Introduction

Priapism is the persistence of erection that is not associated with sexual stimulation [1]. The most common etiology of priapism is intracavernosal injection therapy with vasoactive drugs such as papaverine or prostaglandin E1 (PGE1). The incidence of iatrogenic causes ranges from 0.26% to 10.26% [2-9]. Predictive factors of prolonged erections include young age, good baseline erectile function, and absent coronary artery disease [10]. Intracavernosal agents have a number of utilities in addition to erectile dysfunction treatment. They can facilitate erection for office-based examinations, such as a penile duplex Doppler ultrasonography (PDDU) in the workup of Peyronie’s disease [11]. These patients will almost invariably undergo PDDU for evaluation of erectile function, plaque size, penile curvature, and hemodynamic function [12]. The use of vasoactive agents carries a risk of inducing iatrogenic priapism [13]. Patients receiving these injections in an outpatient setting are at increased risk because of the inability to predict optimal dosing. Furthermore, Deveci et al. [14] reported the prevalence of erectile dysfunction in...
Peyronie’s patients to be approximately 35% (self-reported at presentation), with 18% of those patients having normal results on hemodynamic PDDU studies.

Therefore, given that the majority of Peyronie’s disease patients are expected to have normal or near-normal erectile function, this patient group was chosen to evaluate the risk of iatrogenic priapism following intracavernosal vasoactive agent injection therapy. Phenylephrine has been well described as a method of priapism treatment. The aim of our study was to analyze the utility of “early” prophylactic administration of low-dose phenylephrine in patients with sustained erections after diagnostic injections of vasoactive agents to prevent the deleterious effects of iatrogenic priapism.

**MATERIALS AND METHODS**

A retrospective review of all patients with Peyronie’s disease in a specialized practice was performed to analyze the effects of low-dose phenylephrine as a prophylaxis against iatrogenic priapism. A total of 78 patients underwent a workup for Peyronie’s disease that included a focused history and physical examination as well as PDDU. All patients were given 10 μg of alprostadil, with an additional 10 μg to achieve adequate response (rigidity 4–5) when the initial injection was insufficient. Clinic assessment and grading of penile rigidity (on a scale of 1–5) as well as degree and direction of penile curvature were recorded by a single urologist (H.S.N). Rigidity was classified as 5/5 if there was complete fullness as determined by the same clinician. A score of 3/5 was given if there was 50% fullness. A score of 1/5 was given if there was no fullness or response to vasoactive injection. Subsequently, the patients underwent PDDU to obtain peak systolic velocity (PSV) and end diastolic velocity (EDV). Following the study, the patients were reevaluated at 15 minutes after the completion of the exam (approximately 45–60 minutes after alprostadil injection) to assess for persistent penile rigidity. The patients with unsubsided penile rigidity evaluated as 4 to 5 out of 5 at 15 minutes after the PDDU study were given 200-μg intracavernosal phenylephrine combined with 5 minutes of firm pressure at the injection site to achieve full detumescence. Patients were asked to report any symptoms, including lightheadedness, headaches, or palpitations. Blood pressure and heart rate were monitored within 10 minutes of phenylephrine injection.

A database was compiled to include patient demographics, duration of symptoms, degree and direction of curvature, associated symptoms, erectile function, medical comorbidities, PDDU results, and complications. One patient required immediate phenylephrine reversal because of unbearable discomfort secondary to alprostadil injection (excluded from study results). The remaining 77 patients were divided into 2 groups on the basis of rigidity following the examination: 1–3 vs. 4–5. A total of 44 patients with 4–5 rigidity were further analyzed to determine the proportion with reported erectile dysfunction and the correlation with PDDU analyses. Chi-square with Yates correction and two-tailed t-tests were used to analyze comorbidities, demographics, erectile function, and PDDU measurements where appropriate. Finally, 95% confidence intervals of studies reporting iatrogenic priapism rates were calculated. Microsoft Excel (Microsoft Co., Redmond, WA, USA) was used for all statistical analyses.

**RESULTS**

Of the 77 patients studied, 44 had persistent rigidity (score 4–5) approximately 45 to 60 minutes after receiving alprostadil injection and received phenylephrine reversal. Table 1 reports the patients’ demographic characteristics and comorbidities, which did not differ significantly between the two groups. Table 2 compares the two groups by baseline erectile function as reported by subjective International

