the UCT among children in whom the CDLQI is validated, a subgroup analysis was performed in patients aged 4 to 16 years.

Internal consistency of the UCT was evaluated by Cronbach's α coefficient, calculated by the *Psych* package. Cronbach's α coefficient was interpreted as follows: <0.60 unacceptable, 0.60-065 not desirable, 0.65-0.70 minimally acceptable, 0.70-0.80 respectable, 0.80-0.90 excellent, and >0.90 excessive redundancy[17].

Convergent validity of the UCT was assessed by Pearson partial correlation with the CDLQI using the *ppcor* package in groups with [?]25 patients[18]. Partial correlations were controlled for sex and age. The following strata were used to interpret r values: 0.90-1.00 very strong correlation, 0.70-0.89 strong correlation, 0.40-0.69 moderate correlation, 0.10-0.39 weak correlation, and 0.00-0.10 negligible correlation[19].

Known-groups validity of the UCT was assessed by the Kruskal-Wallis test using established CDLQI disease severity strata: 0-1 no effect, 2-6 small effect, 7-12 moderate effect, 13-18 very large effect, and 19-30 extremely large effect[20].

We considered a CDQLI cut-off value of [?]6 as indicative of poorly controlled disease[21]. Using this cut-off, we assessed the screening accuracy and the area under the curve (AUC) of the UCT in the identification of poorly controlled CU by receiver operating characteristics (ROC) curve via the *pROC* package. Optimal UCT cut-off values were estimated by the Youden index[22]. AUC values were interpreted according to the following cut-off values: [?]0.90 outstanding, 0.80-0.89 excellent, 0.70-0.79 acceptable, 0.50-0.69 poor, and 0.50 no better than chance[23].

Bootstrapping hypothesis testing with 100, 000 iterations was used to evaluate the change in UCT scores from study entry to follow-up between patients who started or increased their dose of sgAHs versus patients who decreased their dose or ceased sgAHs.

RESULTS

Patient Characteristics, Comorbidities, and Management (Table 1)

A total of 52 children with CU were recruited, consisting of 35 patients with solely CSU and 17 patients with CIndU. One CIndU case was delayed pressure urticaria and the remainder were cold urticaria (n=16), of which one had concomitant cholinergic urticaria. Half of the patients recruited were female and the median age of onset of CU was 10.0 years (Interquartile Range [IQR]=5.0-13.0). Median age at study entry was 11.8 years (IQR=6.3-14.5). All patients recruited completed the UCT and CDLQI at study entry with median scores of 8.0 (IQR=7.0-12.0) and 5.0 (IQR=2.0-7.0), respectively. Of the patients recruited, 30 (57.7%) had a low impact on their QoL (CLDQI[?]5), suggesting well-controlled disease. Comorbidities included atopic dermatitis (17.3%), allergic rhinitis (15.4%), asthma (11.5%), food allergy (9.6%), and insect venom allergy (1.9%). Less common comorbidities were autoimmune disease (3.8%), consisting of one case of celiac disease and one case of Crohn's disease. No patients presented with a history of autoinflammatory symptoms (*i.e.,* arthralgia and/or recurrent fever). At study enrolment, almost half (53.8%) of patients were not taking any medication to manage their CU. The remaining patients (46.2%) were managed with sgAHs. No patients were taking omalizumab or oral corticosteroids at study entry.

Internal Consistency (Table 2)

The UCT demonstrated respectable internal consistency in the assessment of CU, CSU, and CIndU at study entry (Cronbach's α=0.73 [95%CI: 0.62, 0.85], 0.74 [95%CI: 0.60, 0.88], 0.73 [95%CI: 0.54, 0.92], respectively). Similarly, in patients aged 4 to 16 years old (N=40) the UCT had respectable internal consistency (Cronbach's α=0.73 [95%CI: 0.61, 0.86]).

Convergent Validity

When controlling for age and sex, UCT scores strongly correlated with CDLQI scores in CU (r=-0.74, P<0.01) and CSU (r=-0.72, P<0.01). A moderate correlation was observed in patients aged 4 to 16 years (r=-0.67, P<0.01). We were unable to assess the convergent validity of the UCT in CIndU patients because of inadequate sample size (N<25).

Known-Groups Validity (Table 3)

Kruskal-Wallis test revealed significantly different UCT scores at different strata of disease severity established by the CDLQI for patients with CU (P<0.01), CSU (P<0.01), and CIndU (P=0.02) at study entry. Subgroup analysis of patients aged 4 to 16 years yielded similar results (P<0.01).

