The management of lower urinary tract symptoms (LUTS) in men has often been associated with benign prostatic obstruction and managed accordingly. In the last three decades, pharmacologic treatment of LUTS became the standard approach to men bothered by voiding and storage symptoms, leaving surgery as a second-line option. Better understanding of LUTS pathophysiology broadened understanding of a number of mechanisms involved in the genesis of LUTS, including occult neurogenic disorders; hormonal and vascular changes associated with ageing, diabetes, obesity, and other conditions leading to metabolic syndrome; and bladder and urothelial disorders. The composite pathophysiology of male LUTS has not yet fully translated to a more sophisticated therapeutic approach, although a number of properly designed randomised trials are helping refine our therapeutic strategy. The clear success of the medical treatment of male LUTS helped change the treatment management of male LUTS, with a large decrease in surgical procedures in favour of widespread use of medications [1]. The number of treated patients has continued to increase in recent years [1]. Notwithstanding the clear success of the medical treatment of male LUTS, real-life data highlight a number of unmet needs, as some of the patients remain bothered and symptomatic despite treatment. Current medical options include (in order of introduction in the formularies) phytotherapeutic agents, α-blockers, 5α-reductase inhibitors (5-ARIs), antimuscarinics, phosphodiesterase type 5 inhibitors, and β3 agonists.

There are no proper animal models of lower urinary tract dysfunction. Animal models of acute urinary obstruction have been somehow misleading and led us believe that storage symptoms such as urgency were caused mainly by increased outlet resistance and that treatment should be aimed at relieving the obstruction [2]. Long-term analysis of patients undergoing transurethral resection of the prostate showed that urgency and detrusor overactivity are cured in about 50% of patients but often recur, suggesting that the problem is not just in the prostate but rather in the bladder and in that part of the nervous system that controls the micturition cycle [3]. Another example of our poor understanding of LUTS is nocturia, which has always been treated regardless of whether or not it is due to nocturnal polyuria. Our overall approach to the diagnosis and treatment of LUTS has matured enormously over the last decade, but as the picture becomes more complex, treatment difficulties increase accordingly.

Randomised trials of pharmacologic treatment of male LUTS showed a significant improvement of symptoms and quality of life, although patients rarely become asymptomatic and symptoms tend to persist, although in milder form [4]. The aetiology of LUTS is multifactorial, and a single drug addresses only part of the problem. Combination treatment of male LUTS is not a novel idea, although it took a long time before the combined use of α-blockers and 5-ARIs proved to be effective over monotherapies [5,6]. A different type of combination treatment was pioneered by Lee and co-workers, who investigated the sequential treatment of LUTS in men with bladder outlet obstruction with or without overactive bladder [7]. Men reporting urgency had a lower chance of improving with α-blockers, but symptoms greatly improved when an antimuscarinic drug was added [7]. The sequential use of drugs is a common way to manage our patients that may certainly be effective, although decisions to step up from single- to dual-drug treatment are often...
based on personal preferences, with large variability among patients, doctors, centres, and countries.

The study from Drake et al addresses the issues of safety and efficacy of a fixed-dose combination of a modified-release formulation of tamsulosin (Omnic OCAS) and solifenacin (Vesiker) in the treatment of male LUTS with 1-yr follow-up [8]. Although the subject may not appear new, the study is of importance because no new fixed-dose combination treatment can be registered unless this type of study is conducted. The study design consists of a 40-wk open extension of a 12-wk randomised trial. The results of the study provide evidence of the safety of this combined treatment over a 1-yr period and maintenance of efficacy over the duration of the open-label extension. Symptom improvement was observed as early as 4 wk, with further improvement up to 16 wk and maintenance over the following weeks up to 1 yr. The overall reduction in International Prostate Symptom Score was 9 ± 5.7 points after the 12-wk randomised trial and 10.1 ± 9.2 points at the end of the open-extension study. A 1.1% retention rate was observed during 52 wk of treatment. The study is of interest because it answers a number of questions that are important in real-life practice. We know that the low adherence to antimuscarinics is mainly due to treatment efficacy that is perceived as lower than expected by the patient, and 1-yr data provide a reasonable horizon for understanding what patients can expect from such combination treatment [9]. Another cause of low adherence is side effects, and safety over a 1-yr period is of importance to understand whether prolonged exposure to such treatment can result in unexpected adverse events [9].

The use of fixed-dose combination treatments is not new in medicine or in urology. The aim is to improve patient adherence and to ensure that patients are exposed to the expected drug dosages. The convenience of a single tablet may be of interest for some of our patients and, hopefully, will improve adherence. Will the fixed-dose combination of Omnic OCAS and Vesiker work for everyone? Certainly not, but it is an important option in our armamentarium that will easily fit the needs of many of our patients. Looking into the management of LUTS due to benign prostatic hyperplasia, we know that most of our patients are treated with α-blockers only, and antimuscarinics are clearly under-utilised in men compared with female patients [10]. It is too early to know how much this fixed-dose combination will help fill the existing unmet needs in the management of male LUTS, but its availability will help our fellow urologists consider the use of antimuscarinics in male patients suffering urgency, among other LUTS. The study by Drake et al [8] is a must-read reference for the practising urologist!

Conflicts of interest: A. Tubaro is a consultant for Allergan Astellas, GSK, and Pfizer. C. De Nunzio is a consultant for GSK and Pierre-Fabre.

References


