

## Podcast

Journal watch: studies with a 'take-home' message'

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# Journal watch



## MIKE KIRBY

Editor for Trends in Urology and Men's Health, picks some interesting recent papers and highlights the 'take-home message'



## Tadalafil effective in reducing pelvic pain

Hiramatsu I, Tsujimura A, Soejima M, et al. Tadalafil is sufficiently effective for severe chronic prostatitis/chronic pelvic pain syndrome in patients with benign prostatic hyperplasia. *Int J Urol* 2020;27:53–7.

This study investigated the efficacy of tadalafil 5mg daily in 74 patients with benign prostatic hyperplasia (BPH) and chronic prostatitis (CP)/chronic pelvic pain syndrome (CPPS) over a 12-week period. Patients were classified as having moderate or severe urinary tract symptoms, and voiding symptoms were compared in those with high ( $\geq 4$ ) and low ( $< 4$ ) pain subscores based on the National Institutes of Health Chronic Prostatitis Symptom Index (CPSI).

At baseline, the CPSI pain subscore was high in 32.4% of patients, and the International Prostate Symptom Score (IPSS) was significantly higher in the group with a high pain score. After treatment, IPSS, CPSI, and pain subscores were all significantly improved. The change in the CPSI scores correlated positively with the change in the IPSS. The decrease in the IPSS was significantly greater in the group with the high pain subscore than the group with the low pain subscore.

### Messages for the clinic

Men with lower urinary tract symptoms (LUTS) may often have BPH, but also complain of lower

abdominal pain and/or perineal discomfort, which has been described as CP or CPSS.<sup>1,2</sup> When assessed by IPSS, the degree of histological prostatic inflammation has been shown to be positively correlated with the severity of LUTS.

CPPS is a difficult condition to treat, but PDE5 inhibitors have been shown to exert an anti-inflammatory effect on endothelial cells, which leads to a reduction in pro-inflammatory cytokines.<sup>3,4</sup> This has been demonstrated in expressed prostatic secretions and semen from men with CPPS whose secretions contained a higher level of TNF alpha, which is one of the markers of inflammation.<sup>5</sup>

In this study, men with the highest pain score also had a higher IPSS. Tadalafil was the treatment of choice because it has been shown to have a positive effect on oxidation, blood flow, inflammation and endothelial function. An interesting finding was that the change in the pain score correlated positively with the change in the IPSS.

Alpha-blockers and 5-alpha reductase inhibitors are the most commonly prescribed medications for BPH. Tadalafil has been approved for the last five years to treat men with BPH, with or without erectile dysfunction. However, until the drug recently became available as a generic, there were cost barriers to initiating this treatment.

This preliminary study suggests that tadalafil is effective in treating

patients with BPH and quite severe CPPS. It therefore seems logical that in patients with BPH, who also complain of perineal discomfort and pain, tadalafil might be a good treatment choice.

Furthermore, the latest Clinical Knowledge Summary from NICE recommends more frequent dosing of Tadalafil 5mg daily, and even up to 10–20mg daily if on-demand treatment fails or is inappropriate. This would seem to settle the issue!

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## Vardenafil: a PDE5i with multiple applications

Santi D, Granata ARM, Guidi A, et al. Six months of daily treatment with vardenafil improves parameters of

*endothelial inflammation and of hypogonadism in male patients with type 2 diabetes and erectile dysfunction: a randomized, double-blind, prospective trial. Eur J Endocrinol 2016;174:513–22.*

This prospective, investigator-initiated, randomised, placebo-controlled, double-blind trial investigated whether long-term chronic treatment with vardenafil improved systemic endothelial function in 54 men with type 2 diabetes mellitus (T2DM) and erectile dysfunction (ED).

The study involved a 24-week treatment phase with vardenafil or placebo, 10mg twice daily and patients were followed up for the same duration. The evaluated parameters included the International Index of Erectile Function 15 (IIEF 15), flow-mediated dilatation (FMD), serum interleukin-6 (IL-6), endothelin 1 (ET-1), testosterone and gonadotropins.

