Letter to the Editor

Autonomic nervous function in patients with atopic dermatitis and its implications for acupuncture treatment: a retrospective study

Atopic dermatitis (AD) is a common chronic inflammatory skin disease, which is caused by a combination of different factors.\(^1\) The results of many studies have established the role of autonomic nervous system (ANS) in mediating the immune system.\(^2,3\) Acupuncture treatment has been widely used as alternative treatment for AD. Previous studies reported that acupuncture controls histamine-induced itch, mainly via the parasympathetic nervous system (PNS).\(^4,6\)

To date, no studies have evaluated the relationship between autonomic function and AD disease severity. To provide the patients with more effective therapy, more studies investigating autonomic function in patients with AD are needed. The aim of this study was to evaluate autonomic dysfunction and its relationship with disease severity in AD.

We collected the data of AD group from retrospective chart review and collected the data of healthy control group prospectively in Dermatology of Korean Medicine at Kyung Hee University Hospital at Gangdong. From these data, we performed a cross-sectional study by comparing two groups. AD was diagnosed by Hanifin and Rajka's criteria, and it was scored using SCORing Atopic Dermatitis (SCORAD). Healthy controls had undergone a general health checkup, as well as laboratory tests, and had shown no abnormal findings. All subjects were aged 18–65 years and were excluded if: (1) any disease known to affect HRV, (2) use of hormone replacement therapy, (3) pregnancy or lactation, or (4) antihistamine, anticholinergic, antidepressant, or contraceptive pill use for at least 4 weeks before the test. After screening, we randomly extracted 30 subjects with AD for each mild to moderate, severe group (total score was mild at <25, moderate at 25–50 and severe at >50), while we randomly extracted 30 healthy subjects who were equally matched to the age and sex distributions of the AD group. All subjects were assessed their heart rate variability (HRV) using SA-3000P\(^6\) (Medicore Inc., Seoul, Korea), with same procedure, similar temperature, humidity, and noise environment.

There were no significant differences in age or sex distribution among the groups. Mild to moderate group had decreased high frequency (HF) compared with control group. Severe group had elevated heart rate (HR) and decreased root mean square of successive differences (RMSSD) and HF compared with control group. There was no significant different parameter between mild to moderate and severe groups. Total SCORAD scores showed negative correlations with RMSSD and HF and positive correlations with HR and ratio of absolute LF to HF power (LF/HF ratio) (Table 1).

The current study has indicated the following: (1) patients with mild AD have higher sympathetic and lower parasympathetic activity compared with healthy controls, and (3) such differences are more pronounced in patients with severe symptoms.

In the childhood period, the itch arises from eczema in atopic patients. However, as the clinical course progresses from childhood to adulthood and become more chronic, and AD is characterized by itch preceding dermatitis.\(^7,8\) Patients with chronic itch often have peripheral as well as central neural hypersensitization.\(^9\) In this state, sensitized itch fibers overreact even to slight stimuli such as heat, sweat, and emotional stress.\(^7\) A previous study reported that atopic subjects exhibit an overactive sympathetic response to induced itching, scratching, and mental stress stimuli, compared to healthy controls, demonstrating a lack of adaptability to such stimuli.\(^7\) Otherwise, PNS plays the role in controlling itch. The vagus nerve is known to modulate neuroimmune communication, anti-inflammatory responses in target organs, and control histamine-induced itch.\(^10\)

Several studies suggested the role of acupuncture on the ANS. Acupuncture stimulation induced alteration in HRV, main via the PNS.\(^6\) Acupuncture enhance the parasympathetic activity and modulate the post-stimulation spatial extent of resting state connectivity networks.\(^5\) The recent study reported that acupuncture reduce itch and skin blood perfusion, by enhancement of the PNS and functional connectivity of putamen and posterior middle cingulate cortex.\(^4\)

In this study, patients with more severe symptoms exhibited higher sympathetic activities, indicating the role of ANS in the chronic progress of AD and itching. Acupuncture is commonly used in the treatment of AD, however, evidences for more effective and individualized therapy were lacking. According to our results, acupuncture treatment would have more therapeutic potential in severe atopic patients, enhancing their parasympathetic activity, subsiding chronic itch, weaken the itch-scratching cycle.

Conflicts of interest

The author declares no conflicts of interest.

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Data availability

Data will be made available upon request.

Author contribution

MHK designed the study, performed the study, analyzed and interpreted the data, and wrote the manuscript. CC analyzed the data and critically revised the manuscript. HJN and BK interpreted

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Table 1
General characteristics, comparison of HRV parameters, and the correlations between total SCORAD score and HRV parameters.

| General characteristics | Controls (n = 30) | Atopic dermatitis subjects (n = 60) | r (p value) |
|-------------------------|------------------|-----------------------------------|-------------|
|                         | Mild to moderate (n = 30) | Severe (n = 30)                  |             |
| Age                     | 27.07 ± 4.88      | 26.83 ± 6.42                     | 26.17 ± 4.70 | 0.799    |
| Sex (male/female)       | 14/16            | 14/16                            | 16/14       | 0.652    |
| HRMSSD                  | 64.90 ± 9.37     | 70.97 ± 10.32                    | 73.4 ± 14.69 | 0.283 (0.028)* |
| LF (ms²)                | 46.46 ± 26.55    | 36.71 ± 19.66                    | 32.52 ± 18.17 | -0.279 (0.028)* |
| HF (ms²)                | 6.10 ± 0.93      | 5.62 ± 0.99                      | 5.66 ± 0.98  | -0.105 (0.425) |
| LF/HF                   | 1.34 ± 0.99      | 1.54 ± 1.34                      | 1.84 ± 1.02  | 0.027 (0.035)* |

HRV = Heart rate variability, SCORAD = SCORing Atopic Dermatitis, HR = heart rate, RMSSD = root mean square of successive differences, LF = low frequency, HF = high frequency, LF/HF = ratio of absolute LF to HF power.
ANOVA and Tukey’s HSD post-hoc test except sex analysis (chi-square analysis), r, Pearson correlation.

1 Significant differences between control and mild to moderate group.
2 Control and severe group.
3 Significant correlations between total SCORAD score and HRV parameters (p < 0.05).

the data and critically revised the data. IC designed the study and critically revised the manuscript. All authors approved the final version of this manuscript.

Ethical statement

The retrospective data of patients with AD in this study was approved a waiver of informed consent by the Institutional Review Board of Kyung Hee University Hospital at Gangdong approved this study (KHNMC-OH-IRB 2014-0010). The data of healthy volunteers in this study was approved by the Institutional Review Board of Kyung Hee University Hospital at Gangdong (KHNMCOH 2018-07-003-001) and written informed consent was obtained from all volunteers prior to enrollment.

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Min Hee Kim
Department of Ophthalmology, Otolaryngology and Dermatology of Korean Medicine, Kyung Hee University, Seoul, Republic of Korea

Chunhoo Cheon
Department of Preventive Medicine, College of Korean Medicine, Kyung Hee University, Seoul, 26 Kyungheedae-ro, Dongdaemun-gu, Republic of Korea

Hae Jeong Nam
Bonghyun Kim
Inhwa Choi*
Department of Ophthalmology, Otolaryngology and Dermatology of Korean Medicine, Kyung Hee University, Seoul, Republic of Korea

* Corresponding author.
E-mail address: inhwajaun@khnmc.or.kr (I. Choi)

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