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Effect of tadalafil 5 mg on post-micturition dribble in men with lower urinary tract symptoms: a multicentre, double-blind, randomized, placebo-controlled trial

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This trial was registered at International Clinical Trials Registry Platform (ICTRP; www.who.int/ictrp; file no. KCT0002232).

Objectives

To compare the effects of taking tadalafil 5 mg and placebo once daily on post-micturition dribble (PMD) in men with lower urinary tract symptoms (LUTS).

Patients and Methods

Our prospective, randomized, double-blind, placebo-controlled, multicentre trial enrolled 102 men with PMD and other LUTS. PMD was assessed using the Hallym Post-Micturition Dribble Questionnaire (HPMDQ) and according to PMD volume. Over a 12-week period, patients took either tadalafil 5 mg (n = 51) or placebo (n = 51) once daily and their HPMDQ and PMD volume results were evaluated. Adverse events (AEs) were also reported.

Results

Over the course of 12 weeks, total HPMDQscores and PMD volumes improved significantly more in the tadalafil group than in the placebo group (reduction of total HPMDQ score of ≥2 points in the tadalafil and placebo group in 68.8% and 31.9% of patients (P < 0.001) and decreased mean PMD volume in the tadalafil and placebo group at 0.48 mL and 0.22 mL, respectively (P = 0.046). Specifically, PMD frequency decreased and quality of life increased significantly more in the tadalafil group than in the placebo group (P = 0.029 and P < 0.001, respectively). Furthermore, 66.7% of the tadalafil group reported moderate and significant PMD improvement, whereas only 4.2% reported that tadalafil was ineffective. Treatment-emergent AEs did not significantly differ between the groups (all P > 0.05), and no serious AEs were observed.

Conclusion

Taking tadalafil 5 mg once daily reduced PMD symptom severity and PMD volume in men with PMD, without inducing serious AEs, more effectively than placebo, suggesting that taking tadalafil 5 mg once daily may be an effective and well-tolerated PMD treatment.

Keywords

lower urinary tract symptoms, men, phosphodiesterase-5 inhibitors, post-micturition dribble

Introduction

It is possible to divide LUTS into storage, voiding and post-micturition symptoms [1]; however, almost all LUTS treatments are focused on storage and voiding symptoms, not on post-micturition symptoms [1,2], and even LUTS research does not focus on post-micturition symptoms. Physicians' and researchers' indifference to post-micturition symptoms may be attributable to the traditional belief that post-micturition symptoms may be a part of the aging process, have a low prevalence, and elicit less discomfort than other LUTS [3–7].

Post-micturition dribble (PMD), a post-micturition symptom, is defined as an involuntary loss of urine immediately after passing urine [2]. It is clearly different from terminal dribble, which is a voiding symptom [2]. PMD occurs in both genders, but seems to be more common in men [6,8]. Contrary to traditional assumptions [3–6], recent evidence

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suggests that PMD prevalence in men may be higher than previously expected. Some studies report PMD prevalence of > 50% [8–10]. Recent studies also suggest that PMD may be one of the most bothersome LUTS in men [8,11,12].

In men, PMD occurs secondary to residual urine in the bulbar and prostatic urethra after urination, but the exact pathophysiology of PMD is unknown [13,14]. Although bulbar urethral massages and pelvic floor muscle exercises are known to be effective in treating PMD, pharmacological treatment has not yet been introduced [15,16].

Several epidemiological studies report that there may be a close association between PMD and erectile dysfunction (ED) [7,17,18]. Recent experimental studies have also shown that corpus cavernosum structural changes may be related to the post-micturition residual urine volume in the bulbous urethra [19–21]. It is well known that phosphodiesterase-5 (PDE-5) isoenzymes are highly expressed in the urethra as well as the corpus cavernosum, bladder and prostate [22]. In addition, once-daily 5 mg tadalafil, a PDE-5 inhibitor, has previously been used to treat storage and voiding LUTS [1]. This suggests that tadalafil 5 mg can potentially be used in PMD treatment. The aim of the present study was to compare the effects of taking tadalafil 5 mg and placebo once daily on PMD in men with LUTS.

