ORIGINAL ARTICLE

Eur Ann Allergy Clin Immunol Vol 58, N.5, 205-209, 2026

Guilherme Azizi, Sérgio Dortas Jr, Alfeu França, José Elabras, Omar Lupi, Solange Valle

Provocation test on stairs: a new accessible method to cholinergic urticaria diagnosis – Azizi-Valle Test

Immunology Service, Hospital Universitário Clementino Fraga Filho (HUCFF-UFRJ), Rio de Janeiro, Brazil

Key words

Cholinergic urticaria; chronic inducible urticaria; provocation test.

Corresponding author
Guilherme Azizi
Immunology Service
Hospital Universitário Clementino Fraga Filho (HUCFF-UFRJ)
Rua Rodolpho Paulo Rocco 255, Ilha do Fundão
Rio de Janeiro (RJ), Brazil 21941-590
ORCID: 0000-0002-4772-1599
E-mail: gazizi247@gmail.com

Doi
10.23822/EurAnnACI.1764-1489.381

Impact statement

This study aims to publicize the presentation of a new diagnostic technique with low technological and safe input, seeking to assist diagnosis outside reference centers and in developing countries.

Summary

Background. *Cholinergic urticaria (CholU) is characterized by itching and/or stinging, painful micro wheals due to systemic heating. There are two standardized protocols to diagnose CholU using an exercise bike with heart rate or warming passive. The objective of the study is to provide an affordable, new, low-tech test to assist the diagnostic.* ***Methods.*** *Cross-sectional study with a convenience sample: 10 with a diagnostic or high suspicion of CholU and 20 participants without suspicion of CholU, recruited in a UCARE from a developing country. After the pre-participation assessment, the provocation test through movements of going up and down a flight of stairs and with a heart rate monitor, an increasing 15 bpm every 5 min until an increase of 90 bpm above the initial level, for 30 min and/or stopped immediately, upon visualization of wheals and with body temperature measured in 3 different locations every 5 min.* ***Results.*** *The group CholU comprised eight females and two males (29.6 y), and the other group had eleven females and nine males (27.2 y). Data analysis demonstrated that in a positive test in a body temperature measured above 37.05 °C and with a variation of 0.35 °C above the initial value, sensitivity of 80% and specificity of 100% in the forehead region and sensitivity of 80% and specificity of 90% in tympanic region.* ***Conclusions.*** *Thus, with the feasibility of reproducing the method, it is expected that this simple and accessible method for diagnosing CholU can be a tool for application, mainly in developing countries.*

Introduction

Urticaria is characterized by the appearance of wheals, angioedema, or both. Chronic urticaria (≥ 6 weeks) can occur spontaneously (chronic spontaneous urticaria) or be motivated by specific stimulation (chronic inducible urticaria - CIndU), which is reported through provocation tests (1).

Cholinergic urticaria (CholU) is a subtype of CIndU with sweat in its genesis and occurs due to systemic heating (2, 3). CholU is characterized by itching and/or stinging, painful papular wheals (1-3 mm) that develop simultaneously with sweating, related to increased body temperature from physical exercise, hot baths, stress, spicy foods or hot drinks; symptoms generally disappear within 1 hour, and these sensations are highly impacted to disturb the quality of life (4). CholU has its incidence and prevalence predominantly between the second and third decades of life (5, 6). There is consensus that an increase in body temperature above 1 °C from baseline, as indicated by a passive warming test while sitting for ≤ 15 min in a 42 °C water bath, confirms the diagnosis of CholU (10). A standardized protocol was proposed to diagnose CholU using an exercise bike with heart rate and temperature control. The patient positions himself on the exercise bike and begins pedaling, being instructed so that the pulse increases by 15 bpm every 5 min, reaching 90 bpm above the basal level after 30 min (14). The time for urticaria to appear is inversely proportional to the intensity of the disease; therefore, the shorter the time for the lesions to occur, the more severe CholU is considered (7-14).

