Intralesional Verapamil for Peyronie's Disease

Lori B. Lerner, MD, Mark D. Tyson, BS, Theresa M. Fairbank, PA-C,
Richard A. Morse, MD, and Matthew A. Thomas, MD

Although this treatment has been used for Peyronie's disease for many years, patient satisfaction with the results is seldom measured. These authors aim to give clinicians a better understanding of what their patients can expect with regard to sexual performance.

Peyronie's disease (PD) is a disorder of the penis characterized by fibrosis of the tunica albuginea.[1] Proliferation of the connective tissue causes formation of a fibrous plaque with excess collagen and ground substance.[2] In severe cases, the plaques can calcify. The disease results in penile curvature, pain, and in some patients, erectile dysfunction (ED).[1] The pathogenesis is unknown and the etiology is unclear. Although trauma often has been thought to be the most likely cause of the disease, most men do not recall any traumatic event.[3]

Recent publications have revealed that PD affects more men than previously appreciated. It is estimated that the disease prevalence in the general population of American men is 8.9%.[4,5] The mean age of affected men is about 54, with as many as 10% presenting at ages younger than 40 years.[6]

It has been shown that pain resulting from PD completely resolves during the natural progression of the disease in 89% of cases, but plaque size and penile curvature remain unchanged or continue to worsen.[7] In 30% of cases, ED ensues and has been shown to result in significant psychological distress.[8,9]

No single treatment for PD has emerged as the gold standard, and all therapies currently utilized have varying degrees of success. Therapies described in medical literature include topical and oral vitamin E; intralesional agents, such as collagenase; and surgical treatments, such as penile grafting and prosthesis placement.[10–13]

Another treatment option, which has been used for almost 13 years, is intralesional verapamil injection.[14,15] Published reports have focused on the success of verapamil injections in reversing the disease process—but not on how the treatment has altered subjective parameters, including patient satisfaction. Therefore, we conducted a study designed to evaluate not only the effectiveness of this treatment method in reducing plaque size and penile curvature but also its effects on erectile and sexual function in a small cohort of veterans with PD.

PARTICIPANTS AND METHODS

Thirteen men with previously untreated PD were included in the yearlong study. All participants had been symptomatic for PD for nine to 36 months prior to their first verapamil treatment. All men were heterosexual and ranged in age from 51 to 78 years (mean [SD], 61.8 [8.2]) at the beginning of the study in August 2003 (Table 1).

Patients were given a penile block consisting of 0.5% bupivacaine followed by a 10-mg dose of verapamil diluted to 10 mL with normal saline. The verapamil solution was injected directly into the penile plaque. Verapamil injections were administered every two to four weeks for a total of 12 treatments. The patients were assessed at three intervals: baseline, after the sixth injection (midpoint), and after the 12th injection (endpoint). Artificial erections were

At the time of this study, **Dr. Lerner** was a staff urologist in the department of urology at White River Junction VA Medical Center (WRJVAMC), White River Junction, VT. She is now a staff urologist in the section of urology at VA Boston Healthcare System and an assistant professor of surgery at Boston University, both in Boston, MA. **Mr. Tyson** is a medical student at Dartmouth Medical School, Hanover, NH. At the time of this study, **Ms. Fairbank** was a physician assistant at WRJVAMC. She is now a medical student at Rush Medical School, Chicago, IL. **Dr. Morse** is the chief of radiology at WRJVAMC. At the time of this study, **Dr. Thomas** was a resident in urology at WRJVAMC. He is now a private practice urologist in Minocqua, WI.

obtained through intracavernosal injections of papaverine.

Manual measurement of the penile curvature was determined using a protractor, plaque size was determined through palpation, and plaque volume was assessed with ultrasound. The same three clinicians, two urologists and a radiologist, were present for each measurement.

Sexual and erectile function were assessed—using the 15-question, validated International Index of Erectile Function (IIEF)[16]—at the baseline, midpoint, and endpoint assessments. Scores for the five IIEF domains (erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction) were determined by adding together the responses to the IIEF questions, as previously described by Rosen and colleagues.[16]

For the erectile function domain, responses to questions 1, 2, 3, 4, 5, and 15 were totaled for a maximum score of 30. Using the erectile function domain score, ED was classified as severe (a score of 6 to 10), moderate (a score of 11 to 16), mild to moderate (a score of 17 to 21), mild (a score of 22 to 25), and no ED (a score of 26 to 30). The orgasmic function domain was the sum of the responses to questions 9 and 10. The sexual desire domain was the sum of questions 11 and 12. The intercourse satisfaction domain was the sum of questions 6, 7, and 8. The overall satisfaction domain was the sum of responses to questions 13 and 14.

We also broke down the five domains of the IIEF into their individual components and assessed relationship satisfaction, penetration ability, desire frequency, overall satisfaction, erection frequency, and maintaining erection at the baseline, midpoint, and endpoint assessments.