Patients and Methods

Patients

Patients were recruited to the present study between November 2017 and June 2018 from three Korean institutions. Approval for the study was obtained from the Korean Ministry of Food and Drug Safety (KMFDS; file no. 31252-2017) and the institutional ethical committees of each institution (file no. 16-12-003 at KSHH, 2016-602-I at DSHH, and 2016-137 at CSHH). The study is registered with the International Clinical Trials Registry Platform (ICTRP; www.who.int/ictrp; file no. KCT0002232). The study design and possible adverse events (AEs) associated with the study medication were explained in detail and the difference between PMD and terminal dribble was also explained based on the standardization of terminology of LUTS by the ICS [2,7]. Participants then signed an informed consent form prior to being randomized to a study arm.

Men aged 20–70 years who had both PMD and other LUTS (IPSS ≥8) and were regularly sexually active for at least 3 months prior to the study were included.

The exclusion criteria included contraindications to PDE-5 inhibitor use, urethral or penile malformations, history of pelvic surgery, neurological and chronic major systemic illnesses, and PDE-5 inhibitor use and ED treatments within 2 weeks prior to the study commencing. Treatments that could affect LUTS and ED were not allowed during the study period; however, patients taking LUTS medication for >1 month prior to the study were included but only if the drug regimen was maintained throughout the study period.

Study Design

Our prospective, randomized, double-blind, placebo-controlled multicentre study consisted of a 1-week baseline period and 12-week double-blind treatment period (Fig. 1).

During the baseline period, patients' characteristics, including medical and sexual history, physical examination results, vital signs, Hallym Post-Micturition Dribble Questionnaire (HPMDQ) score, IPSS, International Index of Erectile Function (IIEF) score, PMD volume, and uroflowmetry results; and laboratory results, including urine analysis results and serum PSA and serum testosterone levels, were recorded.

After the baseline period, patients were randomly assigned, 1:1, to the experimental or control groups. Block randomization was applied for each institution via an independent statistician using a computer-generated coding system. Sealed and labelled medication packages were provided by an independent pharmacist for double-blind conditions. Double-blinding was maintained until the data were finalized.

During the study period, patients were given tadalafil 5 mg (experimental group) or placebo (control group) daily. HPMDQ score, IPSS, IIEF score, PMD volume, and uroflowmetry results were assessed at 4 and 12 weeks post-baseline.

Safety Assessments

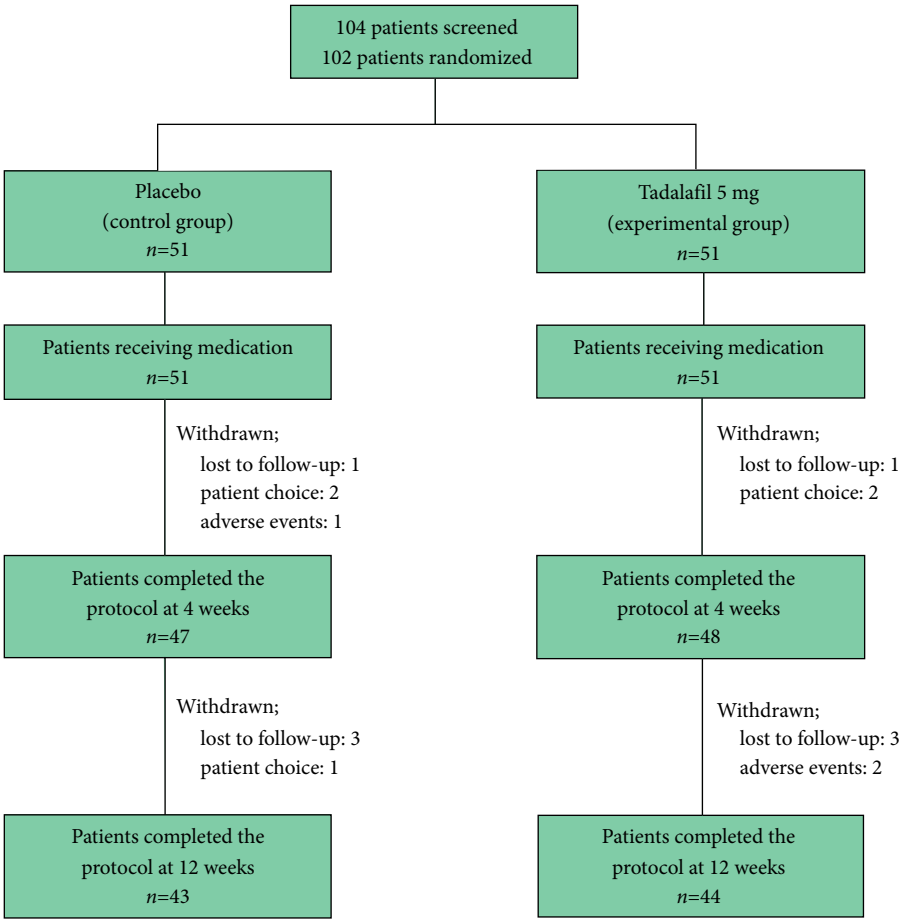
Vital signs, physical examination, and medical history, including concomitant medications, were checked at each visit. Any AEs were reported at onset or during each visit.