International index of erectile function (IIEF) erectile function improved during vardenafil treatment ( $p < 0.001$ ), and by the end of the treatment period, both FMD and IL-6 had also improved significantly ( $p = 0.040$  and  $p = 0.019$ , respectively). FMD correlated with serum testosterone levels ( $p < 0.001$ ). Testosterone levels increased significantly with vardenafil treatment, returning to the eugonadal range in hypogonadal men, without changes in gonadotrophin levels. There were no relevant side-effects from chronic vardenafil treatment.

### Messages for the clinic

T2DM is essentially an inflammatory condition associated with endothelial dysfunction, which in turn leads to the comorbidities that we see every day in clinical practice. Endothelial dysfunction reduces the availability of nitric oxide, which is associated with pro-inflammatory cytokines.<sup>1</sup>

Clinical trials using chronic phosphodiesterase type 5 inhibitors

(PDE5i) in diabetic men have illustrated a beneficial effect on flow-mediated dilatation and IL-6 serum levels.<sup>2</sup>

In this study, the investigators demonstrated a reduction in endothelial inflammation, which was maintained after treatment withdrawal, suggesting a long-lasting positive effect. The increase in testosterone level may be a consequence, of course, of improved sexual activity related to the PDE5i treatment or, perhaps, through a direct effect on testicular vasodilatation, Leydig cell function or both.

The authors speculate that chronic vardenafil treatment, by reducing endothelial dysfunction, may reduce mortality risk, and this has been demonstrated in other observational studies.<sup>3,4</sup>

Older men often have comorbidities, including T2DM, atherosclerosis, endothelial dysfunction and testosterone deficiency. Chronic use of a daily PDE5i drug offers physicians an opportunity to address multiple vascular comorbidities with one therapeutic agent, and move hypogonadal men into the eugonadal range.

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### Nocturia increased in obese patients

*Moon S, Chung HS, Yu JM, et al. The Association Between Obesity and the Nocturia in the U.S. Population. Int Neurourol J 2019;23(2):169–76.*

In this study, the researchers investigated the association between obesity and nocturia, using a nationally representative sample of 14 135 adults from the National Health and Nutrition Examination Survey (NHANES) between 2005–2012.

The methods included multivariate logistic regression analysis to find the odds ratio (OR) of obesity for nocturia, analysis of the OR of BMI for nocturia, and subgroup analysis based on age, sex, and hypertension.

As compared with participants without obesity, those with a BMI  $\geq 30 \text{ kg/m}^2$  had a significantly higher OR for nocturia (OR 1.39, 95% CI 1.28–1.50), and there was a dose-dependent relationship between BMI and OR for nocturia. Similar results were found in the subgroup analysis. Further analysis, using 1:1 matching data, found a significant association between obesity and the prevalence of nocturia (OR 1.25; 95% CI 1.10–1.41).

### Messages for the clinic

Nocturia is a highly prevalent condition that can negatively affect quality of life<sup>1</sup> due to the frequent need to wake up at night to void. It is often associated with comorbidities.<sup>2</sup>

Obesity is a risk factor for type 2 diabetes, hypertension, cardiac disease and stroke, and obesity may well be reversible with a change in lifestyle. Nocturia has been found to be more common in obese patients,<sup>3</sup> and BMI has been positively associated with nocturia in the general population.<sup>4</sup>

The NHANES data set is enormous and has provided plenty of epidemiological data. It is interesting that in this population,

32.7% of the participants had nocturia occurring two or more times per night. This may be the result of increasing urine production or increasing frequency of urination, and may be related to night-time eating or drinking, especially alcohol,<sup>5</sup> and those with central obesity may have increased intrabdominal pressure.<sup>6</sup> Men may suffer from an enlarging prostate, related to the metabolic effects of obesity<sup>5</sup> and obesity may therefore increase the risk of nocturia by causing BPH.<sup>7</sup>

Previous studies have shown that weight reduction<sup>8</sup> and exercise programmes<sup>9</sup> can improve nocturia.

These are data that we can inform our patients about and perhaps provide them with increased

motivation to achieve the necessary weight loss and take more exercise.

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