

Silodosin — a safer alpha-blocker targeting benign prostatic hyperplasia

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Silodosin is a specific alpha-1A receptor inhibitor newly available in South Africa. It offers a real solution to symptoms of BPH especially in those patients with moderate prostate enlargement experiencing nocturia, frequency and incomplete voiding. It can be safely used in patients who cannot tolerate non-selective alpha blockers. The main side-effect is anejaculation, but this seldom leads to drug discontinuation. The rapid action and ongoing effectiveness of the drug offers swift relief for patients.

Keywords: alpha-1A receptor inhibitor, benign prostatic hypertrophy, BPH, lower urinary tract symptoms

Summary

Silodosin is a specific alpha-1A receptor inhibitor which has been available in the US/EU since 2008. According to the European Association of Urology (EAU), benign prostatic hyperplasia (BPH) affects as many as 40% in men in their fifth decade and 90% in men in their ninth decade.¹ Bothersome lower urinary tract symptoms (LUTS) affect both daily activity and sleeping patterns.² By 60 years of age nearly half of all men have symptoms of BPH.

While BPH causes many lower urinary tract symptoms, the most bothersome symptoms for which patients seek treatment includes urinary frequency, nocturia and incomplete emptying – leading to a constant sense of fullness in the bladder. Effectively managing these symptoms is important in improving patient quality of life.^{3,4}

Medical treatment of BPH

Even men with moderate BPH can be severely affected by their symptoms. Effective and safe medical management is important to improving quality of life and delaying the need for surgical intervention.¹

The EUA recommends watchful waiting for patient with only mild LUTS. Patients with moderate to severe symptoms (International Prostate Symptom Score between 7 and 19) should be considered for medical treatment. Choosing an agent depends on the specific symptoms experienced by the patient, risk of progression and co-morbidities.^{1,2}

The most widely used medical treatments available for BPH in South Africa include alpha adrenergic receptor antagonists and 5-alpha-reductase inhibitors or a combination thereof.²

Alpha-blockers

The prostate gland is rich in the expression of alpha-1A receptors, which mediate contraction of the smooth muscle at the urethral sphincter. Alpha-1A receptors are expressed with increasing concentration in elderly patients, making them an important target for BPH treatment.^{2,3}

Inhibiting these receptors allows muscle relaxation of the urethra, aiding in relief of primarily obstructive symptoms.

Up until now in South Africa there have been sensitive but no super selective alpha-1A blockers. General alpha-blockers cause blockade of alpha-1A, alpha-1D and alpha-1B receptors resulting in many unwanted and even dangerous side-effects.²

While the prostate gland only expresses alpha-1A receptors, alpha-1B and alpha-1D receptors are found widely elsewhere in the body — most importantly in the blood vessel walls.^{3,4}

Furthermore, with ageing, the prostate gland expresses a higher concentration of alpha-1A receptors. Since BPH is a disease which primarily affects older men, the targeted action at highly expressed receptors is of greater benefit to this population group.⁴

Prescribers need to monitor blood pressure closely and consider potential drug interactions, limiting the use of these agents. Patients also need to warn their ophthalmologists if they are using these drugs as rarely intraoperative floppy iris syndrome has been reported. Rarely side-effects like nasal congestion and headache have been reported.³

Silodosin

Selectivity

Silodosin is a highly sensitive alpha-1A receptor antagonist with little or no cardiovascular side-effects. It has been shown to have negligible effects on blood pressure and no effect on cardiac repolarization.³

In particular, silodosin has been shown to be more effective than tamsulosin in relieving nocturia, incomplete bladder emptying and frequency.^{3,5}

Tamsulosin is an alpha-1 receptor antagonist available in South Africa for several years. While both tamsulosin and silodosin are alpha-1A receptor antagonists, silodosin has even more specific alpha-1A binding specificity compared to tamsulosin.⁴

Nocturia (≥ 2 episodes per night) occurs in 85% of men with BPH and is considered by sufferers to be the most troublesome of all lower urinary tract symptoms.⁵ There are few treatment options which specifically target these symptoms.⁵

Sustained efficacy

Silodosin works rapidly to reduce obstructive symptoms of BPH. Studies show onset of action within 2–6 hours and clinically significant reduction in IPPS score within the first 3–4 days.³

Patients in trials have continued to experience symptom relief at 12 months after starting treatment.³

In their post hoc analysis, Montorsi *et al.* further concluded that silodosin exhibits significantly better effects to tamsulosin in managing the most bothersome symptoms of BPH — frequency, nocturia and incomplete emptying.³

Safety

The targeted specificity of silodosin to alpha-1A receptors located primarily in the prostate and urethra means that unlike other alpha blockers it can be used safely in patients with already using anti-hypertensives or in whom hypotension is a concern. Dose adjustment is required for patients with severe liver or renal dysfunction. The medication is, however, well tolerated in patients with mild renal failure.³

Unlike most other alpha-1A receptor antagonists, silodosin can also be safely prescribed concomitantly with phosphodiesterase type 5 inhibitors, overall improving patient quality of life.^{1,3}

The most frequent side-effect of silodosin is 'retrograde ejaculation' (RE) occurring in up to 20% of users. Retrograde ejaculation is better termed 'anejaculation' because it occurs due to failure of the vas deferens to contract rather than true RE. Those experiencing the side-effect attain orgasm with reduced seminal fluid release.⁴

Clinically patients treated with silodosin who develop retrograde ejaculation are also those who experience greater LUTS-related symptom improvements. This may be explained by the fact that anejaculation is a direct result of alpha-1A receptor blockade indicating uptake and specific targeting by silodosin.^{4,6}

Symptom relief clearly outweighs side-effects as only a minority of patients (3.9%) discontinued treatment due to RE.³ RE is completely reversible on stopping medication.⁷

New frontiers in BPH

BPH is a frequent issue, especially in ageing men, many of whom cannot tolerate typical alpha blockers. Silodosin provides an additional alpha-1A receptor antagonists, especially targeting symptoms of nocturia, frequency and incomplete voiding.

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Received: 26-05-2014 Accepted: 19-09-2014