Post-Micturition Dribble Assessment

The HPMDQ, a self-administered questionnaire (Appendix S1) was used to assess PMD. It is composed of four questions regarding urination frequency (Question 1), bother (Question 2), quality of life (QoL; Question 3), and response to treatment (Question 4). The answers to the questions are scored in a range of 0–3 [7]. Total HPMDQ score was defined as the sum of the scores in questions 1–3.

Post-micturition dribble was also assessed using PMD volume, which was calculated with a paper test; at each visit, a double-folded paper towel was attached inside the patient's undergarments immediately after urination. After the patient had walked around for 1 min, PMD volume was estimated by

Fig. 1 Patient disposition.



trained researchers using the proportion of wetting on the paper towel.

Both assessments are newly developed and have been used in previous studies [7,23].

Outcome Measures

The primary outcome measure was difference in the change in total HPMDQ score between the tadalafil and the placebo groups at 12 weeks post-baseline.

Secondary outcome measures included differences in the changes in total HPMDQ score, in score for each individual HPMDQ question, and in PMD volume between the groups during the study period. In addition, IPSS and IIEF scores were recorded at each visit.

Statistical Analyses

The study was designed with 80% power and a 5% level of significance to detect a 30% difference in the percentage of patients whose total HPMDQ score decreased by ≥2 points, assuming a common standard deviation of 3.2 between the groups, which was based on the previous literature and our pilot study [23]. A total of 102 patients were enrolled, allowing for a drop-out rate of 20% during the study period because at least 41 patients per group were required for statistical analyses.

The main outcomes in the intention-to-treat population were analysed using a last post-baseline observation carried forward approach. The primary outcome measure was assessed with Pearson's chi-squared test. Secondary outcome measures were assessed using Pearson's chi-squared test and repeated-measures ANOVA with Bonferroni correction. Changes in PMD volume were analysed based on geometric means owing to their positively skewed distribution. Vital signs, physical examinations and medical history were described. AEs were compared using Fisher's exact test.

SPSS Windows version 21.0 (IBM Corp., Armonk, NY, USA) was used for all statistical analyses. All P values were two-sided and a P value of <0.05 was taken to indicate statistical significance.

Results

Patients

Of the 102 patients, 87 completed the follow-up at 12 weeks post-medication (44 and 43 from the tadalafil and the placebo groups, respectively; Fig. 1). The intention-to-treat population comprised 95 patients; 48 and 47 from the tadalafil and placebo groups, respectively.

Fifty-two patients (51.0%) experienced one PMD in three urinations, whereas 24 (23.5%) almost always experienced PMD. Furthermore, 38 patients (37.2%) felt moderate to severe frustration as a result of PMD, whereas two (2.0%) were not frustrated at all. All patients reported a poor QoL as a result of PMD. Only five patients (5.0%), however, were using pads in their daily lives.

Baseline characteristics, including IPSS, IIEF score, HPMDQ score and PMD volume, were similar in the two groups (Table 1).

Post-Micturition Dribble.

At 12 weeks post-baseline, the number of patients whose baseline total HPMDQ score decreased by ≥2 points was significantly higher in the tadalafil group (33 patients, 68.8%) than in the placebo group (15 patients, 31.9%; $P < 0.001$).

