11. Gastrointestinal, Hepato-Biliary-Pancreatic Diseases

Reference

Miyazaki Y, Yamada A, Saitou M. Effect of ninjin-youei-tou on xerostomia induced by oxybutynin hydrochloride. *Shinyaku to Rinsho* (*Journal of New Remedies and Clinics*) 1994; 43: 2613-7 (in Japanese). MOL, MOL-Lib

1. Objectives

To evaluate the efficacy of ninjin'yoeito (人参養栄湯) for improvement of xerostomia induced by oxybutynin hydrochloride.

2. Design

Randomized controlled trial (RCT).

3. Setting

The department of urology of a hospital (although not mentioned, it was probably an outpatient clinic) , Japan.

4. Participants

Sixteen patients who complained of dry mouth out of 20 patients who were diagnosed with psychogenic frequency or unstable bladder (chronic cystitis, neurogenic bladder) and received oxybutynin hydrochloride (6 mg/day) for 2 weeks (all females; mean age, 52.3 years; range, 31–72 years) were examined.

5. Intervention

Arm 1: oxybutynin hydrochloride alone for 2 weeks followed by oxybutynin hydrochloride combined with ninjin'yoeito (人参養栄湯; manufacturer, not specified) (8.1 g/day) for 2 weeks (a total of 4 weeks) (n=8).

Arm 2: oxybutynin hydrochloride alone for 4 weeks (n=8).

6. Main outcome measures

Severity of dry mouth (on a 5-point scale), chewing gum test, frequency of urination evaluated by interview at baseline, 2 weeks, and 4 weeks.

7. Main results

After 2-week treatment with oxybutynin hydrochloride, 16 out of 20 patients (80%) developed xerostomia symptoms (mild in 12 and severe in 4 patients). In arm 1, dry mouth worsened in 5 patients and remained unchanged in 3. In arm 2, dry mouth worsened in no patients, remained unchanged in 2, and improved slightly in 4, and moderately in 2. Dry mouth failed to disappear in any patient in either arm. Response, defined as mild or moderate improvement, was observed in 6 out of 8 patients, yielding a response rate of 75%. The chewing gum test was performed in 3 patients in arm 1 and 4 in arm 2. The total amount of saliva in arm 1 and arm 2 was, respectively, 8.00 mL and 7.30 mL at baseline, 1.27 mL and 1.30 mL at 2 weeks, and 1.13 mL and 2.40 mL at 4 weeks, suggesting that the amount of saliva had increased at 4 weeks. The frequency of urination was 11.875±2.125 times/day at baseline, 8.5±1.125 times/day at 2 weeks, and 8.375±1.0 times/day at 4 weeks in arm 1, and 11.75±2.75 times/day, 8.75±1.625 times/day, and 8.5±1.5 times/day, respectively, in arm 2; there was no between-arm difference.

8. Conclusions

Ninjin'yoeito improves the subjective symptoms of xerostomia induced by oxybutynin hydrochloride but not urinary frequency and therefore is considered to be effective for treating xerostomia induced by oxybutynin hydrochloride.

9. From Kampo medicine perspective

For drug-induced xerostomia, treatment with byakkokaninjinto (白虎加人参湯) or bakumondoto (麦門冬湯) has been frequently reported. Byakkokaninjinto is indicated for patients with *jitsu-sho* (実証, excess pattern) and *netsu-sho* (熱証, heat pattern). Since most patients with nonobstructive dysuria associated with frequency and incontinence are female with *kyo-sho* (虚証, deficiency pattern), ninjin'yoeito may be more effective for dry mouth induced by oxybutynin hydrochloride.

10. Safety assessment in the article

Not mentioned.

11. Abstractor's comments

The authors said: "the study was triggered by the encounter with cases in which polydipsia had developed due to dry mouth induced by this drug (oxybutynin hydrochloride), and urinary frequency was not improved because of the increase in urine output." Clinical practice questions were transformed into research questions, and this RCT was conducted to answer them. Such a study is called a "practice-based study" and provides results that can easily be applied in clinical practice. Although there are some concerns about study design, including the small number of patients and lack of objective assessment of the oral cavity, the authors deserve praise for implementing a practice-based study. Further studies of this treatment are expected.

12. Abstractor and date

Tsuruoka K, 31 October 2008, 1 June 2010, 31 December 2013.