

Sakakibara R¹, Takahashi O², Tateno F³, Yano M⁴, Kishi M³, Tsuyusaki Y³, Yamamoto T⁵, Yamanishi T⁶, Uchiyama T⁶, Yamaguchi C⁶, Yanagisawa M⁷, Awa Y⁷

1. Neurology, Internal Medicine, Sakura Medical Center, Toho University, 2. Clinical Physiology Unit, Sakura Medical Center, Toho University, Sakura, Japan, 3. Neurology, Internal Medicine, Sakura Medical Center, Toho University, Sakura, Japan, 4. Urology, Sakura Medical Center, Toho University, Sakura, Japan, 5. Neurology, Chiba University, Chiba, Japan, 6. Continence Center, Dokkyo Medical College, Tochigi, Japan, 7. Urology, Chiba University, Chiba, Japan

TOLTERODINE ACTIVATES THE FRONTAL MICTURITION AREA OF OAB PATIENTS: A REAL-TIME MEASURE OF OXYHEMOGLOBIN CONCENTRATION CHANGES DURING URODYNAMICS

Hypothesis / aims of study

The incidence of overactive bladder, with or without incontinence, in the general population over 40 years in age is estimated to be 12.4-16.6%. The prevalence increases significantly with age (35–50%). Mechanism of OAB is age related changes in the bladder itself, or central nervous system changes innervating the bladder. Studies concerning OAB have shown urothelial/suburothelial changes and increased bladder afferents, while in the brain the frontal micturition area is deactivated that normally suppresses the bladder¹. Question arises whether anticholinergic medication could reverse the latter. To clarify this, we performed a real-time NIRS (near-infrared spectroscopy)-urodynamic study in OAB patients before and after administration of an anticholinergic agent tolterodine.

Study design, materials and methods

We recruited 13 OAB patients in our outpatient clinic. Most of them were referred patients. They were 9 male, 4 female patients; mean age 73 years, range 46-84 years. Before and after administration of 3 months, 4 mg/day tolterodine, all patients underwent a NIRS-urodynamics according to the International Continence Society standards. Cerebral changes in the oxy-hemoglobin concentration (oxy-Hb) and deoxy-hemoglobin concentration (deoxy-Hb) were sampled by optical topograph systems for NIRS (OMM-3000, Shimazu Inc, Kyoto, Japan, 52 channels being measured simultaneously). Concentration changes in oxy-Hb and deoxy-Hb were calculated based on a modified Beer-Lambert approach². According to the Talairach's brain atlas, the probe array covers the areas 8, 10, 44, 46 and the more anterior parts of the frontal cortex.

Results

Tolterodine ameliorated night-time frequency (by the OAB-symptom scale, $p < 0.05$) and increased first sensation volume (290 ml to 359 ml, $p < 0.01$) significantly, while it did not increase post-void residual volume (20.6 ml to 28.7 ml). The number of patients with detrusor overactivity did not lessen significantly (11 to 9). A real-time NIRS -urodynamic study showed that tolterodine activated the frontal micturition area of OAB patients. It was prominent in Brodmann's area 8,10 of the prefrontal cortex.

Interpretation of result

In the present study, tolterodine increased first sensation volume significantly without marked disappearance of detrusor overactivity. This presumably reflects tolterodine's suppression of the bladder afferent signals. The present study results showed that tolterodine activates the frontal micturition area of OAB patients, particularly Brodmann's area 8,10 of the prefrontal cortex, that has been deactivated presumably by the disease process. This activation seems to be the secondary phenomenon since tolterodine does not easily penetrate the blood-brain barrier³. However, since this is a small study, clarification with a larger study is needed.

Concluding message

A real-time NIRS -urodynamic study showed that tolterodine, an anticholinergic agent, activates the frontal micturition area of OAB patients that was prominent in the Brodmann's area 8,10 of the prefrontal cortex.

