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Original Research Article

PENILE HEMODYNAMIC RESPONSE TO PHOSPHODIESTERASE TYPE V INHIBITORS AFTER CAVERNOSAL SPARING INFLATABLE PENILE PROSTHESIS IMPLANTATION A PROSPECTIVE IMPLANTATION: A PROSPECTIVE RANDOMIZED OPEN-BLINDED END-POINT (PROBE) STUDY

ALI J[1], BANGASH MH[*2], HAMZA M[3], SHAHID M[3], TARIQ F[4], HAMMAD M[5], ASIM F[6]

[1]*ITTEHAD Medical & Diagnostic Complex Karak/type D Hospital Latamber Karak, Pakistan*
[2]*Department of Urology, Mardan Medical Complex Mardan, Pakistan*
[3]*Department of Pharmacy, University of The Punjab Lahore, Pakistan*
[4]*Riphah International University Lahore, Pakistan*
[5]*Faculty of Pharmaceutical Sciences, Shifa College of Pharmaceutical Sciences Shifa Tameer-e-millat University, Islamabad, Pakistan/ Faculty of Management Sciences, School of Business and Management, Riphah International University, Islamabad, Pakistan*
[6]*Department of Pharmacy, The University of Lahore (UOL), Lahore, Pakistan*
**Corresponding author`s email address:* jamrab15@gmail.com

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Abstract: *Oral phosphodiesterase type V inhibitors (PDE5i), such as sildenafil (Viagra), tadalafil (Cialis), and vardenafil (Levitra), have become the first-line pharmacological treatment for most cases of ED. Objective: The main objective of the study is to find the penile hemodynamic response to phosphodiesterase type v inhibitors after cavernosal-sparing inflatable penile prosthesis implantation prospective implantation.* ***Objective:*** *To evaluate the penile hemodynamic response, erectile function, and patient satisfaction associated with PDE5i therapy after cavernosal sparing IPP implantation.* ***Methods:*** *This Prospective Randomized Open-Blinded End-Point (PROBE) was conducted at Mardan Medical Complex Peshawar from June 2024 to December 2024. Data were collected from 25 male patients. Patients underwent cavernosal sparing IPP implantation and were randomly assigned to two groups: Group A (n=13) received PDE5i postoperatively, while Group B (n=12) received a placebo. Hemodynamic measurements using Doppler ultrasound were conducted at baseline, 6 weeks post-surgery, and the 6-month follow-up. International Index of Erectile Function (IIEF) scores and patient satisfaction were also assessed.* ***Results:*** *Group A showed significant improvements in penile hemodynamics compared to Group B, with a higher peak systolic velocity (PSV: 38.7 ± 6.1 cm/s vs. 24.5 ± 5.3 cm/s), reduced end-diastolic velocity (EDV: 4.8 ± 2.3 cm/s vs. 8.9 ± 2.4 cm/s), and improved resistance index (RI: 0.88 ± 0.07 vs. 0.64 ± 0.09) at 6 months. Group A also reported higher IIEF scores and greater satisfaction with sexual function.* ***Conclusions:*** *Cavernosal sparing IPP implantation combined with PDE5i therapy significantly improves penile hemodynamics, erectile function, and patient satisfaction compared to IPP alone. This dual approach offers enhanced outcomes for managing severe ED.*

Keywords: Phosphodiesterase Inhibitors Penile Erection Prostheses and Implants Hemodynamics Erectile Dysfunction

Introduction

Oral phosphodiesterase type V inhibitors (PDE5i), such as sildenafil (Viagra), tadalafil (Cialis), and vardenafil (Levitra), have become the first-line pharmacological treatment for most cases of ED (1). These drugs exert their action by suppressing PDE5 thereby leading to enhanced concentration of cyclic guanosine monophosphate (cGMP). This biochemical reaction enables smooth muscle relaxation in the corpus cavernosum resulting in enhanced penile blood flow during sexual stimulation and erection (2, 3). Nevertheless, it should be noted that, even with ePDE5i, some patient groups such as patients with severe ED or structural abnormalities associated with conditions such as Peyronie's disease or after radical prostatectomy may not gain optimum results (4). It is in such circumstances that more aggressive approaches, including the placement of the inflatable penile prosthesis (IPP), are contemplated. IPP implantation has also been proven to be a safe and long-term treatment in men with refractory ED. The operations of the prosthesis are such that a reservoir is used to allow fluid to be shifted into inflatable cylinders laid within the penis resulting in an erection (5). This enables men to have erections which are not in any way relying on their natural erectile tissues. However, conventional surgery for IPP damages or excises portions of the cavernosal tissue and hence patients are left dependent on the prosthesis to achieve erection post-surgery and pharmacological erections are out of the question (6). For the past years, newer generations of prosthetic surgery have strived to come up with methods that can be integrated into an IPP that would spare as much of the native tissue as possible (7). The necessity of such an approach is based on the preservation of anatomical architecture and functions of the corpus cavernosum enabling the patients to undergo the effects of PDE5 inhibitors after the implantation of the prosthesis. The concept is that, by preserving the cavernosal tissue patients might have a better haemodynamic response to PDE5i which may prove useful in their overall erectile function and satisfaction after implant surgery (8). However, as with most theoretical advantages of cavernosal-sparing IPP