### Table 1. Patient demographics and comorbidities

| Demographic                | Group A (1-3 rigidity) | Group B (4-5 rigidity) | p-value |
|----------------------------|------------------------|------------------------|---------|
| No. of patients            | 33                     | 44                     |         |
| Phenylinephrine reversal   | No                     | Yes                    |         |
| Age (mo), mean             | 53.4                   | 48.7                   | 0.12    |
| Duration of symptoms (mo), mean | 33.9                   | 24.3                   | 0.37    |
| Erectile dysfunction (reported) | 20 (61)               | 18 (41)                | 0.03    |
| Hypertension               | 7 (21)                 | 7 (16)                 | 0.55    |
| Diabetes mellitus          | 1 (3)                  | 4 (9)                  | 0.29    |
| Smoker                     | 3 (9)                  | 3 (7)                  | 0.71    |
| Hyperlipidemia             | 10 (30)                | 17 (39)                | 0.45    |
| Coronary artery disease    | 2 (6)                  | 1 (2)                  | 0.40    |
| No comorbidities           | 16 (48)                | 22 (50)                | 0.89    |

Values are presented as number (%) unless otherwise indicated. *Significant (p<0.05).

### Table 2. Comparison of erectile function with IIEF scores and PDDU hemodynamic values

| Variable                          | Group A (1-3 rigidity) | Group B (4-5 rigidity) | p-value |
|-----------------------------------|------------------------|------------------------|---------|
| No. of patients                   | 33                     | 44                     |         |
| Erectile function (IIEF), n (%)   |                        |                        |         |
| No ED (22-25)                     | 11 (33)                | 26 (59)                | 0.03    |
| Mild (17-21)                      | 11 (33)                | 12 (27)                | 0.57    |
| Moderate (8-16)                   | 5 (15)                 | 5 (11)                 | 0.62    |
| Severe (5-7)                      | 6 (18)                 | 1 (2)                  | 0.02    |
| PDDU                              |                        |                        |         |
| PSV (cm/s), mean                  | 18.86                  | 23.89                  | 0.002   |
| EDV (cm/s), mean                  | 5.46                   | 3.95                   | 0.001   |

IIEF, International Index of Erectile Function; ED, erectile dysfunction; PDDU, penile duplex Doppler ultrasonography; PSV, peak systolic velocity; EDV, end diastolic velocity. *Significant (p<0.05).
Index of Erectile Function [15] categories and objective hemodynamic measurements (mean PSV and EDV). Group B had significantly more patients with normal reported erectile function and better hemodynamic values.

The 44 patients in group B who received phenylephrine were further divided into subgroups, with 26 patients reporting no erectile dysfunction. Comparison of patients with Peyronie’s disease only (PD only) versus patients with Peyronie’s disease and erectile dysfunction (PD+ED) showed that PD only patients had higher PSV and lower EDV than would be expected (Fig. 1). There was a significant difference in PSV for PD only (25.92±7.30) and PD+ED (20.94±5.71, p=0.02). The difference in EDV between the two groups was not significant.

All 44 patients achieved complete detumescence following injection of phenylephrine. There were no reports of hypotension, palpitation, or other adverse effects during or after the study. Average blood pressure change was <10 mmHg systolic. A number of patients (n=12) in both groups had complained of a “throbbing sensation” in the penis for up to 2 hours after the study, but it was difficult to assess whether this transient sensation was due to phenylephrine or to the initial alprostadil injection. The priapism rate was 0%.

Table 3 summarizes the results of a literature search on previous studies of iatrogenic priapism rates resulting from intracavernosal injection of vasoactive agents. All studies were conducted in patients with existing erectile dysfunction, with the incidence of iatrogenic priapism ranging from 0.26% to 10.26%. There were noticeably higher incidences of iatrogenic priapism with papaverine versus alprostadil injections. The use of alprostadil yielded lower rates of priapism, ranging from 0.26% to 0.94% (Table 3).

**DISCUSSION**

Iatrogenic priapism is a serious complication of diagnostic and therapeutic intracavernosal injection of vasoactive agents. The detrimental effects of priapism have been described extensively in the literature as biochemical alterations that produce histologic changes that result in cavernosal damage [16]. Juenemann et al. [17] demonstrated that hypoxia and intracorporeal acidosis occur 4 hours after erection onset as seen in corporal blood gas analysis. This anoxia and acidosis combined with glucose deprivation results in significantly diminished cavernosal smooth muscle tone and irreversible contractile dysfunction [12,18]. Low-flow priapism can result in irreversible cellular damage and corporal fibrosis, which results in significant morbidity of permanent erectile dysfunction [16,19].