For statistical analysis of the IIEF individual component and domain scores, plaque sizes, and penile curvature measurements, two-sample paired *t*-tests with two-tailed significance of $P \leq .05$ were used against the null hypothesis that baseline and endpoint scores would be the same. All statistical calculations were performed using Stata version 9.0 (StataCorp LP, College Station, TX) for Mac OS X (Apple Inc, Cupertino, CA).

RESULTS

Plaque size and penile curvature

The mean decrease in plaque area from baseline to endpoint was –4.6 cm^2 ($P = .001$; 95% CI, 7.1 to 2.1 cm^2), and the mean decrease in penile curvature was –13.8º ($P = .008$; 95% CI, 23.3º to 4.2º) (Table 2). Since some patients had biplanar curvatures, the scores for penile curvature were standardized to one overall value for ease of statistical analysis.

It is interesting to note that two patients experienced a slight increase in overall penile curvature (of less than 5º) despite decreases in plaque area. One of these patients had been symptomatic with PD for only nine months at baseline. All patients reported complete resolution of pain with erection at the endpoint assessment.

Sexual function

Of the 13 study participants, one (7%) was found to have severe ED, four (31%) had moderate ED, three (23%) had mild ED, and five (39%) had no ED.

Table 1. Baseline patient characteristics (n = 13)

Characteristic	Mean (SD)
Age (years)	61.8 (8.2)
Duration of PD[a] (months)	21.3 (8.7)
Penile curvature (º)	66.3 (8.7)
Plaque area (cm^2)	7.1 (4.4)

[a]PD = Peyronie's disease.

Statistically significant improvements from baseline to endpoint were observed for the overall satisfaction domain ($P = .02$), orgasmic function domain ($P = .04$), and sexual desire domain ($P = .05$) (Table 3). Improvements also were observed for the erectile function and intercourse satisfaction domains, though these improvements were not statistically significant.

The most statistically significant improvements for the individual components of the IIEF were observed for relationship satisfaction ($P = .008$) and penetration ability ($P = .04$) (Figure). The other four sexual measures (overall satisfaction, desire frequency, erection frequency, and ability to maintain erections) had *P* values ≤ .1.

IS THE SEXUAL EXPERIENCE IMPROVED WITH VERAPAMIL?

The statistically significant decreases in plaque area and penile curvature that we observed in our study further support the established use of verapamil in alleviating these symptoms

Table 2. Change in plaque size and penile curvature from baseline to endpoint

Measurement	Mean at baseline (SE)	Mean at endpoint (SE)	Mean change (SE)	*P* value
Plaque area (cm^2)	7.1 (1.2)	2.5 (0.4)	–4.6 (1.4)	.001
Penile curvature (º)	66.3 (8.7)	52.5 (8.5)	–13.8 (4.4)	.008

Table 3. Change in IIEF[a] domain scores from baseline to endpoint

IIEF domains[b]	Mean score at baseline (SE)	Mean score at endpoint (SE)	Mean change (SE)	*P* value
Overall satisfaction	6.4 (0.7)	7.4 (0.9)	1.0 (0.4)	.02[c]
Orgasmic function	8.4 (0.3)	9.5 (0.3)	1.1 (0.5)	.04[c]
Sexual desire	6.3 (0.6)	6.9 (0.7)	0.6 (0.3)	.05[c]
Erectile function	24.6 (1.3)	25.2 (1.2)	0.6 (1.6)	.68
Intercourse satisfaction	10.6 (0.6)	10.7 (1.0)	0.1 (0.6)	.85

[a]IIEF = International Index of Erectile Function. [b]Ranges of the possible scores for the IIEF domains are as follows: overall satisfaction, 2–10; orgasmic function, 0–10; sexual desire, 2–10; erectile function, 1–30; and intercourse satisfaction, 0–15. [c]Statistically significant to the .05 level.

of PD. Whether or not these improvements are clinically significant, however, is debatable. One challenge with studies involving verapamil treatment for PD is the lack of a randomized, controlled design. Without a control arm it is difficult to evaluate the efficacy of verapamil in light of potential confounders or bias.

We set out, however, to evaluate whether any improvements in penile curvature and plaque size represented improvements in the overall sexual experience for the particular men in this study—with the goal of giving clinicians a better understanding of what their patients can expect with regard to sexual and erectile perfor-