Figure 2 shows the changes in the mean total HPMDQ score during the study period. At 4 weeks post-baseline, total HPMDQ scores significantly decreased for both groups ($P < 0.001$ and $P = 0.012$ for the tadalafil and placebo groups, respectively). Afterwards, in the placebo group, the total HPMDQ score decrease was maintained up until 12 weeks post-baseline ($P = 0.743$), whereas, in the tadalafil group, the total HPMDQ score gradually decreased within the same time ($P = 0.001$). The decrease was significantly greater in the tadalafil group than in the placebo group ($P < 0.001$).

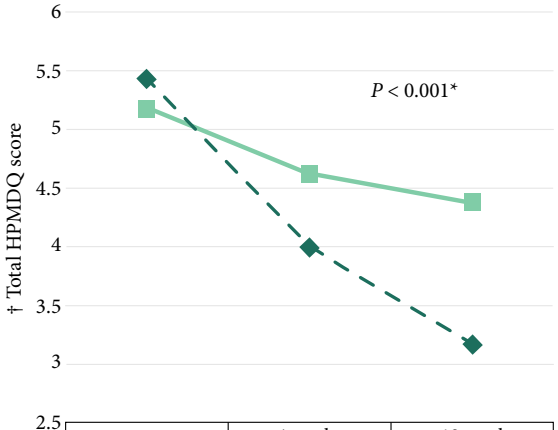
Figure 3 shows the proportion of patients whose baseline HPMDQ score for each question decreased by ≥1 point at 12 weeks post-baseline. The improvement in PMD frequency (Question 1) and QoL (Question 3) scores was significantly greater in the tadalafil group than in the placebo group ($P = 0.029$ and <0.001, respectively). Additionally, the improvement in bother (Question 2) scores tended to be greater in the tadalafil group than in the placebo group, but this was not statistically significant ($P = 0.259$). For the treatment response question (Question 4), two patients (4.2%) from the tadalafil group answered 'not at all', 14 (29.2%) answered 'slightly improved', 21 (43.8%) answered 'moderately improved', and 11 (22.9%) answered 'a lot improved', whereas seven (14.9%), 24 (51.1%), 11 (23.4%), and five (10.6%) patients from the placebo group provided these respective answers (Appendix S2). Significantly more

Table 1 Baseline demographic and clinical characteristics.

Variable	Placebo group (n = 51)	Tadalafil group (n = 51)	P
Age, years, mean (SD)	62.6 (6.5)	60.8 (7.3)	0.464*
Systemic blood pressure			
Systolic, mmHg, mean (SD)	124.5 (11.8)	126.3 (9.3)	0.488*
Diastolic, mmHg, mean (SD)	77.5 (10.0)	79.6 (8.1)	0.341*
Body mass index, kg/m^2, mean (SD)	24.3 (2.2)	24.6 (3.8)	0.739*
PSA, ng/mL, mean (SD)	1.2 (1.0)	1.2 (1.0)	0.779*
Total testosterone, ng/mL, mean (SD)	4.9 (1.5)	5.5 (2.8)	0.330*
Urine analysis			
Haematuria, n (%)	17 (33.3)	7 (13.7)	0.204†
Pyuria, n (%)	7 (13.7)	8 (15.7)	1.000†
Total IPSS, mean (SD)	14.4 (6.7)	14.7 (6.0)	0.781*
Storage IPSS, mean (SD)	5.5 (2.9)	5.8 (2.7)	0.573*
Voiding IPSS, mean (SD)	8.9 (4.8)	8.9 (4.7)	0.967*
Q_{max}, mL/s, mean (SD)	18.6 (9.7)	16.1 (7.8)	0.225*
PVR, mL, mean (SD)	20.8 (36.1)	21.3 (19.2)	0.946*
IIEF			
Erectile function, mean (SD)	15.5 (9.2)	15.4 (9.3)	0.966*
Orgasmic function, mean (SD)	5.1 (3.6)	5.6 (3.4)	0.466*
Sexual desire, mean (SD)	5.7 (2.1)	5.5 (2.0)	0.570*
Intercourse satisfaction, mean (SD)	5.5 (3.9)	5.9 (3.6)	0.601*
Overall satisfaction, mean (SD)	5.1 (2.0)	5.1 (2.1)	0.962*
Total HPMDQ	5.18 (2.01)	5.43 (1.82)	0.504*
Question 1 (frequency), mean (SD)	1.7 (0.8)	1.7 (0.8)	0.811*
Question 2 (bother), mean (SD)	1.5 (0.7)	1.5 (0.8)	0.691*
Question 3 (QoL), mean (SD)	2.0 (0.9)	2.2 (0.8)	0.158*
PMD volume, mL, mean (SD)	1.02 (0.19)	0.97 (0.20)	0.654‡