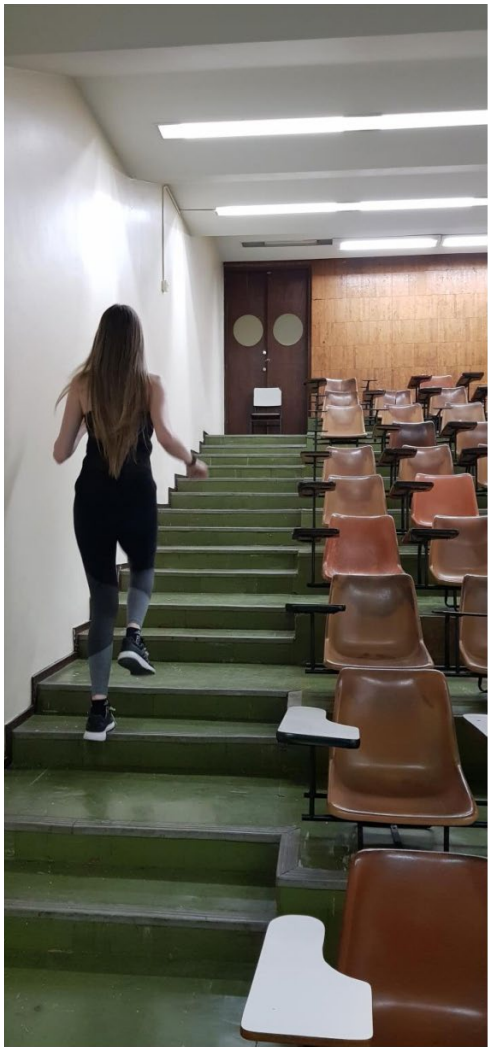
© 2026 Associazione Allergologi Immunologi Italiani Territoriali e Ospedalieri - AAIITO. Published by Edra Media S.r.l. All rights reserved

In this way, the site team of this study asked if it would be possible to provide a simple, affordable, low-tech test with statistically reliable indices to assist specialists and primary care diagnoses, especially in environments outside reference centers and in developing countries.

Materials and methods

Cross-sectional intervention study with a convenience sample, in which 30 participants were divided into two groups: 10 with a diagnostic and/or high clinical suspicion of CholU and twenty participants without clinical suspicion of CholU and with other CIndU, who were recruited from the Urticaria Centers of Reference and Excellence (UCARE) Immunology Service outpatient clinic in a developing (Human Development Index - HDI = 0.76) and tropical country. All were between 12-65 years old, both sexes and with body mass index (BMI) in the range 18.5-30 kg/m^2.

Figure 1 *- Provocation test to CholU on stairs.*



The exclusion criteria were to avoid corticosteroids for 15 days, antihistamines for 7 days, or anti-IgE therapies for 6 months before the test. They should not regularly use immunosuppressive therapy, have a comorbidity that makes it impossible to practice physical activity, have been suspected of exercise-induced anaphylaxis, or have skin comorbidities that could make it impossible to assess the body surface. The patient should not have performed physical exercise in the last 24 hours before the test or ingested stimulant medications.

On the previous visit, the participant underwent a complete clinical examination, electrocardiogram, and Physical Activity Readiness Questionnaire (PAR-Q) to avoid unfavorable outcomes and increase safety in the test. On the second day (7 to 15 days after the first visit), the participants underwent the CholU provocation test on stairs. The acclimatization time was 20 min, during which the participant underwent temperature measurement in 3 sites (forehead, oral and tympanic) using a digital infrared thermometer. The provocation test was carried out in a room or auditorium with a controlled ambient temperature of 20-23 °C by moving up and down a flight of stairs (13 steps) with a slow. It gradually increased initial speed through the evaluator's commands, aiming to obtain an increase of 15 bpm every 5 min until a rise of 90 bpm above the initial level, for 30 min. A heart rate monitor (Polar F11®) was adapted to the patient's chest using a chest strap suitable for the instrument and to the wrist using a watch-type marker (**figure 1**).

The provocation test was stopped immediately, regardless of the period elapsed, upon visualization of pruritic wheals associated with erythema characteristic of CholU. Body temperature was measured in 3 different locations every 5 min with interruptions that did not exceed 10 seconds. In addition, a small amount of starch and iodine was placed on the individual's dorsal region to analyze the positivity regarding the appearance of sweat during the diagnostic test. The ambient temperature (°C) and relative humidity (%) were measured.