Patients with Peyronie’s disease are intuitively thought to be at higher risk for iatrogenic priapism because a substantial number of these patients have normal erectile function. As shown in Table 3, previous studies that at-

![Figure 1. Comparison of penile duplex Doppler ultrasonography values in patients receiving low-dose phenylephrine. PD, Peyronie disease; PD+ED, Peyronie disease and erectile dysfunction. *Significant (p < 0.05).](image)

| Source | No. of patients | Erectile dysfunction (%) | Vasoactive agent | Priapism rate (%) | 95% Confidence interval |
|--------|----------------|-------------------------|-----------------|------------------|------------------------|
| European alprostadil study group [2] (1998) | 848 | 100 | Alprostadil (PGE1) | 0.94 | (0.48-1.85) |
| Linet et al. [6] (1996) | 683 | 100 | Alprostadil (PGE1) | 0.73 | (0.31-1.70) |
| Perimenis et al. [8] (2001) | 423 | 100 | Alprostadil (PGE1) | 0.71 | (0.15-2.07) |
| Porst [9] (1996) | 4,577 | 100 | Alprostadil (PGE1) | 0.26 | (0.15-0.45) |
| Kilic et al. [5] (2010) | 672 | 100 | Papaverine | 2.68 | (1.59-4.23) |
| Perimenis et al. [8] (2001) | 262 | 100 | Papaverine | 1.91 | (0.62-4.45) |
| Metawea et al. [7] (2005) | 250 | 100 | Papaverine and phentolamine | 10.00 | (6.47-14.76) |
| Coombs et al. [3] (2012) | 1,412 | 100 | Various | 0.50 | (0.24-1.03) |
| Domes et al. [4] (2012) | 117 | 100 | Various | 10.26 | (5.97-12.08) |
| Our study, with phenylephrine px | 44 | 41 | Alprostadil (PGE1) | 0.00 | (0.00-8.03) |

PGE1, prostaglandin E1; px, prophylaxis.
temped to identify iatrogenic priapism rates were con-
ducted in patients with existing erectile dysfunction. In
fact, we were unable to identify any studies that specifically
reported on the use of intracavernosal injections in pa-
tients with a similar erectile function profile as our
patients. Thus, the findings of this pilot study underscore
the safety and efficacy of preemptive and “early” use of in-
tracavernosal phenylephrine injection to achieve detu-
mescence, particularly in patients with normal baseline
erectile function.

Intracavernosal phenylephrine for reversal of prolonged
erections has been well established as an important ther-
apeutic intervention that is safe and effective [20-25].
Azocar et al. [26] noted that 93.1% of cases achieved detu-
mescence and no adverse complications were identified.
Munarriz et al. [22] demonstrated that high-dose intra-
cavernosal phenylephrine (mean dose, 2059±807 μg) can
be used for management without adverse effects or sig-
ificant changes in vital signs. We found that a minimal
dose of 200 μg of phenylephrine resulted in complete detu-
mescence without any adverse effects.

Our experience with Peyronie’s disease patients showed
59% to have normal erectile function. All patients who had
persistent penile rigidity (score of 4-5) approximately 45
to 60 minutes after alprostadil injection received pho-
ylactic phenylephrine. All patients achieved complete detu-
mescence, without any cases of iatrogenic priapism.
Although the published studies reviewed in Table 3 also re-
ported low rates of iatrogenic priapism, the patient pop-
ulation studied was different from the typical Peyronie’s
disease patient, as discussed above.

Thus, in our study, absent a proactive intervention with
vasoactive agents (i.e., reversal with an alpha adrenergic
agent), it would be expected that a number of patients will
have prolonged, painful erections that require further pharma-
ologic injections, penile aspiration, or surgical in-
tervention after induction of an erection with papaverine
or PGE1. This further treatment entails additional un-
necessary and stressful time spent with a health care pro-
vider, as well as expenditure of more health care dollars in
the form of added visits to emergency rooms and urgent
care centers. Furthermore, the persistence of erection can
be alarming and exceedingly uncomfortable for patients
who have already endured the discomfort of intrac-
avernosal injection therapy for PDDU. Preempting the
emergency management of priapism by identifying those
patients at higher risk for developing iatrogenic priapism
can minimize stressors on both patients and the health care
system. Although waiting in the office and receiving vaso-
active injection requires spending extra time at the office
at the outset, this brief intervention will lead to better out-
comes overall by reducing the chances of more extensive
and time-consuming interventions if the same patient
were to present to the Emergency Department or the physi-
cian’s office after a 3- to 4-hour priapism episode.

Our study was limited by sample size, given that
Peyronie’s disease is fairly uncommon. In addition, the
dose of 200 μg of phenylephrine resulted in complete detu-
mescence without any adverse effects,

CONCLUSIONS

Prophylactic phenylephrine reversal of strong erections
persisting beyond 60 minutes following vasoactive in-
duction is warranted to prevent the deleterious physio-
logical effects of prolonged erections, especially in patients
who are at higher risk. Future studies should incorporate
well-defined endpoints with larger sample sizes to explore
the incidence of iatrogenic priapism secondary to diag-
nostic procedures.
CONFLICTS OF INTEREST
The authors have nothing to disclose.

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