*HPMDQ, Hallym Post-Micturition Dribble Questionnaire; IIEF, International Index of Erectile Function; PMD, post-micturition dribble; PVR, post-void residual urine volume; Q_{max}, maximum urinary flow rate; QoL, quality of life. *Student's t-test. †Pearson's chi-squared test. ‡Geometric mean was used owing to the positively skewed distribution.*

Fig. 2 Changes of total Hallym Post-Micturition Dribble Questionnaire (HPMDQ), scores during the study period. *Repeated-measures ANOVA. †Total HPMDQ score was defined as the sum of the scores in question 1, 2 and 3 of HPMDQ.



	Baseline	4 weeks	12 weeks
Placebo	5.18 ± 2.01	4.62 ± 1.92	4.38 ± 2.07
Tadalafil	5.43 ± 1.82	4.00 ± 2.02	3.17 ± 2.15

patients in the tadalafil group reported a better treatment response than in the placebo group ($P = 0.013$).

Figure 4 shows the changes in the mean PMD volume during the study period. In the tadalafil group, the mean (range) PMD volume at baseline and at 12 weeks was 0.97 ± 0.20 (0.30–1.77) mL and 0.49 ± 0.26 (0–1.52) mL, respectively, with a mean decrease of 0.48 ± 0.46 mL (49.5%). PMD volumes significantly decreased from baseline at 4 weeks post-baseline ($P = 0.022$), and then gradually decreased up until 12 weeks post-baseline ($P = 0.034$). In the placebo group, the mean (range) PMD volume at baseline and at 12 weeks was 1.02 ± 0.19 (0.30–1.59) mL and 0.80 ± 0.20 (0.30–1.58) mL, respectively, with a mean decrease of 0.22 ± 0.28 mL (21.6%). Baseline PMD volumes did not decrease at 4 weeks post-baseline ($P = 0.081$), but did decrease at 12 weeks ($P = 0.041$). The decrease in PMD volume during the study period was significantly greater in the tadalafil group than in the placebo group ($P = 0.046$).

IPSS

In the tadalafil group, the total, storage and voiding IPSS decreased significantly from baseline at 12 weeks (mean decreases 5.69 ± 4.95, 2.67 ± 3.12, and 3.02 ± 3.93, respectively; $P < 0.001$, respectively). In the placebo group, these variables also significantly decreased within the same period (mean decreases 3.55 ± 5.69, 1.36 ± 2.60, and 2.19 ± 3.94, respectively; $P < 0.001$, $P = 0.001$, and $P < 0.001$, respectively). The decreases in total and storage IPSSs were significantly greater in the tadalafil group than in the placebo group ($P = 0.046$ and 0.022, respectively), but the decreases in voiding IPSS were not significantly different between the groups ($P = 0.398$; Appendix S3).

International Index of Erectile Function

In the tadalafil and placebo groups, the erectile function domain score significantly increased at 12 weeks post-baseline (mean increase = 5.76 ± 6.14 and 2.16 ± 4.58, respectively; $P < 0.001$ and $P = 0.013$, respectively); however, the increases in erectile function domain score were significantly greater in the tadalafil group than in the placebo group ($P = 0.010$; Appendix S4).

Fig. 3 The proportions of patients with reduction of baseline each question score of Hallym Post-Micturition Dribble Questionnaire by ≥1 point at 12 weeks. (a) question 1, (b) question 2, (c) question 3. *Pearson's chi-squared test. QoL, quality of life.

