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# Self-Reported Provoking Physical Factors in Patients with Chronic Urticaria: A Questionnaire Study

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Dear Editor:

Although chronic urticaria (CU) is classified as either chronic spontaneous urticaria (CSU) or chronic inducible urticaria (CIndU), CSU patients can be susceptible to provoking physical factors. Recent guidelines recommend that physicians identify and characterize the eliciting physical triggers of CU<sup>1,2</sup>. However, little is known about the frequency and clinical significance of self-reported provoking physical factors in CU patients. The aim of this study was to evaluate the frequency of self-reported provoking physical factors in patients with CU using a questionnaire. Also, we investigated the clinical differ-

ences between patients with or without provoking physical factors.

Patients who presented with wheals and/or angioedema lasting at least 6 weeks were diagnosed with CU by a single dermatologist in our out-patient clinic between September 2006 and February 2017, were asked to complete a questionnaire about provoking physical factors. The questionnaire included queries about whether or not common physical factors (dermographism, pressure, cold, and cholinergic stimuli) provoke urticaria. Our questionnaire also included detailed questions about the patient's demographics and medical history, such as age,

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gender, disease duration at the time of the survey, and three-generation family history of CU. In some patients, laboratory findings including total serum IgE and erythrocyte sedimentation rate (ESR) were evaluated, and autoimmunity was evaluated using the autologous serum skin test (ASST), according to the guidelines<sup>3</sup>. The results of the questionnaire, demographic and laboratory findings were retrospectively reviewed. To identify any clinically significant risk factors of self-reported provoking physical factors, we compared demographic and laboratory findings between patients with self-reported provoking physical factors and patients without them using the Mann-Whitney U-test. A  $p$ -value  $<0.05$  was considered statistically significant. The study protocol was approved by the Institutional Review Board of the Seoul St. Mary's Hospital, The Catholic University of Korea (KC16RISI0976). A total of 287 patients with CU agreed to participate in the study and completed a questionnaire. The mean participant age was 32.6 years, and the mean disease duration at the time of the survey was 20.0 months. The subject population was predominantly female (54.4%, 156/287). The proportion of patients with a family history of CU was 35.9% (103/287). The proportion of CU patients who reported provoking physical factors was 78.0%. Dermographism (52.6%, 151/287) was the most commonly reported physical factor, followed by cholinergic stimuli (51.6%, 148/287), pressure (32.1%, 92/287), and cold (21.6%, 62/287). The proportions of patients who reported none, one, two, three, and four kinds of provoking physical factors were 22.0% (63/287), 30.7% (88/287), 26.5% (76/287), 18.1% (52/287), and 2.8% (8/287), respectively. ASST results were positive in 58.3% of patients. Elevated ESR ( $>20$  mm/h) and IgE levels ( $>100$  IU/ml) were found in 19.2% (28/146) and 54.0% (135/250) of patients, respectively. The mean age of patients with provoking physical factors

was significantly lower than that of patients without these factors ( $p=0.038$ ), and disease duration at the time of the survey in patients with provoking physical factors was significantly longer than patients without them ( $p=0.002$ ). The proportions of female patients ( $p=0.021$ ) and family history of CU ( $p=0.002$ ) were significantly higher among CU patients with provoking physical factors than among patients without them. There were no significant differences in the proportions of positive ASST, elevated ESR, and elevated total immunoglobulin (IgE) between the two patient groups (Table 1).

Seventy-eight percent of our patients reported at least one or more provoking physical factors. To our knowledge, there are only two other studies of self-reported provoking physical factors associated with CU. Kozel et al.<sup>4</sup> reported that 182 of 220 CU patients (82.7%) were suspected to have CIndU according to their questionnaire-based evaluation. However, they did not provide proportions for the physical factors in their study. Sánchez et al.<sup>5</sup> reported that 186 of 245 CU patients (75.9%) had a provoking physical factor. The most common factor they identified was dermographism (40.8%), followed by pressure (25.3%), cold (22.8%), and cholinergic stimuli (15.5%). The overall proportion of provoking physical factors in their study was consistent with our results. However, we found higher proportions of cholinergic stimuli and pressure than did the previous studies. This discrepancy could be explained by differences in the study populations and questionnaires used. In our study, 48.3% of 151 patients who reported dermographism as a provoking physical factor also reported pressure as a provoking factor. The high frequency of pressure as a provoking factor could be due to patient difficulty differentiating between the two stimuli. The high frequency of cholinergic stimuli could be explained by the demographic characteristics of our study population: a

**Table 1.** Comparison between CU patients with or without self-reported provoking physical factors

Variable	Physical factors (+) (n = 224, 78.0%)	Physical factors (–) (n = 63, 22.0%)	$p$ -value <sup>†</sup>
Age (yr)	31.1 (16.9)	37.9 (19.1)	0.038
Disease duration (mo) <sup>‡</sup>	22.7 (46.4)	9.9 (18.7)	0.002
Female	129 (57.6)	27 (42.9)	0.021
Family history of CU	91 (40.6)	12 (19.0)	0.002
Positive ASST*	46/78 (59.0)	21/37 (56.8)	0.82
Laboratory findings			
Elevated ESR ( $>20$ mm/h)*	19/113 (16.8)	9/33 (27.3)	0.18
Elevated IgE ( $>100$ IU/ml)*	103/195 (52.8)	32/55 (58.2)	0.46

Values are presented as mean (standard deviation) or number (%). CU: chronic urticaria, ASST: autologous serum skin test, ESR: erythrocyte sedimentation rate, IgE: immunoglobulin E. \*Not all patients underwent ASST, ESR, and IgE. <sup>†</sup>The  $p$ -value was calculated from comparisons between CU patients with or without self-reporting provoking physical factors using the Mann-Whitney U-test. <sup>‡</sup>Disease duration at the time of the survey.

few young male patients visited our clinic to obtain medical reports for military service. Previous studies reported that 44%~62% of patients with suspected CIndU were only diagnosed after further provocation tests and diagnostic work-up<sup>4,6</sup>. This discrepancy could be explained by the tendency of patients with CU to overestimate the role of their triggers<sup>5</sup>. Along with our results, these findings suggest that CIndU diagnosis could be difficult with history-taking alone or even with a questionnaire. We found that the presence of provoking physical factors indicated a more chronic CU course. CU patients without self-reported provoking physical factors were diagnosed with CSU, while CU patients with these factors included both CIndU patients and CSU patients with provoking physical factors. Silpa-archa et al.<sup>7</sup> conducted a retrospective study of the natural history of CU among 1,200 patients, and they found that CIndU patients tended to have a longer disease course than CSU patients. In our study, CU patients who reported provoking physical factors tended to be younger, female, and have a family history of CU. There might also be demographic differences between CIndU and CSU patients. A limitation of our study was that our study population was recruited from a single tertiary referral center, and provocation tests were not performed for all patients, with the exception of dermographism. Also, our questionnaire was not validated. In conclusion, we found that 78.0% of CU patients had at least one self-reported provoking physical factor, and those patients tended to be younger, female, have longer disease duration at the time of the survey, and have a family history of CU. These results can help physicians understand patients' perspectives and the clinical significance of self-reported physical factors in CU.

## CONFLICT OF INTEREST

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The authors have nothing to disclose.

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