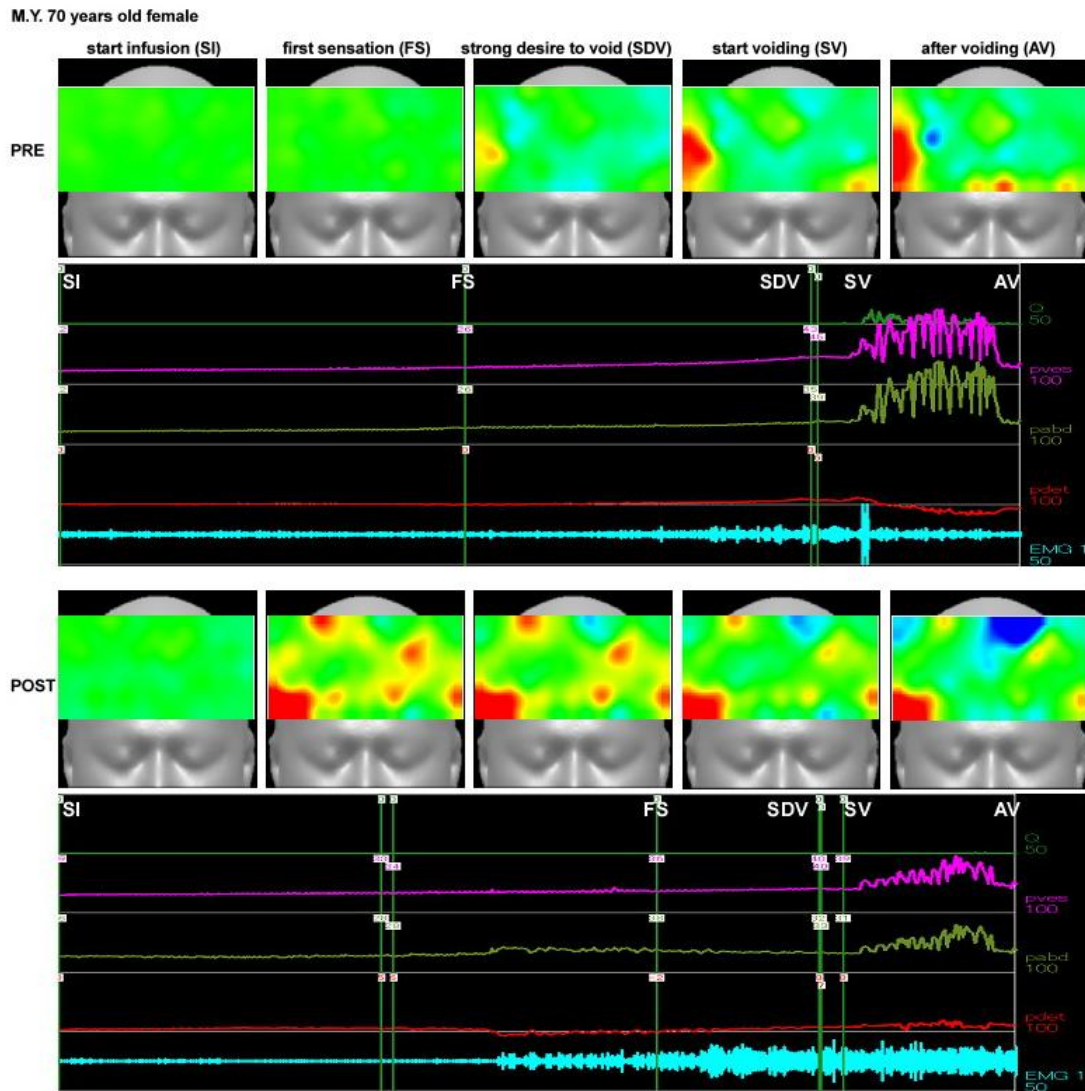


Figure 1 M.Y. showing an increase in oxyhemoglobin concentration in the frontal micturition area before and after administration of 3 months, 4 mg/day tolterodine. Note that time scale is different between PRE and POST.

References

1. Cerebral control of the bladder in normal and urge-incontinent women. *NeuroImage* 2007; 37, 1–7.
2. Real-time measurement of oxyhemoglobin concentration changes in the frontal micturition area: an fNIRS study. *NeuroUrol Urodyn.* 2010; 29: 757-764.
3. Effects of tolterodine, trospium chloride, and oxybutynin on the central nervous system. *J Clin Pharmacol.* 2001; 41: 636-644

Disclosures

Funding: No funding **Clinical Trial:** No **Subjects:** HUMAN **Ethics Committee:** Ethics committee in Sakura Medical Center, Toho University **Helsinki:** Yes **Informed Consent:** Yes