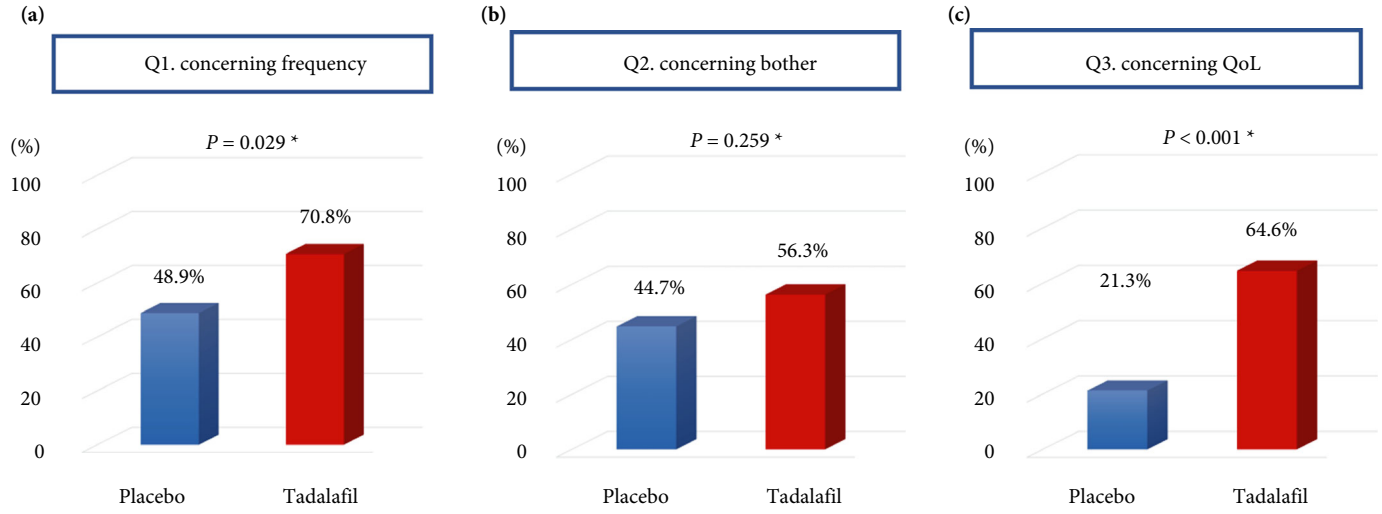
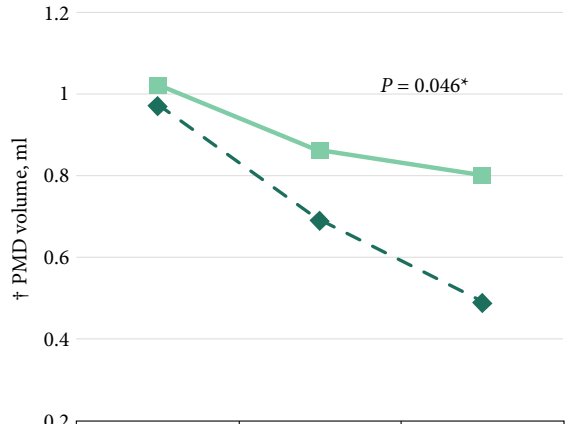


Fig. 4 Changes of volume of post-micturition dribble (PMD) during the study period. *Repeated-measures ANOVA. †Geometric mean was used owing to the positively skewed distribution.



	Baseline	4 weeks	12 weeks
Placebo	1.02 ± 0.19	0.86 ± 0.20	0.80 ± 0.20
Tadalafil	0.97 ± 0.20	0.69 ± 0.20	0.49 ± 0.26

In terms of orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction domains, scores tended to increase in both groups during the study period; however, no significant differences were found in the mean domain score increases between the two groups (P = 0.209, 0.543, 0.161, and 0.409, respectively).

Safety

Treatment-emergent AEs (TEAEs) in the tadalafil and placebo groups occurred in seven (13.7%) and three patients (5.9%), respectively (Table 2). No significant differences were found in the incidence of TEAEs between two groups (P = 0.318). Almost all TEAEs were mild, and no serious TEAEs were observed. Additionally, clinically significant changes in vital signs and physical examination findings were not observed.

Table 2 Treatment-emergent adverse events occurring in patients during the study period.

