

LETTER TO THE EDITOR

Successful treatment of chronic urticaria with a Japanese herbal medicine, yokukansan

Dear Editor,

Chronic urticaria is characterized by recurrent wheals and pruritus presenting on all or most days for more than 6 weeks. Approximately 80–90% of patients with chronic urticaria have no specific external cause for their disease, which is therefore labeled “chronic spontaneous urticaria”.¹ Histamine H1-antagonists are the central treatment of urticaria. For patients whose symptoms are not controlled by H1- antagonists alone, adjunctive treatments such as leukotriene receptor antagonists, histamine H2-antagonists, systemic steroid and cyclosporin A are available. However, a substantial proportion of patients are

intractable in spite of these conventional remedies. Recent reports have suggested that psychotropic drugs could be candidate drugs for chronic urticaria.^{2,3} We report herein five cases of chronic urticaria successfully treated with Yokukansan (YKS, *Yi-gan san* in Chinese), a traditional Japanese Kampo medicine that proved to ameliorate psychiatric symptoms.

The first case was a 27-year-old woman who had suffered from chronic urticaria for 9 months despite pharmacotherapy. Her wheals had never been controllable with various antihistamines or other anti-allergic drugs (case 1 in Table 1). Oral bepotastine

Table 1. Chronic urticaria cases treated with yokukansan

Case	Age and sex	Duration before YKS treatment	Ineffective drug history	Drugs just before YKS treatment	Score* change 2 weeks after YKS treatment
1	27 years/female	9 months	Cetirizine hydrochloride, d-chlorpheniramine maleate, pranlukast hydrate, olopatadine hydrochloride, fexofenadine, ebastine, cyproheptadine hydrochloride hydrate, bepotastine, azelastine hydrochloride	Bepotastine, azelastine hydrochloride	6 → 0
2	65 years/female	9 months	Prednisolone, dexamethasone, cetirizine hydrochloride, bepotastine, olopatadine hydrochloride, hydroxyzine pamoate, tranexamic acid, ebastine, montelukast sodium	Ebastine, montelukast sodium dexamethasone	6 → 1
3	65 years/female	4 months	Olopatadine hydrochloride	Olopatadine hydrochloride	5 → 0
4	20 years/female	5 months	Loratadine, epinastine hydrochloride, fexofenadine	Fexofenadine	6 → 4
5	58 years/female	7 months	Prednisolone, dexamethasone, olopatadine hydrochloride, mequitazine, epinastine hydrochloride, bepotastine, cetirizine hydrochloride, cyproheptadine hydrochloride hydrate, azelastine hydrochloride	Azelastine hydrochloride, cetirizine hydrochloride, dexamethasone	6 → 3

*Disease activity score in accordance with the EAACI/GA2LEN/EDF guideline: definition, classification and diagnosis of urticaria.

and azelastine hydrochloride was given without any benefit. We added YKS 7.5 g/day. Two weeks later, the patient's skin condition and itching were completely controlled. Her disease activity score, measured in accordance with the EAACI/GA2LEN/EDF guideline: definition, classification and diagnosis of urticaria¹ improved from 6 to 0. No adverse effects were observed. We also detected slight to marked response to YKS in other four intractable cases as shown in Table 1.

To our knowledge, this is the first report to describe the beneficial effects of YKS in the treatment of chronic urticaria. Administration of YKS might be a suitable complementary therapy for intractable chronic urticaria. In the field of psychodermatology, increasing evidences have shown mutual interactions between psychosocial stress and dermatological diseases/symptoms including chronic urticaria.⁴ In addition, antidepressants have proved to have therapeutic effects on chronic urticaria.² Recently, mirtazapine, a noradrenergic and specific serotonergic antidepressant with antihistaminergic properties, has also been reported to be effective in controlling chronic urticaria.^{3,5}

Yokukansan was originally developed in the 16th century as a remedy for restlessness and agitation in children and has been used as an anti-anxiety agent for the treatment of neurosis, insomnia and nocturnal crying in children. Recent reports have suggested that YKS is effective in treating psychiatric diseases.^{6,7} The psychopharmacological mechanism of YKS remains to be established, while current animal studies suggest that YKS may exert its effectiveness through the serotonergic and dopaminergic systems in the brain.⁸ It is of note that YKS was also demonstrated to inhibit the development of atopic dermatitis-like lesions in isolated NC/Nga mice.⁹ Our case report presenting beneficial effects on chronic urticaria suggest that YKS may be considered as one of the complementary drugs for chronic urticaria. According to Jiang *et al.*,⁹ shown in atopic dermatitis, the favorable effects of YKS might be attributable to a reduction of stress-related reactions in the central nervous system or a direct attenuation of skin inflammation, although the underlying mechanism

remains to be elucidated. Further *in vitro/in vivo* experiments and clinical researches using a double-blind placebo-controlled design should be performed in order to clarify the effectiveness of YKS on chronic urticaria.

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