158

Sugaya K[1], Onaga T[2], Nishijima S[1], Miyazato M[1], Ogawa Y[1]
1. Division of Urology, Faculty of Medicine, University of the Ryukyus, 2. Department of Urology, Okinawa Kyodo Hospital

SERUM CHOLINESTERASE LEVELS IN PATIENTS WITH OR WITHOUT OVERACTIVE BLADDER AND/OR NEUROGENIC BLADDER

Aims of study
It has been reported that acetylcholine is not only produced by nerve terminals but also by the bladder epithelium, and that acetylcholine production by this epithelium increases after bladder outlet obstruction occurs. Acetylcholine derived from the bladder epithelium has been suggested to activate bladder smooth muscle cells and afferent nerve terminals via muscarinic receptors. For the treatment of overactive bladder (OAB), anticholinergic agents are mainly used. These drugs can usually improve OAB symptoms without inhibition of micturition, suggesting that anticholinergic agents block the action of acetylcholine released from the bladder epithelium on bladder smooth muscle cells and afferent nerve terminals. Serum cholinesterase (ChE) is an enzyme that metabolises acetylcholine. The serum ChE level is one of the indices of hepatic protein synthesis, but ChE also metabolises acetylcholine in the bladder wall. In order to confirm whether the serum ChE level is related to the occurrence of OAB, serum ChE and other biochemical markers of liver function were compared in relation to the presence/absence of OAB and/or neurogenic bladder (NB).

Patients and methods
The subjects were selected from among outpatients who consulted the Department of Urology at our hospital from July to December 2004. Patients who met the following criteria were selected; 1) the presence/absence of OAB was described in their medical records within one year before the study, 2) biochemistry tests (including ChE) had been done within one year at a routine health check or mass screening at our hospital, and 3) serum GOT, GPT, and creatinine levels were within the normal range. Patients taking cholinesterase inhibitors or cholinergic agents, were excluded, as well as patients with acute cystitis, acute prostatitis, bladder cancer, or proteinuria. From the medical records of the subjects, the original disease, concomitant illnesses, medications, progress of OAB, serum total protein (TP), albumin (ALB), liver function tests (GOT, GPT, gamma-GTP, T-Bil, ALP, LDH, LAP, ZTT), and ChE (dimethoxy benzoylthiocholine method, reference range: 100-240 IU/L) were examined. Then the relationship between the presence of OAB with or without NB and the serum ChE level was examined, as well as that between the serum ChE level and other biochemical data. Moreover, a qualified urologist comprehensively evaluated the efficacy of medication by determining each patient's satisfaction with the treatment and assigning them to 1 of 4 categories (excellent: 3 points, good: 2 points, fair: 1 point, no change or worse: 0 points) at 2 months after the start of treatment, and the relationship between the therapeutic outcome and the serum ChE level was also examined. Results are reported as the mean ± standard deviation.

Results
The number of outpatients during the investigational period was 1017, and 200 of them met the requirements for this study. Among these 200 patients, there were 31 patients (20 males and 11 females aged 74 ± 8 years) with both NB and OAB (NB-OAB), 49 patients (37 males and 12 females aged 75 ± 7 years) with OAB but without NB (OAB), and 120 patients (72 males and 48 females aged 67 ± 12 years) without OAB (non-OAB). In the NB-OAB group, 10 patients (32%) had cerebrovascular disease, and 7 patients (23%) had spinal canal stenosis. In the OAB group, all 37 men had BPH with or without chronic prostatitis, and while 6 of the 12 women had non-bacterial chronic cystitis including urethral syndrome. The serum ChE level was significantly lower in the OAB group (143 ± 32 IU/L) than in the NB-OAB group (164 ± 40 IU/L, $p = 0.035$) or non-OAB group (166 ± 45 IU/L, $p = 0.002$). There was no significant difference of the serum ChE level between the NB-OAB and non-OAB groups. The serum TP level (6.8 ± 0.6 g/dl) of the OAB group was also significantly ($p = 0.035$) lower than that (7.0 ± 0.6 g/dl) of the non-OAB group. There were no differences of the values of other biochemical parameters among the OAB, NB-OAB, and non-OAB groups. The serum ChE level showed the strongest positive correlation ($r = 0.396$) with serum ALB, followed by serum TP ($r = 0.349$). There was only a significant gender difference of the gamma-GTP level. NB-OAB and OAB patients were treated by using anticholinergic agents with or without adrenergic alpha one receptor antagonists or Chinese herbal medicines. In the OAB group, higher serum ChE levels were associated with a better therapeutic outcome ($p = 0.011$).

Interpretation of results
The serum ChE level of OAB patients was significantly lower than that of NB-OAB or non-OAB patients. The serum TP level of OAB patients was also significantly lower than that of non-OAB patients. Moreover, a higher serum ChE was associated with a better therapeutic outcome in the OAB group. These results suggest that lower serum ChE levels are related to the occurrence and poor response of OAB in patients who do not have NB. Circulating ChE is produced in the liver, and it is thought that serum ChE may also metabolise acetylcholine secreted by the bladder epithelium. The amount of ChE in the serum is not enough for rapid elimination of a large quantity of acetylcholine secreted by parasympathetic nerve terminals in the bladder when the micturition reflex is activated. However, when the amount of acetylcholine secreted by the bladder epithelium increases in the state of bladder outlet obstruction and exceeds the metabolic capacity of ChE produced by the liver, it is possible that OAB develops.

Concluding message
There were significant positive correlations between serum ChE and serum TP or ALB, suggesting that a protein-rich diet may assist in the treatment of OAB in patients without NB.

FUNDING: NONE
DISCLOSURES: NONE
HUMAN SUBJECTS: This study did not need ethical approval because Patients' individual informations are protected, and their names are not clarified. but followed the Declaration of Helsinki Informed consent was not obtained from the patients.