TEAE	Placebo group (n = 51)	Tadalafil group (n = 51)	P*
Overall, n (%)	3 (5.9)	7 (13.7)	0.318
Headache, n (%)	1 (2.0)	2 (3.9)	1.000
Dyspepsia, n (%)	–	1 (2.0)	1.000
Urticaria, n (%)	1 (2.0)	–	1.000
Hot flushing, n (%)	1 (2.0)	2 (3.9)	1.000
Myalgia, n (%)	–	2 (3.9)	0.495

*TEAE, treatment-emergent adverse event. *Fisher's exact test.*

Discussion

The present study demonstrates that taking tadalafil 5 mg once daily is effective in treating storage LUTS and ED, similarly to recent studies [1]. This treatment also decreased PMD volume and symptom severity in our patients with LUTS. To our knowledge, this is the first study to suggest that tadalafil may be effective in treating PMD.

Recent epidemiological studies suggest that PMD may be one of the most common LUTS in men [8–10]. The population-based Tampere Ageing Male Urologic Study (TAMUS), which involved > 7000 men, revealed a PMD prevalence rate of 58.1% [9]. The internet-based Epidemiology of LUTS study, which involved > 14 000 men, reported an overall prevalence rate of 46.2% [10]. It is also suggested that PMD might be one of the most bothersome LUTS for men [8,11,12]. In a population-based study involving > 1700 men, PMD was defined as a moderate or severe bother symptom [11]. In the TAMUS study, men aged 30–40 years experienced the most bother from PMD [12]. Furthermore, post-micturition symptoms, including PMD, commonly overlap with other LUTS [8], thereby causing further aggravation. Even with this recent evidence, PMD seems to be outside of physicians' interests owing to standard beliefs regarding PMD [3–7], and diagnostic tools and treatment options for PMD are currently lacking [7,16].

In men, PMD occurs because of urine residue in the bulbar urethra after urination [16]; however, the mechanism through which residual urine remains after urination is not fully understood. One of the main proposed mechanisms is that bulbocavernosus muscle weakness results in the muscle's failure to contract at the end of urination, leading to residual urine [13]. Consequently, providing bulbar urethral massages immediately after urination and pelvic floor muscle exercises to compensate for this weakness is a widely used method for relieving PMD [15,16]. Another possible mechanism is a poor milk-back of urine into the bladder at the end of urination as a result of incompetent external urethral sphincter or bladder neck obstruction [13].

To our knowledge, only one study has assessed the efficacy of PDE-5 inhibitors in treating PMD in a randomized controlled trial [23]. Ko et al. [23] assessed the effects of taking udenafil 75 mg, a PDE-5 inhibitor, once daily, for 12 weeks, on PMD in 138 patients. As in present study, the authors used the HPMDQ and paper test to assess the severity of PMD. They reported that PMD was improved in 61.7% patients in the udenafil group, whereas in 26.9% patients PMD was improved in the placebo group, suggesting that taking udenafil 75 mg once daily may be an effective PMD treatment; however, more patients were lost to follow-up than the authors initially expected. Moreover, patient losses attributable to AEs and withdrawal from the study were

greater in the udenafil group than in the placebo group. These limitations may lower the statistical power of the results and lead to study bias.

The present study has several advantages over the study by Ko et al., even though their results were similar. Firstly, our study had enough power for statistical analyses. Only seven (13.7%) and eight (15.7%) patients from the tadalafil and placebo groups, respectively, dropped out during the study period. Secondly, various PMD aspects were assessed by each question of HPMDQ and PMD volume. In the present study, tadalafil improved PMD frequency, discomfort, PMD volume and patients' QoL. Furthermore, 66.7% of patients reported moderate or a lot of improvement in PMD symptoms after taking tadalafil, whereas only 4.2% of patients reported that tadalafil was not effective at all. Finally, tadalafil can be easily used for PMD treatment, because tadalafil, unlike udenafil, has been globally licensed for LUTS treatment [1].