Screening Accuracy

ROC analysis revealed excellent screening accuracy of the UCT in the discrimination of poorly controlled CU at study entry (Figure 1A, AUC=0.82 [95%CI: 0.71, 0.93]). For CU, the optimal cut-off value of the UCT was determined to be [?]10 (sensitivity=95.5%, specificity=63.3%). Similarly, screening accuracy of the UCT in CSU at study entry also indicated excellent accuracy (Figure 1B, AUC=0.86 [95%CI: 0.74, 0.98]), also with an optimal cut-off of [?]10 (sensitivity=100.0%, specificity=65.0%). The UCT had acceptable accuracy in the discrimination of poorly controlled CIndU (Figure 1C, AUC=0.75 [95%CI: 0.50, 1.00]), with an optimal cut-off of [?]10 (sensitivity=85.7%, specificity=60.0%). Subgroup analysis of children aged 4 to 16 years also revealed an acceptable screening accuracy of the UCT (Figure 1D, AUC=0.79 [95%CI: 0.65, 0.93]), with an optimal cut-off of [?]10 (sensitivity=92.9%, specificity=65.4%).

Validity at Follow-up

Of the 52 patients contacted for follow-up, 33 (63.5%) responded after a median of 1.2 years (IQR=0.92, 1.9) after study entry. Of the 33 responders, 4 (12.1%) patients' CU has since resolved. Of the remaining patients, 28 completed the UCT and 27 completed the CDLQI as well, with median scores of 13.5 (IQR=11.8-15.0) and 2.0 (IQR=1.0-5.0), respectively. The UCT had respectable internal consistency in the evaluation of CU (Cronbach's α=0.74 [95%CI: 0.59, 0.89]). At follow-up, the UCT moderately correlated with CDLQI scores (r=-0.59, P<0.01) and could distinguish between different disease severities by Kruskal-Wallis test (P<0.01). Moreover, the UCT had excellent discrimination of poorly controlled urticaria (Figure

1E, AUC=0.81 [95%CI: 0.56, 1.00]), with an optimal cut-off of [?]9 [sensitivity=87.5%, specificity=66.7%]. Patients who started taking or increased their dose of sgAHs after study entry (N=14) had a greater increase in UCT scores from study entry to follow-up than patients who decreased or ceased sgAHs (N=12) (mean change in UCT=5.3 versus 2.1, respectively, P=0.04).

DISCUSSION

Our study is the first to validate the use of the UCT in the evaluation of pediatric CU. We demonstrated that the UCT has adequate internal consistency, convergent validity, known-groups validity, and screening accuracy when compared to the CDLQI at study entry and at follow-up. Similar results were observed in subgroup analyses of CSU and CIndU patients, although we were unable to assess the convergent validity of the UCT in CIndU cases because of inadequate sample size. Furthermore, a greater increase in UCT scores was observed in patients who started or increased their dose of sgAHs, which exemplifies the clinical relevance of the UCT.

Results of the validation of the UCT in adult CU were largely consistent with our study. Internal consistency of the UCT in adult CU was excellent (Cronbach's α=0.84)[14], whereas our results revealed respectable internal consistency in pediatric CU (Cronbach's α=0.73). Validation of the Turkish UCT revealed lower internal consistency of the UCT in CIndU compared to CSU (0.89 versus 0.68, respectively), whereas values were similar in our results[17]. Although DLQI and CDLQI scores are not directly comparable[24], in adult CU, UCT scores strongly negatively correlate with DLQI scores (Spearman's rho=-0.72)[25]. Consistent with our results in children, the UCT can distinguish between known-groups of disease severity in adults[17,26]. Screening accuracy (*i.e.,* AUC) of the UCT in adult CU was also excellent, although slightly higher than in our findings (0.89 versus 0.82, respectively)[14]. We found a slightly lower optimal cut-off for poorly controlled CU in children (UCT[?]10) than was determined for adults (UCT[?]11)[14]. A cut-off of 10 in children had a poorer specificity (63.3% versus 70.8%) but greater sensitivity (95.5% versus 89.9%) than a cut-off of 11 in adults[14]. The discrepancy between the cut-off of poorly controlled CU in adults and children may be because no studies exist formally validating a CDLQI cut-off for poorly controlled CU. Despite using a previously published CDLQI cut-off[21], misclassification bias may persist.

