



Original Research Article

Comparative Effectiveness of "On-Demand" vs. "Scheduled Bi-weekly" Tadalafil in Hemodialysis Patients: A Real-World Retrospective Analysis

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Abstract: **Objective:** To compare the effectiveness, tolerability, and treatment adherence of on-demand versus scheduled bi-weekly tadalafil in male patients undergoing maintenance hemodialysis with erectile dysfunction. **Methods:** This retrospective comparative study was conducted at Faisalabad Medical university Allied Hospital 1 from June 2024 to June 2025 included 65 male patients receiving maintenance hemodialysis with a documented diagnosis of erectile dysfunction. Patients were categorized according to tadalafil prescribing pattern into an on-demand group (n = 33) and a scheduled bi-weekly group (n = 32). Demographic and clinical characteristics, duration of hemodialysis, comorbidities, erectile function scores, sexual satisfaction, quality-of-life indicators, treatment adherence, and adverse events were extracted from medical records. **Results:** Among 65 male hemodialysis patients, 33 received on-demand tadalafil and 32 received scheduled bi-weekly tadalafil. Baseline characteristics were comparable, with mean ages of 49.6 ± 8.7 and 51.2 ± 9.1 years and dialysis duration of 3.8 ± 1.6 and 4.1 ± 1.9 years, respectively. Erectile function improved in both groups; however, the scheduled bi-weekly group showed greater improvement, with scores increasing from 11.1 ± 3.4 to 19.9 ± 3.8 compared with 11.4 ± 3.1 to 16.8 ± 3.6 in the on-demand group. Sexual satisfaction (81.3% vs. 63.6%), quality-of-life improvement (78.1% vs. 57.6%), and treatment adherence (84.4% vs. 66.7%) were higher with scheduled dosing. **Conclusion:** Both on-demand and scheduled bi-weekly tadalafil are effective in managing erectile dysfunction in hemodialysis patients. Scheduled bi-weekly tadalafil offers superior improvements in erectile function, sexual satisfaction, quality of life, and treatment adherence without compromising safety, supporting its consideration as a preferred dosing strategy in this population.

Keywords: Dysfunction, Hemodialysis, Patients, Effective, Management, Tadalafil.

INTRODUCTION

Erectile dysfunction (ED) is very prevalent in men under maintenance hemodialysis and can be attributed to an intricate interaction of organic,

psychological, and treatment-related factors [1]. Chronic kidney disease (CKD) and end-stage renal disease (ESRD) are linked to accelerated atherosclerosis, endothelial dysfunction, autonomic

neuropathy, chronic inflammation, oxidative stress, anemia, and calcium-phosphate metabolic disturbances, which compromise normal erectile physiology [2]. Moreover, hormonal imbalances, including decreased levels of testosterone, abnormal secretion of the luteinizing hormone, and hyperprolactinemia, also contribute to sexual dysfunction in this group of people [3]. In addition to biological processes, the psychosocial load of long-term dialysis, such as depression, anxiety, body image issues, relationship stress, and decreased self-confidence, makes a significant contribution to the emergence and maintenance of ED [4]. The effects of erectile dysfunction on hemodialysis patients go far beyond sexual performance. Several studies have established that ED is closely related to lower health-related quality of life, low emotional well-being, lower levels of treatment satisfaction, and disturbed interpersonal relationships [5]. Sexual health is an unmet need in many patients and is often not addressed during their usual nephrology visits, whether due to time limits or cultural issues or the notion that sexual function is a secondary issue relative to survival and dialysis adequacy. But according to the patient-centered care approach, ED is also being identified as a crucial element of the holistic care of ESRD [6,7].