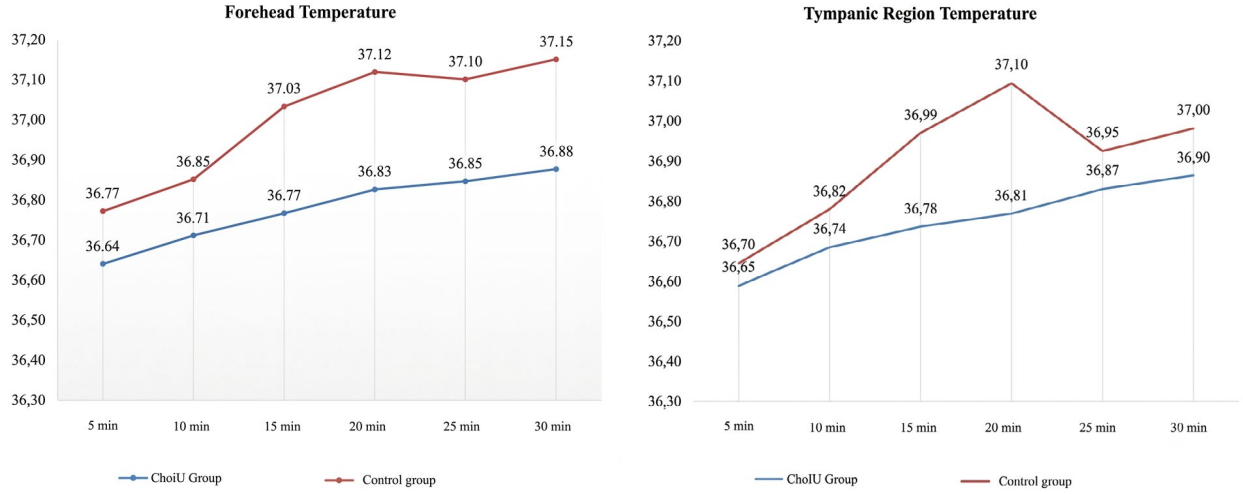
The research (CAAE 57071122.6.0000.5257) was approved by the local ethics committee on August 4, 2022, after being submitted for consideration by CEP/HUCFF-UFRJ (C.E.P. number: 5.562.556.). The participants signed the informed consents.

Results

The sample from the group CholU was composed of eight female and two male participants, with an average age of 29.6 years (18-55 y) and an average BMI of 23.5 kg/m² (20.2-28.8 kg/m²). Proportionally, the control group had eleven female and nine male participants, with an average age of 27.25 years (19-52 y) and an average BMI of 24.2 kg/m² (21.4-29.2y).

All patients presented a reactive starch-iodine test during physical activity, demonstrating sweat associated with the test. Among

Figure 2 *- Average temperature variations between both groups.*



the control group, 14 individuals were observed with dermographism, four with cold urticaria, one with vibratory urticaria and another with solar urticaria. All tests were conducted at a controlled temperature between 20 °C and 23 °C, with an average relative humidity of 66% (58%-72%).

The final temperatures among the subjects and sites were: final oral temperature of the group with CholU (average 37.1 °C, standard deviation = 0.277) *vs* participants without CholU (average 36.85 °C, standard deviation 0.161); P-value = 0.013. The forehead temperature in the study group with CholU (average 37.17 °C, standard deviation = 0.295) *vs* control group (average 36.88 °C, standard deviation = 0.159); P-value = 0.001. The tympanic temperature in the study group with CholU (average 37.14 °C, standard deviation 0.26) *vs* control group (average 36.9 °C, standard deviation = 0.13); P-value = 0.002. All patients with positive provocation tests showed an increase of 0.5 °C compared to basal temperature (**figure 2**).

Data analysis demonstrated that in a positive CholU provocation test, presenting clinical characteristics compatible with the disease, in a temperature measured in the forehead region above 37.05 °C and with a variation of 0.35 °C above the initial temperature value, sensitivity is 80% and specificity is 100%. The probability of obtaining a positive result for CholU, considering the variation in the forehead temperature and variation in this temperature at the end of the exam if the person has the disease, is 80%. In contrast, the probability of obtaining a negative result for CholU, considering the variation in forehead temperature and this temperature at the end of the exam if the person does not have the disease, is 100%. The positive predictive value (100%) and negative predictive value (90%) depend on the specificity and sensitivity and the prevalence of the disease in the population investigated.