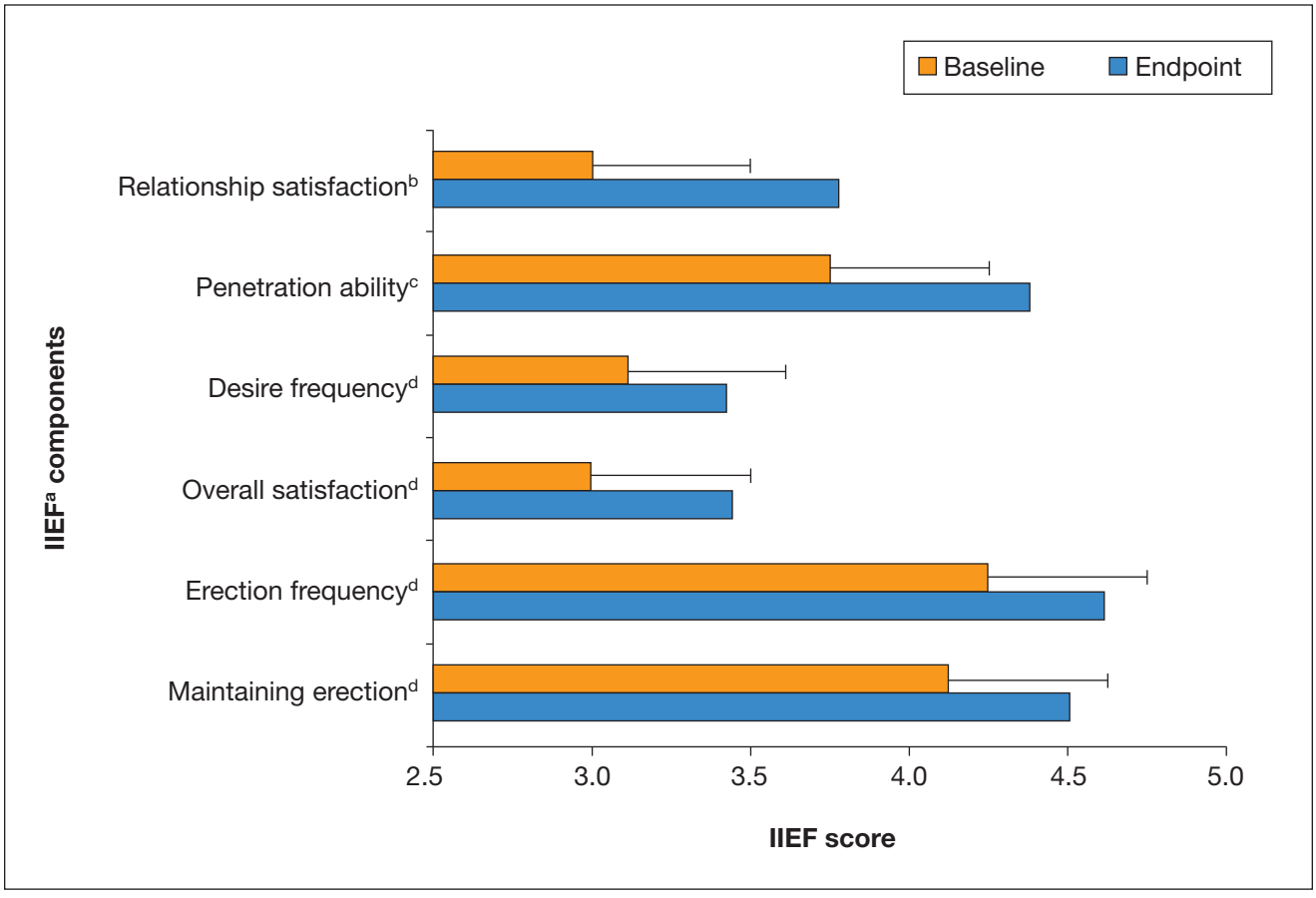

Figure. Baseline and endpoint scores of six individual components of the IIEF. [a]IIEF = International Index of Erectile Function. [b]*P* = .008. [c]*P* = .04. [d]*P* ≤ .1.

mance. The fact that we found significant improvements in three of the five domains measured by the IIEF supports the assertion that the observed improvements in plaque size and penile curvature with verapamil are clinically significant enough to improve the sexual lives of these men. The "overall satisfaction" of the cohort was the most statistically significant improvement (P = .02) and could represent improved sexual and erectile function as a result of improved penile structure (along with the observed improvement in orgasmic function and sexual desire).

A possible explanation for the statistically insignificant improvements in the other two IIEF domains (erectile function and intercourse satisfaction) is that the average baseline values for the erectile function domain already were quite high. A significant improvement would be difficult to achieve given that almost half of the cohort did not present with ED at baseline. In fact, only 38% presented with moderate to severe ED, and the overall baseline erectile function domain mean (SD) score for the cohort—24.6 (1.3)—falls in the upper tier of mild ED.

The prominent improvement we observed in satisfaction with partners and ability to penetrate components of the IIEF were likely secondary to the decreases in penile curvature and pain during intercourse as a result of the verapamil treatment and not necessarily directly due to the verapamil itself. Although improvements were observed in most of the other individual components of the IIEF, statistical significance to the .05 level was difficult to achieve with the low statistical power of this cohort size.

CONCLUSION

In this cohort of veterans, intralesional verapamil treatment led to reductions in plaque size and curvature of the penis, which led to statistically significant improvements in three of the five sexual and erectile domains measured by the IIEF. This indicates verapamil may have a beneficial effect not only in correcting the penile deformities commonly seen in PD but also in improving the sexual and erectile dysfunctions that frequently accompany PD symptoms. The long-term efficacy of verapamil for treating erectile and sexual dysfunction resulting from PD is not known, however, and requires further investigation.

Author disclosures

The authors report no potential or actual conflicts of interest with regard to this article.

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