The mechanism through which PDE-5 inhibitors treat PMD is not known. One hypothesis is that PDE-5 inhibitors strengthen the urethro-corporocavernosal reflex. On urination, sinusoidal corpora muscle relaxation and cavernosa muscle contraction are suggested to be mediated through the urethro-corporocavernosal reflex [19]. These changes seem to cause a mild degree of penile tumescence and stretch, which can assist in urinary flow and may allow urine to be easily discharged, leading to relieving PMD [19,24,25]. Other hypotheses focus on the corpus spongiosum and pelvic floor muscles, including the bulbocavernosus and ischiocavernosus muscles. PDE-5 inhibitors act on the corpus spongiosum as well as the corpus cavernosum to restore elasticity to the sinusoids, which may correct dilated bulbar urethrae [23]. The bulbocavernosus and ischiocavernosus muscles, which are closely associated with PMD, contract to prevent blood from leaking during erections [26]. Like pelvic floor muscle exercises, chronic treatment with PDE-5 inhibitors may help strengthen the bulbocavernosus and ischiocavernosus muscles.

The IPSS questionnaire is the most widely used questionnaire for evaluating LUTS [1]. However, PMD cannot be assessed using the IPSS questionnaire because there are no questions concerning PMD, therefore, most studies use the Danish Prostatic Symptom Score (DAN-PSS-1) questionnaire or other questionnaires developed by researchers to assess PMD. The DAN-PSS-1 questionnaire cannot evaluate PMD frequency and PMD-related QoL, although it can evaluate PMD symptom severity and PMD-related bother [27]. To assess PMD in detail we used the HPMDQ, which was modified from validated questionnaires including the IPSS, Premature Ejaculation Diagnostic Tool, DAN-PSS-1, and Patients' Global Impression of Change scale, based on the standardization of terminology of LUTS by the ICS [2,7]. The HPMDQ has been introduced in scientific peer-reviewed journals [7,23]; however, further studies are needed to determine the clinical usefulness of the HPMDQ.

Few studies have quantitatively measured PMD volume. Recently, Yang et al. [7] assessed PMD volume in 205 men aged ≥40 years with LUTS. They showed that PMD volume in the men without ED was ~1.2 mL, while it was ~2.1 mL in men with ED [7]. Similarly, PMD volume at baseline was ~1.0 mL in the present study, which is smaller than would be expected empirically. After taking tadalafil 5 mg once daily, the PMD volume decreased by 49.5%.

The present study has some limitations. Firstly, the HPMDQ has not been validated for assessing PMD, but it has been introduced in scientific peer-reviewed journals [7,23]. Secondly, all patients included in the present study had an IPSS ≥8, representing moderate and severe LUTSs. The results cannot be directly applied, therefore, to patients with mild LUTS. Thirdly, the patient blinding might have not been properly performed because of the unique effects and AEs of tadalafil, although this concern has always been an issue in studies using PDE-5 inhibitors. Finally, all patients included in the study were Korean and the effect of tadalafil on PMD may differ when applied to other ethnicities. Recent evidence suggests, however, that Asian men, including Korean men, experience similar LUTS-related and ED-related effects and AEs to Western men after taking tadalafil once daily [28,29].

In conclusion, taking tadalafil 5 mg once daily reduced PMD symptom severity and PMD volume in men with PMD and other LUTS more effectively than placebo. The present results also show that tadalafil does not induce serious TEAEs. These results suggest that taking tadalafil 5 mg once daily may be an effective and well-tolerated PMD treatment, and suggest that PDE-5 inhibitors have a potential role in treating PMD.

Acknowledgements

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Conflicts of Interest

This study was approved by the Korean Ministry of Food and Drug Safety (KMFDS).

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Abbreviations: AE, adverse event; DAN-PSS-1, Danish Prostatic Symptom Score; ED, erectile dysfunction; IIEF, International Index of Erectile Function; HPMDQ, Hallym Post-Micturition Dribble Questionnaire; PDE, phosphodiesterase; PMD, post-micturition dribble; QoL, quality of life; TAMUS, Tampere Ageing Male Urologic Study; TEAE, treatment-emergent adverse event.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. The Hallym Post-Micturition Dribble Questionnaire.
Appendix S2. The proportions of answers to question 4 (response to treatment) of Hallym Post-Micturition Dribble Questionnaire at 12 weeks.
Appendix S3. Changes in IPSS during the study period.
Appendix S4. Changes in International Index of Erectile Function during the study period.