The phosphodiesterase-5 (PDE5) inhibitors have revolutionized the treatment of the erectile dysfunction and the therapy is regarded as first line treatment in most groups of patients including the chronic kidney disease patients [8]. Specifically, the pharmacokinetics of Tadalafil make it a choice of drug to use in patients under dialysis. It has a long half-life that enables it to have a long therapeutic activity that provides flexibility in the on-demand and schedule dosage regimens [9]. Notably, tadalafil is majorly hepatically metabolized with little excretion during hemodialysis, hence the volume of dose changes is comparatively easy to alter in relation to renally excreted drugs [10]. However, cardiovascular comorbidities, regular antihypertensive usage, and prone to intradialytic hypotension are the causes that make dosing approaches in this high-risk population an issue of concern [11]. Two primary patterns of tadalafil prescriptions are frequently used in the daily clinical practice: on-demand dosing in the presence of the expected sexual activity, and regular, planned dosing without reference to the time of sexual activity [12]. Both methods have possible benefits and drawbacks especially when using hemodialysis. On-demand dosing can decrease total drug exposure, decrease pill burden, reduce the effects of the medication and could provide patients with more control to use drugs [13]. This plan can be very attractive to people who have a low sexual activity or have issues with medication side effects. On the other hand, bi-weekly dosing might offer greater stability in blood concentrations of the drug, less anxiety about

timing of sexual activity, better spontaneity and possibly increased sexual confidence and relationship satisfaction generally [14].

Objective

To compare the effectiveness, tolerability, and treatment adherence of on-demand versus scheduled bi-weekly tadalafil in male patients undergoing maintenance hemodialysis with erectile dysfunction.

METHODOLOGY

This was a **retrospective comparative study** conducted at Faisalabad Medical university Allied Hospital 1 from June 2024 to June 2025. The study included a total count of 65 male patients who were on maintenance hemodialysis who had been diagnosed with erectile dysfunction. Review of the available eligible patient records that fulfilled the inclusion criteria was used as a non-probability consecutive sampling. The inclusion criteria included that the patients had to be males aged 18 years or above, on maintenance hemodialysis with a minimum of three months and with a known diagnosis of erectile dysfunction. The study only considered patients who had been placed on tadalafil either on-demand or on a scheduled bi-weekly regimen but with complete medical history whose follow-ups could be reviewed. Patients were not included in case they had a history of unstable angina, fresh myocardial infarction, or severe heart failure, or were taking concomitant nitrate therapy. Other exclusion criteria were a severe hepatic impairment, known hypersensitivity to phosphodiesterase-5 inhibitors, incomplete medical records, and a history of a known psychiatric disease that could create difficulties in the correct evaluation of sexual functioning.

Data Collection

A structured data extraction form was used to extract data in medical records. The variables that were measured were age, duration of hemodialysis, comorbidity (diabetes mellitus, hypertension, and cardiovascular disease), dialysis vintage, co-prescribed drugs, and tadalafil dosing schedule. The prescribing pattern of tadalafil that was recorded in the medical record of patients was used to group them into two groups. The patients in Group A were on an on-demand basis of tadalafil, which was taken before expected sexual activity. Group B encompassed the patients who had been given tadalafil based on a regular bi-weekly dosage regardless of the time when they are sexually active. The outcome measures of erectile functions were through documented erectile dysfunction assessment scores. Patient-reported sexual satisfaction and quality-of-life indicators, as well as, adverse events that included headache, dizziness, hypotension, dyspepsia, and back pain were also checked. The main result was that the erectile activity increased according to the recorded scores on

assessment. The group of secondary outcomes consisted of patient-reported sexual satisfaction, quality-of-life, treatment adherence, and adverse event frequency.

Data Analysis

Data were analyzed using SPSS version 2.0. Continuous variables were summarized as mean $\pm$ standard deviation, while categorical variables were expressed as frequencies and percentages. Comparative analysis between the two groups was performed using appropriate statistical tests, and a p-value <0.05 was considered statistically significant.

RESULTS

Data were collected from 65 patients, patients in the on-demand tadalafil group had a mean age of 49.6 ± 8.7 years, while those in the scheduled bi-weekly group had a mean age of 51.2 ± 9.1 years ($p = 0.46$). The mean duration of hemodialysis was 3.8 ± 1.6 years in the on-demand group and 4.1 ± 1.9 years in the scheduled group ($p = 0.52$). Diabetes mellitus was present in 19 patients (57.6%) receiving on-demand tadalafil and 18 patients (56.3%) in the scheduled group ($p = 0.91$). Hypertension was observed in 27 patients (81.8%) in the on-demand group and 26 patients (81.3%) in the scheduled group ($p = 0.96$). Cardiovascular disease was documented in 11 patients (33.3%) receiving on-demand tadalafil compared with 12 patients (37.5%) in the scheduled bi-weekly group ($p = 0.72$).

