

FOWLER SYNDROME-CLINICAL CHARACTERISTICS AND STUDIES ON OVARIAN INNERVATION.

Hypothesis / aims of study

Fowler syndrome (FS) is characterized by the presence of polycystic ovaries and urinary retention. The etiology of FS is not well known yet. External urethral sphincter enlargement was suggested to be the most important factor of the lower urinary tract functional disturbances. Changes observed both in the hormonal milieu and in the function of the gonad could be of crucial importance, too. Therefore we decided to study the ovary innervation in women with the clinically diagnosed FS.

Study design, materials and methods

200 patients with the polycystic ovary syndrome (mean age 20.4 years, range 18-33) were studied. Screening was targeted at disclosure of voiding disturbances in these patients (voiding difficulties, post void residual, urgency, frequency, pain during voiding). After identification of such patients a full urodynamic study and volumetry of the external urethral sphincter using transrectal ultrasound were performed. Fowler syndrome was diagnosed if the external urethral sphincter volume was greater than 2 cm³ and the maximum urethral closure pressure (performed accordingly to Brown-Whickman) was higher than 80cm H₂O.

During laparoscopic cauterization of the ovarian cysts, ovary samples were obtained and processed for immunohistochemistry. Ovary innervation was studied with the single immunolabeling technique using the primary antisera against neuropeptide Y (NPY), vasoactive intestinal polypeptide (VIP), peptide histidine-isoleucine (PHI), galanin (GAL) and substance P (SP). Double labeling using the anti-GAL, anti-NPY and anti-SP antibodies was also performed. Control ovaries were obtained from age-matched patients undergoing different gynecological procedures, requiring ovary resection.

Results

Fowler syndrome was diagnosed in 10 patients (mean age 19.5 years, range 18-33 years) out of 13 with polycystic ovary syndrome and voiding disturbances. No patient had complete urinary retention. All patients were complaining of pain in the lower abdomen, decrease of urinary flow rate and increased voiding frequency.

In the urodynamic examination urine flow in a characteristic "saw teeth" shape was found (mean maximum flow rate 16.2 ml/s, range 12.4 to 22.8 ml/s). Maximum cystometric bladder capacity was 429ml in the average (range 222ml to 635ml) and mean post void residual was 30 ml (range 20-200ml). Maximum urethral closure pressure was 115cmH₂O in the average (range 87 to 128 cm H₂O). In the transrectal ultrasound the mean external urethral sphincter volume was 2.8cm³ (range 2.4 to 5.5 cm³)

The majority of the changes in the ovary innervation were observed within the cortical stroma. An increase in the numbers of VIP-, PHI- and GAL-positive nerve fibers in patients with FS were observed, when compared to control specimens. Double-immunostaining revealed a very prominent increase in the density of GAL-positive, but NPY-negative nerve fibers. A less pronounced increase in the number of GAL- and NPY-positive, as well as SP-positive, but GAL-negative terminals was also observed. Within the tunica albuginea we did not observe any nerve fibers positive to the examined substances except for NPY positive nerve fibers, which density was decreased in patients with FS.

Interpretation of results

Fowler syndrome is a rare disease, present in about 0.5% of patients with polycystic ovary syndrome, accordingly to our studies. Its clinical manifestation is not homogenous and the complete urinary retention occurs very rarely (no such cases in examined patients).

Clinical symptomatology of our patients differ from that presented by Fowler in the classical syndrome description, however both voiding problems and polycystic ovaries were present in all our patients. We also described enlargement of the external urethral sphincter in these patients. The reason of different clinical manifestation could be the time elapsed from the onset of the disease till the moment of diagnosis. Another interesting finding are the innervation changes within the ovaries (not described in regular polycystic ovaries), which could be the true cause of the syndrome. One can speculate that altered hormonal milieu and altered neuropeptides expression within the ovaries could give rise to the morphological and functional imbalance within the lower urinary tract

Concluding message

In our study we described a group of females with enlargement of the external urethral sphincter and PCOS, without urinary retention, having however voiding difficulties. or The origin of these problems could be probably attributed to the changes in ovarian functions, that, in turn may be caused by altered pattern of both the sympathetic and parasympathetic innervation of the ovary.

DISCLOSURES: NONE

HUMAN SUBJECTS: This study was approved by the Medical Academy of Warsaw Ethical Committee and followed the Declaration of Helsinki Informed consent was obtained from the patients.