Treatment of overactive bladder: Past, present, and future

Conventional treatment of overactive bladder (OAB) includes behavioral therapy, life style modification and medical treatment with antimuscarinics.1 In patients who fail the second line treatment, electrical stimulation or surgical therapy might be the rescue modality. Although these treatments are effective in relief of urgency and urgency urinary incontinence in about 70% of OAB patients, around 30% of patients are still with inadequate treatment and poor quality of life and only about 30% of them can adhere to antimuscarinic treatment.2-3 In patients who fail the first antimuscarinic therapy, adding a second antimuscarinic agent might be effective in >30% of patients; however, intolerable adverse events and large postvoid residual (PVR) remain problems to be solved.4 It is mandatory to have a guideline for physicians to follow for the treatment for OAB refractory to conventional therapy. In this issue, Wang et al5 proposed the guidelines for adult patients with OAB. It is the first OAB guideline for Taiwanese physicians and patients to follow.

In recent decades, intravesical botulinum toxin A (BoNT-A) injection has been widely used to decrease urgency or urgency urinary incontinence in OAB patients.6-7 BoNT-A injection has been found to decrease sensory receptors such as P2X3 and TRPV1 in suburothelial nerve fibers, which results in reduction of sensory urgency and decrease in detrusor contractility.8 Currently, 100 U BoNT-A injection has been approved to use in refractory OAB patients in the USA, Europe, and many Asian countries and has been shown to improve the quality of life of patients.9-10 Although BoNT-A injection may increase PVR and the incidence of urinary tract infection, the reduction of urgency severity was associated with an improved satisfactory outcome.11 After the 1st month after BoNT-A injection, patients may enjoy an improved quality of life. However, before we recommend this treatment to refractory OAB patients, careful patient selection and informed consent are extremely important to avoid unexpected adverse events and patients dissatisfaction.

Mirabegron, a β3-adrenoceptor agonist, is a new class drug for the treatment of OAB. The mechanism of β3-adrenoceptor is different from antimuscarinic agents. Concerning the Adverse effects (AE) with antimuscarinic drugs, the pooled safety data indicate that mirabegron may be a valuable treatment option for patients with OAB.12 Animal study and clinical urodynamic study have shown that detrusor contractility does not decrease after mirabegron treatment.13 In this issue, Kuei et al14 review the recent advances in therapeutic application of mirabegron on OAB. Another Taiwanese clinical trial (Clinical trial. gov. ID: NCT01043666) of mirabegron has demonstrated that the daily frequency episode can be reduced after mirabegron therapy and no clinically relevant adverse events were identified in OAB patients. The results of this clinical trial are similar to that reported in the USA, Europe, and Japan.15-17 Given that dry mouth and dysuria are the chief cause of discontinuation of antimuscarins because of poor tolerability, mirabegron has been considered as a potentially first line medical treatment for OAB patients.

Intravesical administration of liposomes into the wounded urothelium may improve the dysfunctional urothelium and provide an alternative treatment for interstitial cystitis/bladder pain syndrome. In addition, in rat models of hypersensitive bladder, intravesical instillation of liposomes could reduce the bladder hypersensitivity induced by intravesical potassium chloride or acetic acid without compromise of voiding function.18 One pilot study has demonstrated that intravesical lipotoxin instillation can effectively reduce frequency and urgency episodes 1 month after treatment in OAB patients. The PVR did not increase, and all patients were free of urinary tract infection after the treatment.19 Another two-center, double-blind, randomized, placebo controlled study enrolled patients with OAB who were inadequately managed by antimuscarinics.20 At Week 4 after treatment, lipotoxin significantly decreased total frequency per 3 days. Total urgency and overactive bladder symptom score also significantly decreased in the lipotoxin group. These results support that BoNT-A delivered by liposomes might be better than with injection; thus the therapeutic effects might be limited to the urothelial sensory nerves without compromise to detrusor contractility. Hung et al,21 in this issue, review the clinical application of liposomes and lipotoxin in lower urinary tract dysfunction. The clinical results of lipotoxin in the treatment of interstitial cystitis/bladder pain syndrome and OAB support the liposomes as an efficient vehicle for delivering of BoNT-A without the need for injection.

In conclusion, we can see a change of the promised treatment modalities of OAB, which move toward a more effective and safer future to our patients. Mirabegron may become the first line medication treatment for OAB. If inadequate, adding antimuscarinic agent at a small dose may provide efficient results. For patients with OAB and undesired adverse events after antimuscarinic therapy, intravesical liposomes encapsulated BoNT-A might be a suitable treatment. Finally, in patients with OAB refractory to all kinds of treatments, intravesical BoNT-A injection may be the last treatment.

Conflicts of interest

The author declares that he has no financial or non-financial conflicts of interest related to the subject matter or materials discussed in the manuscript.

Sources of Funding

No funding was received for the work described in the article.