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implantation, there is sparse information about the long-term results and the degree by which they enable preserved or improved response to PDE5 inhibitors (9). Previous investigations concerning IPP largely concentrated on mechanical permanency, patient satisfaction and the rate of complications, and to this date, no studies have investigated the relationship between IPP and PDE5 inhibitors. Knowledge of the penile hemodynamic response to PDE5i in patients with cavernosal-sparing IPP could be clinically relevant in providing us with clues toward the best therapeutic management of any given patient with complex or refractory ED (10). Cavernosal artery injury is possible during corporal dilatation in the course of penile prosthesis implantation procedures. This would deny the corpora its normal blood supply and make the corporae be supplied by the dorsal and bulbourethral arteries only (11). They could then probably have been compressed by these tight dressings applied postoperatively against the underlying cylinders resulting in distal ischemia. Other species of arteries involved in erectile mechanisms include cavernosal arteries which also have an indirect involvement in glandular tumescence. The glans penis which comprises the bulb and acquired part of the penis receives its blood supply from the dorsal arteries and the terminal prevalar branches of the spongiosal arteries. Dorsal and circumflex veins constrict during glandular tumescence probably due to the compression from the sideward-directed corpora of the cavernosal and the elastic connective tissues, supplied by the cavernosal arteries. Therefore, the absence of glans engorgement may be one of the indirect complications of cavernosal artery injury during penile prosthesis implantation (12). Further, several patients lost subjective penile tumescence and experienced a reduction in penile girth as evidenced through corpora tissue injury. The main objective of the study is to find the penile hemodynamic response to phosphodiesterase type v inhibitors after cavernosal-sparing inflatable penile prosthesis implantation prospective implantation.

Methodology

This Prospective Randomized Open-Blinded End-Point (PROBE) was conducted at Mardan Medical Complex from June 2024 to December 2024. Data were collected from 25 male patients. Male patients aged between 40 and 75 years.Diagnosis of ED lasting more than 12 months, unresponsive to PDE5 inhibitors.Candidates for IPP due to severe ED caused by various etiologies (vascular, post-prostatectomy, Peyronie's disease, or diabetes).Any contraindications to PDE5 inhibitors, such as severe cardiovascular disease or concurrent use of nitrates.Prior penile surgery other than IPP.Psychological or neurological disorders affecting sexual function. Patients were randomly assigned to two groups: Group A (n=13): received PDE5 inhibitors post-operatively.Group B (n=12): received a placebo as a control. The randomization was performed using a computer-generated random sequence to ensure equal distribution across both groups. Blinding was applied only to the endpoint evaluations; while both patients and the surgical team were aware of the group assignment (open phase), the investigators assessing the hemodynamic outcomes were blinded to the treatment groups. All patients underwent cavernosal sparing IPP implantation, performed by a single experienced urologist to ensure consistency in technique. The procedure aimed to minimize trauma to the cavernosal tissue, preserving as much of the erectile tissue as possible to allow for potential pharmacological response to PDE5 inhibitors. The prosthesis used was the three-piece inflatable penile prosthesis, selected for its high success rate and patient satisfaction. The cylinders were inserted into the corpora cavernosa with careful attention to minimizing damage to the surrounding cavernosal tissue. All patients received post-operative care and education on using the prosthesis. Following a 6-week post-operative recovery period, during which no pharmacological treatments were administered, patients in Group A began taking a PDE5 inhibitor (sildenafil 50 mg) on-demand, at least 30 minutes before sexual activity. Patients in Group B received a placebo under the same conditions. The primary outcome was the penile hemodynamic response to PDE5 inhibitors. Hemodynamic measurements were performed using Doppler ultrasound at baseline (pre-surgery), 6 weeks post-surgery (before initiating PDE5 inhibitors or placebo), and at the end of the 6-month follow-up period. Data were analyzed using SPSS software (v.25). Continuous variables, such as Doppler ultrasound measurements, were analyzed using paired t-tests and analysis of variance (ANOVA) to compare pre-and post-operative values between the two groups. Categorical variables, such as patient satisfaction and complications, were compared using the chi-square test.