Table 1. Baseline Demographic and Clinical Characteristics of Study Participants (N = 65)

Variable	On-Demand Tadalafil (n = 33)	Scheduled Bi-weekly Tadalafil (n = 32)	p-value
Age (years), mean $\pm$ SD	49.6 ± 8.7	51.2 ± 9.1	0.46
Duration of Hemodialysis (years), mean $\pm$ SD	3.8 ± 1.6	4.1 ± 1.9	0.52
Diabetes Mellitus, n (%)	19 (57.6)	18 (56.3)	0.91
Hypertension, n (%)	27 (81.8)	26 (81.3)	0.96
Cardiovascular Disease, n (%)	11 (33.3)	12 (37.5)	0.72
Smoking History, n (%)	9 (27.3)	10 (31.3)	0.71

At baseline, mean erectile function scores were low and comparable between groups, measuring 11.4 ± 3.1 in the on-demand group and 11.1 ± 3.4 in the scheduled bi-weekly group ($p = 0.74$). At follow-up, both groups demonstrated improvement; however, patients receiving scheduled bi-weekly tadalafil achieved a significantly higher mean score of 19.9 ± 3.8 compared to 16.8 ± 3.6 in the on-demand group ($p = 0.002$). The mean improvement from baseline was significantly greater in the scheduled group, with an increase of 8.8 ± 2.6 points, compared to an increase of 5.4 ± 2.1 points in the on-demand group ($p < 0.001$).

Table 2. Erectile Function Scores Before and After Treatment

Erectile Function Score	On-Demand Tadalafil (n = 33)	Scheduled Bi-weekly Tadalafil (n = 32)	p-value
Baseline Score, mean $\pm$ SD	11.4 ± 3.1	11.1 ± 3.4	0.74
Follow-up Score, mean $\pm$ SD	16.8 ± 3.6	19.9 ± 3.8	0.002
Mean Change from Baseline	$+5.4 \pm 2.1$	$+8.8 \pm 2.6$	<0.001

Sexual satisfaction improved in 21 patients (63.6%) receiving on-demand tadalafil and in 26 patients (81.3%) receiving scheduled bi-weekly tadalafil ($p = 0.04$). Improvement in sexual health-related quality of life was reported by 19 patients (57.6%) in the on-demand group and 25 patients (78.1%) in the scheduled group ($p = 0.03$). Good treatment adherence was documented in 22 patients (66.7%) using on-demand tadalafil, compared with 27 patients (84.4%) in the scheduled bi-weekly group ($p = 0.04$). Missed or irregular dosing was more common in the on-demand group, affecting 11 patients (33.3%), compared to 5 patients (15.6%) in the scheduled group ($p = 0.04$).

Table 3. Sexual Satisfaction, Quality of Life, and Treatment Adherence

Outcome Variable	On-Demand Tadalafil (n = 33)	Scheduled Bi-weekly Tadalafil (n = 32)	p-value
Improved Sexual Satisfaction, n (%)	21 (63.6)	26 (81.3)	0.04
Improved Sexual-related QoL, n (%)	19 (57.6)	25 (78.1)	0.03
Good Treatment	22 (66.7)	27 (84.4)	0.04

Adherence, n (%)			
Missed / Irregular Doses, n (%)	11 (33.3)	5 (15.6)	0.04

Headache was reported in 5 patients (15.2%) in the on-demand group and 8 patients (25.0%) in the scheduled bi-weekly group ($p = 0.32$). Dyspepsia occurred in 4 patients (12.1%) receiving on-demand tadalafil and 7 patients (21.9%) receiving scheduled therapy ($p = 0.29$). Flushing was reported in 3 patients (9.1%) in the on-demand group and 6 patients (18.8%) in the scheduled group ($p = 0.24$). Dizziness was documented in 2 patients (6.1%) using on-demand tadalafil and 5 patients (15.6%) in the scheduled bi-weekly group ($p = 0.21$). Symptomatic hypotension was infrequent, occurring in 1 patient (3.0%) in the on-demand group and 2 patients (6.3%) in the scheduled group ($p = 0.52$).