A positive provocation test for CholU, presenting compatible clinical characteristics, at a temperature measured close to the tympanic region above 37.05 °C and with a variation of 0.35 °C above the initial temperature value, sensitivity is 80% and specificity of 90%. The positive predictive value (80%) and negative predictive value (90%) depend on the specificity and sensitivity and the prevalence of the disease in the population investigated. The oral temperature did not present statistically relevant values. However, it showed an increase in temperature like the other sites and above the control group (**figures 3, 4**).

Discussion and conclusions

This study looked for a simple, affordable, low-tech test that could help diagnose CholU, especially in environments outside reference centers and in developing countries. This technique is a new method controlled by a frequency meter and performed on stairs, which proved to be objective and reproducible for the diagnosis of CholU. As in other tests proposed in the literature, all CholU patients showed characteristic signs and symptoms but not in healthy controls (4, 14).

The method's sensitivity and specificity assessment presented robust values, mainly using two temperature measurement sites (forehead region and tympanic region). The values exceeded 80% sensitivity and 90% specificity, validating the method and providing reliability for its implementation in daily practice. However, measuring temperature in the oral region did not present statistically robust values, but the increase in temperature above the values of the control group was noticeable.

The method proved reproducible and bearable for the sample, as there were no interruptions during the test due to fatigue. However, going up and down stairs also presents itself as a limitation

Figure 3 *- Flowchart to diagnostic cholinergic urticaria through provocation testo on stairs.*

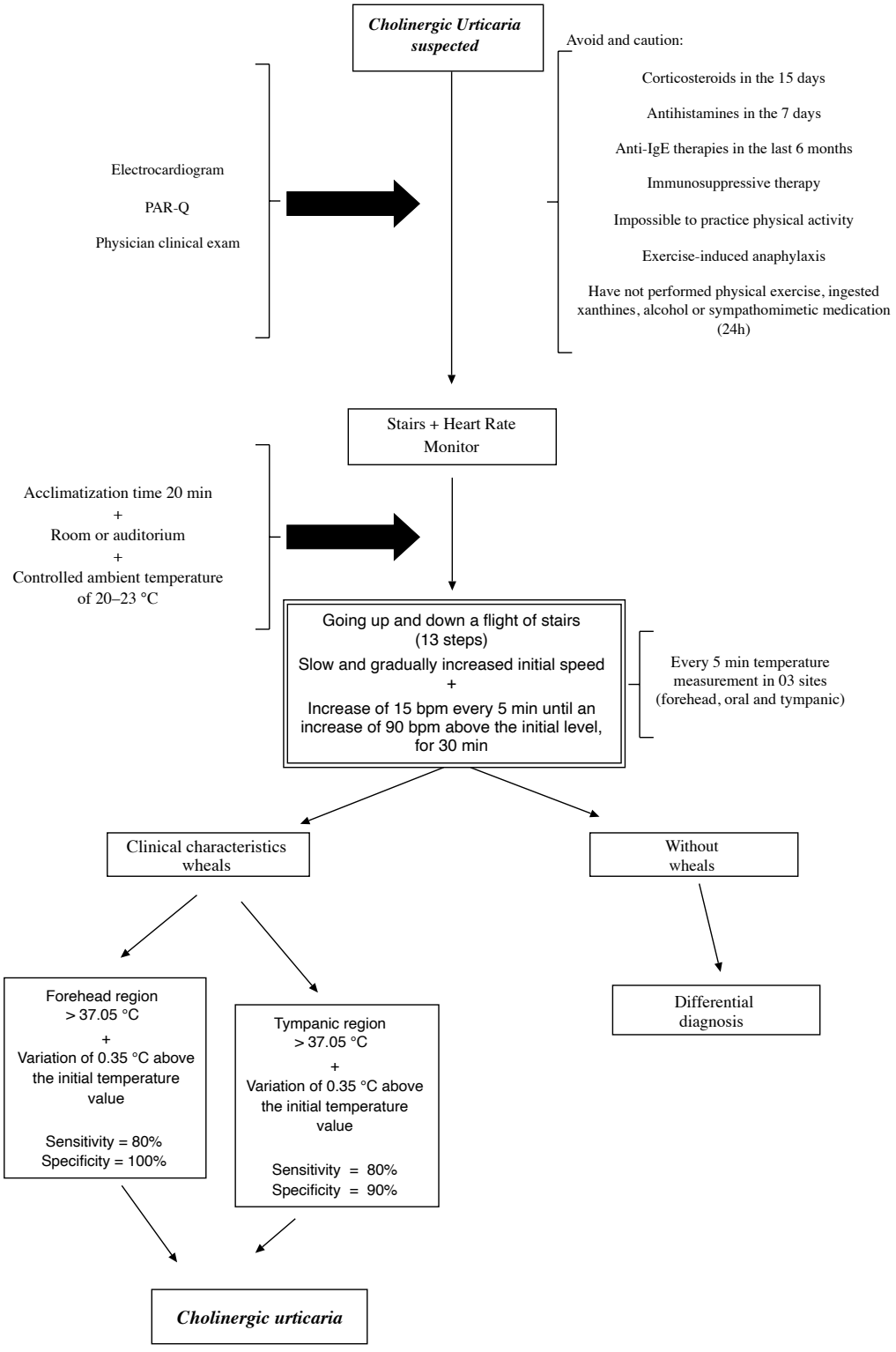
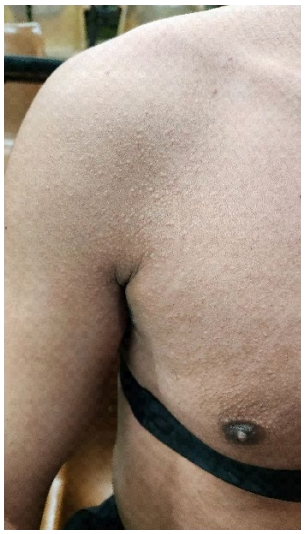


