



## Editorial

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# A Clinician's Perspective on the Mechanism of $\beta_3$ -Adrenoceptor Agonists in the Bladder

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Bladder function consists of 2 opposite functions, contraction and relaxation, of the 2 connected organs (bladder and urethra). In addition, these organs have a characteristic of changing each function in accordance with 2 successive phases of micturition (storage and voiding). For this reason, anticholinergic agents that can block only one function (i.e., contraction) cannot keep up with the changes that occur according to the phases of micturition and suppress the contraction function during storage and voiding phases, resulting in voiding difficulty or urinary retention. This theoretical background of anticholinergic treatment is a significant weakness in the clinical use of medicines in patients. This should be noted when prescribing the drug to patients, thereby limiting the use of medications. The high placebo effect in patients with voiding dysfunction [1] indicates that the central nervous system has a great influence on micturition. This suggests a high likelihood of limiting use of the drug, due to the fear of the recognized adverse effects. To overcome these shortcomings, much effort is being made to develop drugs that block afferent nerve impulses in the bladder rather than anticholinergic drugs that block efferent impulses only. However, although several developments and experimental verifications have been conducted, such as drugs acting on some receptors in the afferent nerves of the bladder [2], only few drugs lead to clinical trials. The beta-3 adrenergic receptor agonist is the first successfully developed afferent-blocking drug, although the effect may be partial. It is an important merit for clinicians to use drugs that do not need explanation of the side effects of anticholinergic drug to patients. Therefore, the

exact theoretical background of the unexplained part of some drugs should be studied.

When I met my mentor, Professor Karl-Erik Andersson a few years ago at an international conference, I remember that he said, "The bladder is an interesting organ because there is so much we do not know yet". He also mentioned that the bladder has a more complicated regulatory system than the heart. In my opinion, patients with voiding dysfunction are more difficult to manage than those with a heart disease. The heart is regulated only by the autonomic nervous system, whereas the bladder is controlled not only by the autonomic nervous system but also by the central nervous system. Patients with heart diseases already know that they are unable to control their hearts to their will. In the bladder, the autonomic nervous system actually plays a role in bladder contraction, but the brain can regulate only the onset of micturition. Therefore, patients assume that they can control all the mechanisms of micturition. Thus, clinicians should first make patients with voiding dysfunction understand that they cannot fully control the bladder and that the subjective symptoms can be quite different from the objective observations.

Although many drugs have been found and used for voiding dysfunction, the theoretical background to support this is still unclear. From the standpoint of clinicians, many basic studies have revealed much information on the function of the bladder, but research studies that link these functions with the micro-anatomical structure are not enough. From this point of view, Karl-Erik Andersson's paper [3] suggests an important implica-



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tion, which paves the way for future research. Our editorial board members and I feel unlimited glory about the publication of this paper by Karl-Erik Andersson in the *International Neurourology Journal* (INJ). In the future, the INJ hopes to receive clinical trials and meaningful basic research to support it. We sincerely hope that INJ will play a role as a global channel between basic research studies and clinical outcome for future meaningful development of treatments of voiding dysfunction in the world.

• **Conflict of Interest:** No potential conflict of interest relevant to this article was reported.

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