No tools exist to evaluate CU symptom control and severity in children, thereby limiting the evaluation of outcomes, progression, and management in pediatric CU trials[5,13]. Patient reported outcome tools, like the UCT, have been recommended as endpoints in clinical trials[27] and in the assessment of adult CU[15]. Although the UAS7 has not been specifically validated in pediatric CSU, current pediatric guidelines suggest that it may be used in the evaluation of pediatric CSU[3,5]. However, the UAS7 has several limitations compared to the UCT. Firstly, the UAS7 is only designed to assess CSU and not CIndU[28]. Secondly, the UAS7 must be completed prospectively, which poses logistical and compliance challenges. Thirdly, the UAS7 does not evaluate angioedema or disease control. Therefore, the retrospective nature of the UCT, the ability to assess CIndU, and the evaluation of angioedema and disease control strongly favours the use of the UCT in the evaluation of pediatric CU and in future clinical trials[14].

Our study is subject to some limitations. The low sample size precluded the evaluation of the test-retest probability of the UCT. Therefore, we recommend future multi-center studies validating the use of the UCT in children. The recall periods of the UCT and the CDLQI are not the same (28 versus 7 days, respectively). Therefore, it is possible that acute exacerbations of CU were captured by the UCT and not the CDLQI. This discrepancy could reduce the convergent validity and the known-groups validity of the UCT and may lead to the misclassification of patients in the assessment of screening accuracy. Although the CDLQI is only validated in children aged 4 to 16 years[8], our study included children of any age, which may bias the results. However, subgroup analysis of only patients aged 4 to 16 years yielded largely consistent results with the entire sample. Furthermore, the CLDQI is not a CU-specific tool; therefore, concomitant dermatologic diseases (*i.e.,* atopic dermatitis) may have elevated the CDLQI scores, which would not have been detected by the UCT. Despite the flaws of the CLDQI, it is the only validated questionnaire that can be used in pediatric CU.

In conclusion, our findings validate the use of the UCT as a patient reported outcome in the assessment of pediatric CU and CSU. Larger studies are necessary to validate the convergent validity of the UCT in pediatric CIndU.

FIGURES AND TABLES

Table 1. Patient demographics, comorbidities, and management

Variable	CSU	CIndU	Total
Demographics	**Demographics**	**Demographics**	**Demographics**
Participants N (%)	35	17	52
Female sex N (%)	15 (42.9)	11 (64.7)	26 (50.0)
Median age of symptom onset in years (IQR)	7.0 (3.4-13.0)	10.0 (8.0-13.0)	10.0 (5.0-13.0)
Median age at study enrolment in years (IQR)	7.4 (5.8-14.4)	11.9 (8.7-14.8)	11.8 (6.3-14.5)
Median disease duration in years (IQR)	0.8 (0.4-1.6)	1.0 (0.7-2.2)	0.8 (0.4-2.0)
Median baseline UCT score (IQR)	8.0 (7.0-12.0)	10.0 (6.0-12.0)	8.0 (7.0-12.0)
Median baseline CDLQI score (IQR)	4.0 (1.0-8.0)	5.0 (4.0-6.0)	5.0 (2.0-7.0)
Well-Controlled Disease (CDLQI[?]5)	20 (57.1)	10 (58.8)	30 (57.7)
Comorbidities	**Comorbidities**	**Comorbidities**	**Comorbidities**
Asthma N (%)	3 (8.6)	3 (17.6)	6 (11.5)
Atopic dermatitis N (%)	4 (11.4)	5 (29.4)	9 (17.3)
Allergic rhinitis N (%)	5 (14.3)	3 (18.8)	8 (15.4)
Food allergies N (%)	4 (11.4)	1 (5.8)	5 (9.6)
Insect sting allergy N (%)	1 (2.9)	0 (0)	1 (1.9)
Autoimmune disease N (%)	1 (2.9)	1 (5.8)	2 (3.8)
Celiac disease N (%)	0 (0)	1 (5.8)	1 (1.9)
Crohn's disease N (%)	1 (2.9)	0 (0)	1 (1.9)
Autoinflammatory disease N (%)	0 (0)	0 (0)	0 (0)
Management	**Management**	**Management**	**Management**
Second generation H1-antihistamines N (%)	14 (40.0)	10 (58.8)	24 (46.2)
Short-course oral corticosteroids N (%)	0 (0.0)	0 (0.0)	0 (0.0)
Omalizumab N (%)	0 (0.0)	0 (0.0)	0 (0.0)
No medication N (%)	21 (60.0)	7 (41.2)	28 (53.8)