Figure 4 *- Cholinergic urticaria during provocation testo on stairs.*



of the method, as patients suspected of CholU with risks inherent to the practice of physical activity or musculoskeletal limitations cannot perform the provocation test.

The average onset of signs and symptoms characteristic of CholU occurred at 19.5 minutes (10-30 min). In this study, the correlation within the studied sample – between the moment of onset of the characteristic manifestations of CholU and severity – was not evaluated. These parameters were assessed in another study (14) and demonstrated an inversely proportional correlation between the speed at which lesions appear and the severity of the disease.

The temperature of the provocation test environment was artificially controlled and varied between 20 °C and 23 °C. However, it is not possible to control only the relative air humidity; therefore, the partial results showed an average relative air humidity of 66% (58%-72%), characteristic of a tropical region with high rainfall levels such as Rio de Janeiro.

Many studies present a progressive increase in body temperature reaching 1°C as a direct correlation with the appearance of pruritic micropapular lesions associated with intense erythema in patients with CholU (4, 14). However, the sample evaluated and presented in partial results demonstrated lower values as an average variation above 0.5 °C between the initial and final temperatures.

Thus, the results demonstrate the feasibility of reproducing the method and its consistency with the clinical findings characteristic of the disease. Therefore, it is expected that this simple and accessible method for diagnosing CholU can be a tool for application, mainly in developing countries, regions with difficulty obtaining high technological support, and the Public Health System. Therefore, it will assist in diagnosing a condition that is extremely harmful to the quality of life of the affected individual.

Fundings

None.

Contributions

GA: formal analysis, investigation, methodology, project administration, writing – original draft, resources, software, supervision, validation. SDJ, JE: formal analysis, investigation, methodology. AF, OL, SV: writing – original draft, investigation, methodology. GA, SV: data curation, writing - review & editing.

Conflict of interests

SDJ declares lecture fees from AstraZeneca Brazil and G.S.K. Brazil. SDJ and SV declare lecture fees from Novartis Brazil. SV declared lecture fees from Takeda, Brazil. GA and AF have no conflicts of interest to declare. OL declares fees from Sanofi Brazil. JE declares lecture fees from Sanofi Brazil, G.S.K. Brazil and AstraZeneca Brazil.