Result

Table 1 presents the patients' baseline characteristics and preoperative measurements, including age, BMI, duration of erectile dysfunction (ED), comorbid conditions such as diabetes and hypertension, and preoperative penile hemodynamic and erectile function scores. Both groups, Group A (PDE5i) and Group B (Placebo), had comparable baseline values, ensuring a balanced comparison. Key metrics like age (58.5 ± 8.7 years) and preoperative PSV (28.5 ± 5.2 cm/s) reflect a homogenous study population. Table 2 summarizes penile hemodynamic parameters assessed via Doppler ultrasound pre-surgery, at six weeks post-surgery, and at six months post-surgery. Group A (PDE5i) demonstrated significant improvements in Peak Systolic Velocity (PSV), End-Diastolic Velocity (EDV), and Resistance Index (RI) compared to baseline and the placebo group, indicating better penile vascular health ($p < 0.05$). Table 3 highlights improvements in the International Index of Erectile Function (IIEF) scores across different domains, showing significant gains in erectile function, intercourse satisfaction, orgasmic function, and overall satisfaction in Group A at six months ($p < 0.05$). Table 4 reports patient satisfaction scores using the Visual Analog Scale (VAS), with Group A (PDE5i) achieving significantly higher satisfaction (8.3 ± 1.1) compared to Group B (5.7 ± 1.6). Table 5 examines sexual activity metrics, including average monthly sexual encounters and prosthesis or PDE5i use. Group A reported higher natural erections (45%) and average sexual encounters (5.1 per month) compared to Group B, where all participants relied on prostheses. These findings underscore the efficacy of PDE5 inhibitors in enhancing sexual function and satisfaction post-surgery.

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Table 1: Patients' Characteristics and Preoperative Baseline Measurements

Characteristic	Group A (PDE5i) (n=13)	Group B (Placebo) (n=12)	Total (n=25)
Age (years)	59.1 ± 7.5 (45–72)	57.8 ± 9.2 (44–73)	58.5 ± 8.7 (44–73)
Body Mass Index (BMI)	26.5 ± 3.1 (22.3–31.4)	27.2 ± 2.9 (23.1–32.0)	26.8 ± 3.0 (22.3–32.0)
Duration of ED (years)	6.8 ± 2.2 (3–10)	7.1 ± 2.6 (3–12)	6.9 ± 2.4 (3–12)
Diabetes (%)	6 (46%)	5 (42%)	11 (44%)
Hypertension (%)	5 (38%)	4 (33%)	9 (36%)
Preoperative PSV (cm/s)	28.9 ± 4.8 (20.1–34.7)	28.1 ± 5.3 (19.6–33.9)	28.5 ± 5.2 (19.6–34.7)
Preoperative EDV (cm/s)	7.3 ± 2.0 (4.1–10.2)	7.6 ± 2.2 (4.0–10.8)	7.5 ± 2.1 (4.0–10.8)
Preoperative IIEF Score	12.6 ± 3.2 (8–17)	12.2 ± 3.7 (7–16)	12.4 ± 3.5 (7–17)

Table 2: Penile Hemodynamic Parameters (Doppler Ultrasound)

Parameter	Pre-Surgery	6 Weeks Post-Surgery	6-Month Follow-Up (Group A - PDE5i)	6-Month Follow-Up (Group B - Placebo)
Peak Systolic Velocity (PSV) (cm/s)	28.5 ± 5.2	22.3 ± 4.9	38.7 ± 6.1*	24.5 ± 5.3
End-Diastolic Velocity (EDV) (cm/s)	7.5 ± 2.1	9.1 ± 1.8	4.8 ± 2.3*	8.9 ± 2.4
Resistance Index (RI)	0.73 ± 0.09	0.59 ± 0.08	0.88 ± 0.07*	0.64 ± 0.09

**Significant improvement compared to baseline and placebo group ($p < 0.05$).*

Table 3: International Index of Erectile Function (IIEF) Scores

Domain	Baseline (All Patients)	6-Month Follow-Up (Group A - PDE5i)	6-Month Follow-Up (Group B - Placebo)
Erectile Function	12.4 ± 3.5	23.1 ± 4.2*	14.7 ± 3.9
Intercourse Satisfaction	5.2 ± 1.8	8.9 ± 1.3*	5.1 ± 1.4
Orgasmic Function	4.9 ± 2.0	7.2 ± 1.5*	4.3 ± 1.6
Overall Sexual Satisfaction	5.6 ± 2.2	9.8 ± 2.0*	5.6 ± 2.1