Table 2. Internal consistency of the UCT

Item	N	Mean (St
Chronic Urticaria at Study Entry	**Chronic Urticaria at Study Entry**	**Chronic**
UCT-1	52	2.1 (1.3)
UCT-2		2.7 (1.2)
UCT-3		1.9 (1.5)
UCT-4		2.1 (1.4)
Chronic Spontaneous Urticaria at Study Entry	**Chronic Spontaneous Urticaria at Study Entry**	**Chronic**
UCT-1	35	2.1 (1.3)
UCT-2		2.6 (1.3)
UCT-3		1.9 (1.6)
UCT-4		2.0 (1.4)
Chronic Inducible Urticaria at Study Entry	**Chronic Inducible Urticaria at Study Entry**	**Chronic**
UCT-1	17	2.1 (1.2)
UCT-2		2.8 (1.0)
UCT-3		1.8 (1.5)

Item	N	Mean (St
UCT-4		2.4 (1.2)
Chronic Urticaria Ages 4-16 at Study Entry	**Chronic Urticaria Ages 4-16 at Study Entry**	**Chronic**
UCT-1	40	2.2 (1.3)
UCT-2		2.8 (1.2)
UCT-3		2.1 (1.5)
UCT-4		2.2 (1.4)
Chronic Urticaria at Follow-up	**Chronic Urticaria at Follow-up**	**Chronic**
UCT-1	28	2.6 (1.2)
UCT-2		3.2 (1.3)
UCT-3		3.4 (0.9)
UCT-4		3.2 (1.1)

Table 3. Known-groups validity of the UCT

CDLQI Strata (Score Range)	N	Mean
Chronic Urticaria at Study Entry	**Chronic Urticaria at Study Entry**	**Chronic**
No effect (0-1)	13	12.6
Small effect (2-6)	21	9.3
Moderate effect (7-12)	15	6.1
Very large effect (13-18)	2	1.5
Extremely large effect (19-30)	1	1.0
Chronic Spontaneous Urticaria at Study Entry	**Chronic Spontaneous Urticaria at Study Entry**	**Chronic**
No effect (0-1)	10	12.5
Small effect (2-6)	11	9.0
Moderate effect (7-12)	12	6.3
Very large effect (13-18)	1	1.0
Extremely large effect (19-30)	1	1.0
Chronic Inducible Urticaria at Study Entry	**Chronic Inducible Urticaria at Study Entry**	**Chronic**
No effect (0-1)	3	13.0
Small effect (2-6)	10	9.6
Moderate effect (7-12)	3	5.3
Very large effect (13-18)	1	2.0
Extremely large effect (19-30)	0	N/A
Chronic Urticaria Ages 4-16 at Study Entry	**Chronic Urticaria Ages 4-16 at Study Entry**	**Chronic**
No effect (0-1)	11	12.6
Small effect (2-6)	18	9.6
Moderate effect (7-12)	9	6.7
Very large effect (13-18)	2	1.5
Extremely large effect (19-30)	0	N/A
Chronic Urticaria at Follow-up	**Chronic Urticaria at Follow-up**	**Chronic**
No effect (0-1)	12	14.8
Small effect (2-6)	13	10.2
Moderate effect (7-12)	2	11
Very large effect (13-18)	0	N/A
Extremely large effect (19-30)	0	N/A

Figure 1. Receiver operating curves of the UCT in the categorization of poorly controlled urticaria (CDLQI [?]6). **A)** CU at study entry (optimal cut-off: [?]10 [sensitivity=95.5%, specificity=63.3%], AUC=0.82

[95%CI: 0.71, 0.93]). **B)**CSU at study entry (optimal cut-off: [?]10 [sensitivity=100.0%, specificity=65.0%], AUC=0.86 [95%CI: 0.74, 0.98]). **C)**CIndU at study entry (optimal cut-off: [?]10 [sensitivity=85.7%, specificity=60.0%], AUC=0.75 [95%CI: 0.50, 100.0]). **D)**CU in children aged 4 to 16 years at study entry (optimal cut-off: [?]10 [sensitivity=92.9%, specificity=65.4%], AUC=0.79 [95%CI: 0.65, 0.93]). **E)** CU at follow-up (optimal cut-off: [?]9 [sensitivity=87.5%, specificity=66.7%], AUC=0.81 [95%CI: 0.56, 1.00]).

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