References

1. Zuberbier T, Abdul Latiff AH, Abuzakouk M, Aquilina S, Asero R, Baker D, et al. The International EAACI/GA²LEN/EuroGuiDerm/APAAACI Guideline for the Definition, Classification, Diagnosis and Management of Urticaria. The international EAACI/GA²LEN/EuroGuiDerm/APAAACI guideline for the definition, classification, diagnosis, and management of urticaria. Allergy. 2022;77(3):734-766. doi: 10.1111/all.15090.
2. Junior SDD, Azizi GG, Sousa ACM, Lupi O, França AT, Valle SOR. Urticárias crônicas induzidas: atualização do tema. Arq Asma Alerg Imunol. 2020;4(3):305-316. doi: 10.5935/2526-5393.20200047.
3. Pozderac I, Lugović-Mihić L, Artuković M, Stipić-Marković A, Kuna M, Ferček I. Chronic inducible urticaria: classification and prominent features of physical and non-physical types. Acta Dermatovenerol Alp Pannonica Adriat. 2020;29(3):141-148.
4. Fukunaga A, Oda Y, Imamura S, Mizuno M, Fukumoto T, Washio K. Cholinergic Urticaria: Subtype Classification and Clinical Approach. Am J Clin Dermatol. 2023;24(1):41-54. doi: 10.1007/s40257-022-00728-6.
5. Hirschmann JV, Lawlor F, English JS, Louback JB, Winkelmann RK, Greaves MW. Cholinergic urticaria. A clinical and histologic study. Arch Dermatol. 1987;123(4):462-7. doi: 10.1001/archderm.123.4.462.
6. Zuberbier T, Althaus C, Chantraine-Hess S, Czarnetzki BM. Prevalence of cholinergic urticaria in young adults. J Am Acad Dermatol. 1994;31(6):978-81. doi: 10.1016/s0190-9622(94)70267-5.
7. Fukunaga A, Bito T, Tsuru K, Oohashi A, Yu X, Ichihashi M, et al. Responsiveness to autologous sweat and serum in cholinergic urticaria classifies its clinical subtypes. J Allergy Clin Immunol. 2005;116(2):397-402. doi: 10.1016/j.jaci.2005.05.024.
8. Nakazato Y, Tamura N, Ohkuma A, Yoshimaru K, Shimazu K. Idiopathic pure sudomotor failure: anhidrosis due to deficits in cholinergic transmission. Neurology. 2004;63(8):1476-80. doi: 10.1212/01.wnl.0000142036.54112.57.
9. Adachi J, Aoki T, Yamatodani A. Demonstration of sweat allergy in cholinergic urticaria. J Dermatol Sci. 1994;7(2):142-9. doi: 10.1016/0923-1811(94)90088-4.
10. Magerl M, Altrichter S, Borzova E, Giménez-Arnau A, Grattan CE, Lawlor F, et al. The definition, diagnostic testing, and management of chronic inducible urticarias - The EAACI/GA(2) LEN/EDF/UNEV consensus recommendations 2016 update and revision. Allergy. 2016;71(6):780-802. doi: 10.1111/all.12884.
11. Oda Y, Fukunaga A, Tsujimoto M, Hatakeyama M, Washio K, Nishigori C. Combined cholinergic urticaria and cold-induced cholinergic urticaria with acquired idiopathic generalized anhidrosis. Allergol Int. 2015;64(2):214-5. doi: 10.1016/j.alit.2014.12.004.
12. Fukunaga A, Washio K, Hatakeyama M, Oda Y, Ogura K, Horikawa T, et al. Cholinergic urticaria: epidemiology, physiopathology, new categorization, and management. Clin Auton Res. 2018;28(1):103-113. doi: 10.1007/s10286-017-0418-6.
13. Montgomery SL. Cholinergic urticaria and exercise-induced anaphylaxis. Curr Sports Med Rep. 2015;14(1):61-3. doi: 10.1249/JSR.0000000000000111.
14. Altrichter S, Salow J, Ardelean E, Church MK, Werner A, Maurer M. Development of a standardized pulse-controlled ergometry test for diagnosing and investigating cholinergic urticaria. J Dermatol Sci. 2014;75(2):88-93. doi: 10.1016/j.jdermsci.2014.04.007.