Table 4. Adverse Events Associated with Tadalafil Use

Adverse Event	On-Demand Tadalafil (n = 33)	Scheduled Bi-weekly Tadalafil (n = 32)	p-value
Headache, n (%)	5 (15.2)	8 (25.0)	0.32
Dyspepsia, n (%)	4 (12.1)	7 (21.9)	0.29
Flushing, n (%)	3 (9.1)	6 (18.8)	0.24
Dizziness, n (%)	2 (6.1)	5 (15.6)	0.21
Symptomatic Hypotension, n (%)	1 (3.0)	2 (6.3)	0.52
Serious Adverse Events	0	0	—

DISCUSSION

The current retrospective analysis has provided comparisons of the on-demand and scheduled bi-weekly tadalafil regimens in men undergoing regular hemodialysis maintenance and discovered that both regimens were viable in enhancing the erectile functions, and scheduled bi-weekly regimen showed better overall results. The complex nature of erectile dysfunction of hemodialysis patients is the result of the interplay between vascular disease, impaired endothelial functioning, hormonal imbalance, and psychosocial stressors, and thus selection of treatment is of paramount importance in this group of patients. The two groups were very similar in terms of baseline demographic and clinical variables, age, duration of hemodialysis and diabetes, hypertension, and cardiovascular disease. This comparability implies that most of the differences in the results could have been explained by the tadalafil dosing plan and not due to the confounding factors in the baseline [15]. The erectile performance was improved in both groups, but more significantly in patients who were treated by scheduled bi-weekly intake of tadalafil. The greater mean increase in the scores of erectile functioning in this group indicates that the regular dosing can offer a longer and more pharmacologic activity and endothelial responsiveness than episodic dosing. Earlier studies have also indicated the higher consistency of the erectile responsiveness to scheduled regimens of tadalafil in chronic disease groups [16].

There were also better sexual satisfaction and sexual health-related quality-of-life outcomes in the scheduled bi-weekly group. A high percentage of patients had improved patient satisfaction and quality-of-life indicators than patients who used on-demand

therapy. This could be attributed to a lower degree of performance anxiety and increased spontaneity with scheduled dosing. By eliminating the necessity of the exact time of the medication intake, which is typical of the patients of hemodialysis, the lack of frequent fatigue and bodily restrictions will have a positive impact on the psychological comfort and interpersonal relationships of the patient [17]. Past studies have repeatedly demonstrated that those treatment programs that permit spontaneity are more likely to result in increased levels of satisfaction and improved perceived well-being of sex. The compliance with the treatment was significantly better in the group of patients who were given the bi-weekly tadalafil on schedule. Planned dosing can be smoother to fit the lifestyle of patients already used to regular dialysis routines, but on-demand use would depend on prediction and opportunity, which can be irregular [18]. Clinically, it is also significant to promote better adherence because it has a direct impact on the efficacy of treatment and patient satisfaction. Past studies in chronic illness environments have also shown that more people would be able to adhere to a stable dosage schedule than to as-needed treatment [19]. The two tadalafil therapies were relatively tolerable. Mild adverse reactions that included headache, dyspepsia, flushing, and dizziness were slightly more common in the scheduled bi-weekly group, but the occurrences were self-limiting, and no one stopped treatment. Notably, symptomatic hypotension was not very common in both groups, which raises a major concern about safety in hemodialysis patients [20,21]. Such results are in line with other studies that tadalafil is safe to use in patients receiving maintenance hemodialysis, provided that proper precautions are observed. One

should note a number of limitations. The study can be limited in its ability to provide cause-and-effect relationships due to the retrospective nature of the study, and the relatively small size of the sample can decrease statistical power. Also, the medical records dependency can have resulted in underreporting of adverse events or subjective outcomes. There was no long-term outcome or partner-report scale. Despite these shortcomings, the research gives practical and real-world evidence that can be used in the daily clinical practice.

CONCLUSION

It is concluded that both on-demand and scheduled bi-weekly tadalafil regimens are effective in improving erectile function in male patients undergoing maintenance hemodialysis. However, scheduled bi-weekly tadalafil demonstrated superior improvement in erectile function scores, sexual satisfaction, quality-of-life indicators, and treatment adherence, with an acceptable and comparable safety profile. These findings suggest that a scheduled bi-weekly dosing strategy may be a more practical and effective option for managing erectile dysfunction in hemodialysis patients, particularly in those who prefer greater spontaneity and structured medication routines.

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