LUTS, alpha-blockers and men's health

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With an increasing number of men presenting with lower urinary tract symptoms (LUTS), erectile dysfunction (ED) and the metabolic syndrome, Roger Kirby suggests that it is time to review current treatment approaches to avoid making some problems worse, and to try combinations of treatments that may be more beneficial for our patients.

Lower urinary tract symptoms, which most commonly develop as a result of benign prostatic hyperplasia (BPH), are extremely prevalent. Ninety percent of men reaching the age of 80 can be expected to have histological BPH, and more than half of them will suffer significant LUTS. As the global population ages, more and more men are destined to experience impairment of their quality of life (QoL) as a consequence of prostatic enlargement and associated bladder outflow obstruction. Their partners may also suffer because of the disabling symptoms that trouble their spouse or partner.

It seems clear, however, that men with LUTS are often reluctant to seek medical advice. Perhaps they assume that frequency of micturition and reduction of their flow rate is simply a natural consequence of ageing; alternatively, some may fear that, if they consult a urologist, he or she may advise surgery and this might have negative consequences for their sex life. It has been clearly demonstrated that there is
a strong correlation between LUTS and ED. Indeed, the greater the International Prostate Symptom Score (IPSS), the more likely the sufferer is to experience sexual dysfunction. Moreover, the combination of LUTS and ED often has a very negative impact on QoL. Men suffering both sets of symptoms are often mainly concerned about further deterioration of the latter.

Another important social trend of the 21st century is the so-called ‘tsunami’ of weight gain. In men, this is characterised by central obesity and very often accompanied by the other three features that comprise the ‘metabolic syndrome’, namely, diabetes, hypertension and hyperlipidaemia. There is now a well-recognised association between obesity and LUTS. As a consequence, urologists and GPs are likely to be seeing more and more patients with a combination of urological symptoms and clinical features of the metabolic syndrome. Significantly, men with central obesity are very likely to have early sexual dysfunction, low morning testosterone levels, and signs and symptoms of hypogonadism. The reason for this is thought to be the role of lectins and cytokines secreted by intra-abdominal fat in suppressing pituitary luteinising hormone (LH), with consequent reduction of production of testosterone from the Leydig cells of the testes.

CURRENT TREATMENT
There are several alpha-blockers available for the treatment of LUTS secondary to BPH. In most countries, around 80% of men treated for these symptoms receive a slow-release formulation of an alpha-blocker as first-line therapy. Tamsulosin has selective affinity for the alpha-1A adrenoceptor and alfuzosin is also ‘uroselective’; however, doxazosin has more balanced selectivity for all three subtypes of the alpha-1 adrenoceptor: alpha-1A, alpha-1B and alpha-1D. These differences may have important clinical consequences. Several studies have suggested that doxazosin has a greater beneficial impact on both LUTS and urinary flow rate than tamsulosin or alfuzosin. Moreover, the profound selectivity of tamsulosin for the alpha-1A adrenoceptor probably accounts for the development of anejaculation, which is often troublesome to patients, as well as the so-called ‘floppy iris syndrome’, which is bothersome to eye surgeons performing cataract surgery.

Following the publication of the MTOPS (Medical Therapy of Prostatic Symptoms) study of the combination of doxazosin and finasteride, and the subsequent randomised trial of tamsulosin and dutasteride, many clinicians opted for dual therapy with an alpha-blocker and a 5-alpha reductase inhibitor (5-ARI) for their patients with LUTS. However, it is clear from the clinical trial data that many patients on this combination suffered sexual dysfunction as a result of the medication. The 5-ARI appeared to cause loss of libido, reduced ejaculate volume and erectile dysfunction in some patients, while tamsulosin sometimes resulted in anejaculation.

ALTERNATIVE APPROACH
An alternative approach to combination therapy in men with both LUTS and ED is to combine an alpha-blocker with a phosphodiesterase 5 inhibitor (PDE5I). Since doxazosin has been shown to be mildly beneficial to sexual function, it might be considered the alpha-blocker of choice in this situation. Once the patient is stable on this medication, or alternatively on alfuzosin, a PDE5I such as tadalafil (Cialis) 5mg or sildenafil 25mg (increasing if necessary to 50mg or 100mg) once a day can be safely added without significant risk of inducing postural hypotension.

From a men’s health standpoint, the use of an alpha-blocker with balanced adrenoceptor selectivity, such as doxazosin, makes good sense. It not only rapidly and effectively improves bothersome LUTS, but also has a positive rather than negative impact on sexual function. It is also potentially beneficial in many of the comorbidities that many of the more elderly patients with LUTS also suffer from. For example, doxazosin reduces blood pressure in hypertensive patients, but has no clinically significant effect in normotensive individuals.

The combination of LUTS and ED can have a very negative impact on quality of life
Doxazosin also improves lipid profile, and reduces insulin resistance and platelet stickiness. It may be usefully deployed in patients with pre-diabetes and those who have coronary artery disease. Of course, in overweight individuals, medication should also be combined with advice about lifestyle and diet. In cases where the comorbidities are more severe, other medications, such as a statin or metformin for diabetes, and a first-line antihypertensive, such as amlodipine, may be required to reduce cardiovascular risk and promote normoglycaemia and normotension. In men with demonstrable hypogonadism and no clinical features of prostate cancer, testosterone replacement therapy may also be indicated.

CONCLUSION
In conclusion, it seems clear that many men presenting with LUTS resulting from BPH suffer significant comorbidities, the most troublesome of which is often ED. Rather than treat them with a medication or medications that may further impair sexual function, treatment with an alpha-blocker that is safe and rapidly effective, as well as mildly beneficial for this important aspect of life, seems reasonable. If further help is required, a PDE5I can safely be added later and other comorbidities treated appropriately as required. The
net result may be a happier, healthier cohort of men who no longer avoid seeking help for their urinary symptoms for fear of receiving a medical treatment or operation that could impact negatively on their sexual performance.

Declaration of interests
Roger Kirby has lectured in the Middle East and Asia on behalf of Pfizer.

REFERENCES