**Significant improvement compared to baseline and placebo group ($p < 0.05$).*

Table 4: Patient Satisfaction (VAS Scores)

Group	Mean Satisfaction Score (VAS)
Group A (PDE5i)	8.3 ± 1.1
Group B (Placebo)	5.7 ± 1.6

Table 5: Sexual Activity and Prosthesis Usage

Group	Average Sexual Encounters/Month	% Using Prosthesis	% Using PDE5i (Natural Erections)
Group A (PDE5i)	5.1	55%	45%
Group B (Placebo)	3.3	100%	0%

Discussion

The results of this prospective study demonstrate that patients who undergo cavernosal sparing inflatable penile prosthesis (IPP) implantation can achieve significant hemodynamic improvements when treated with phosphodiesterase type V inhibitors (PDE5i) postoperatively. This is likely to have been caused by the raised peak systolic velocity (PSV), and reduced end-diastolic velocity (EDV) also accompanied by improved resistance index (RI) in Group A (PDE5i group) as contrasted with Group B (placebo group) where changes were minimal. Thus, the data presented here imply that PDE5 inhibitors combined with cavernosal sparing approaches provide a synergistic mechanism for improving mechanical and pharmacologic erectile function. (13, 14). The idea behind cavernosal sparing IPP implantation is to make as large a portion of the natural corporal tissue available as possible so that patients might someday be candidates for PDE5i medications after surgery. On the other hand, the Group B patients who only consumed a placebo had less enhancement of PSV than the subjects of Group A. The study also pointed out positive changes in the EDV and RI of the rats given PDE5i treatment. ImpROVEMENT in EDV was observed from 7. 3 cm/s to 4. 8 cm/s in Group A but the efficiency of blood reservoir or venous leakage in severe ED patients, which disturb them from having a maintained erection (15). The RI, which is a sign of cavernosal artery function, increased also in Group A from 0. 73 to 0. 88, reflecting its enhanced vascular and erectile status. This implies that PDE5 inhibitors have a place besidesdocsensitizing the blood vessels to allow increased inflow, but they also have a role to play in decreasing outflow from the bruise, in other words, allowing for better-increased erections (16). The increase of only these parameters in Group B points that intact penile microcirculation may not be enough even the use of prosthesis alone to improve penile blood flow, especially

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the factor of venous leakage. This supports the hypothesis that cavernosal sparing surgery with PDE5 inhibitors may have the advantage in the improvement of erectile function after surgery. (17). Cavernosal sparing IPP implantation and PDE5i therapy have several clinical benefits as below. First, it gives patients more diverse choices for the treatment of ED, thereby offering patients the opportunity to have erection through implants or chemical means by taking PDE5 inhibitors. This is highly significant to the male users who opine that besides having a prosthesis, they can be flexible in satisfying their sexual desires unpredictably.

Conclusion

It is concluded that cavernosal-sparing inflatable penile prosthesis (IPP) implantation, combined with postoperative phosphodiesterase type V inhibitors (PDE5i), significantly enhances penile hemodynamics and erectile function. Patients receiving PDE5i showed improved arterial inflow, reduced venous leakage, and higher satisfaction compared to those on placebo, suggesting a synergistic benefit from preserving cavernosal tissue and pharmacological intervention. This dual approach offers greater flexibility in managing erectile dysfunction post-surgery.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.
Ethics approval and consent to participate
Approved by the department concerned. (IRBEC-TCHLUO-0973/2/23)
Consent for publication
Approved
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Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

JAMSHID ALI (Urologist)
Coordination of collaborative efforts.
Study Design, Review of Literature.
MUSADDIQ HUSSAIN BANGASH (Consultant Urologist)
Conception of Study, Development of Research Methodology Design, Study Design, Review of manuscript, final approval of manuscript.
Conception of Study, Final approval of manuscript.
MUHAMMAD HAMZA (Research Scholar)
Manuscript revisions, critical input.
Coordination of collaborative efforts.
MEHAK SHAHID (Research Scholar)
Data acquisition, analysis.
Manuscript drafting.
FATIMA TARIQ (Senior Lecturer)
Data entry and Data analysis, drafting article.
MUHAMMAD HAMMAD
Data acquisition, analysis.
Coordination of collaborative efforts.
FAHAD ASIM (Lecturer)
Data acquisition, analysis.
Manuscript revisions, critical input.

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