

THE EFFICACY OF YOKUKANSAN, JAPANESE TRADITIONAL HERBAL MEDICINE, ON NOCTURIA DUE TO NIGHT-TIME AWAKENING

Lower urinary symptoms can be divided into urinary storage symptoms, voiding symptoms, and post-micturition symptoms. Nocturia is a urinary storage symptom that has a considerable impact on the quality of life of both men and women affected by it [1]. It can be caused by various factors including night-time awakening. Western sleep medicines are often prescribed for patients with nocturia due to night-time awakening. However, the use of sleep medicines, particularly in elderly patients, is a concern because of the risk of drug dependence and incidence of adverse effects such as muscle relaxation.

Yokukansan (yi-gan san in Chinese) is a traditional herbal medicine commonly used in Japan because of its efficacy in preventing difficulty in the initiation and maintenance of sleep, as well as its safety profile. However, there is no report regarding the efficacy of traditional herbal medicine on nocturia due to night-time awakening. The aim of this study was to examine the efficacy of Yokukansan on nocturia caused by night-time awakening.

Study design, materials, and methods

Consent was obtained from patients admitted to our facility for nocturia due to night-time awakening. Patients with a neurogenic bladder, urinary tract infection, or urological malignant tumor were excluded. The participants were treated with 2.5 g of Yokukansan® (TJ-54) three times a day for 12 weeks. Drugs used for the improvement of urinary function and sleep that were administered before participation in this study were not changed during the study. Overactive bladder symptom score (OABSS) and hours of undisturbed sleep (HUS) prior to the first awakening were determined before treatment and 12 weeks after treatment to evaluate the efficacy using the Pittsburgh sleep quality index (PSQI). A P value of less than 0.05 was considered to indicate statistical significance.

Results

Twenty-four patients (12 male and 12 female) with a mean age of 74.4 ± 9.8 years participated in this study after giving consent. While 3 patients complained of difficulty in swallowing the drug because of its bitterness, all patients completed this study without any particular adverse event. The total OABSS decreased from 4.6 ± 1.7 (before treatment) to 2.8 ± 1.9 (after treatment) ($P < 0.001$), while night-time frequency (OABSS Q2) decreased from 2.6 ± 0.6 to 1.8 ± 0.9 ($P < 0.001$). The actual number of night-time voiding reduced from 3.7 ± 2.2 times to 2.2 ± 1.8 times ($P < 0.001$).

Interestingly, the score for daytime frequency (OABSS Q1) also decreased from 0.5 ± 0.7 to 0.2 ± 0.4 ($P = 0.049$). Furthermore, the actual number of daytime urinary frequency reduced from 7.4 ± 2.1 times to 6.1 ± 1.7 times ($P = 0.002$). In addition, urgency (OABSS Q3) also significantly improved ($P = 0.003$). HUS prolonged from 2.4 ± 0.6 hours to 3.3 ± 1.2 hours ($P = 0.002$) and PSQI decreased from 7.6 ± 3.1 to 5.7 ± 1 ($P < 0.001$).

Changes in pre- and post-treatment OABSS

	0 W	12 W	P value
Q1 (daytime frequency)	0.5 ± 0.7	0.2 ± 0.4	0.049
Q2 (night-time frequency)	2.6 ± 0.6	1.8 ± 0.9	<0.001
Q3 (urgency)	1.3 ± 0.9	0.8 ± 0.9	0.003
Q4 (urgency incontinence)	0.2 ± 0.5	0.1 ± 0.3	0.180
Total score	4.6 ± 1.7	2.8 ± 1.9	<0.001

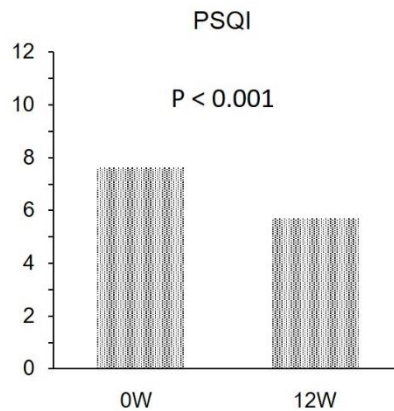
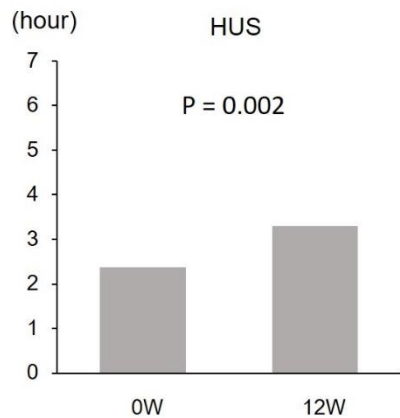
Interpretation of results

Treatment with Yokukansan for nocturia due to night-time awakening was effective and significantly improved night-time frequency and quality of sleep. Administration of Yokukansan also significantly improved OABSS Q1 and Q3. It has been shown that Yokukansan exerts sedating effects via its partial agonist effect on 5-HT_{1A} receptor and downregulation of 5-HT_{2A} receptors. The effects of serotonin on urinary frequency, particularly OAB, have been recently highlighted. There are various subtypes of serotonin, and among these, the stimulation of 5-HT_{2A} receptor has been reported to cause bladder contraction.

In this study, administration of Yokukansan improved daytime urinary frequency and urgency, as well as night-time frequency. Therefore, the effect of Yokukansan on serotonin receptors may be exerted in the bladder, as well as in the central nervous system.

Concluding message

The efficacy of Yokukansan in patients with nocturia due to night-time awakening was confirmed. Although the study subjects were relatively old, treatment with Yokukansan successfully improved the quality of sleep without causing major side effects. Moreover, administration of Yokukansan improved daytime urinary frequency and urgency. Thus, further clinical investigation including application to OAB is desired in the future.



HUS: Hours of undisturbed sleep
 PSQI: Pittsburgh sleep quality index
 SD: Standard deviation

References

1. Neurourol Urodyn. 2010;29:623-628.

Disclosures

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