ORIGINAL RESEARCH—PEYRONIE'S DISEASE

Combination of Penile Traction, Intralesional Verapamil, and Oral Therapies for Peyronie's Disease

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ABSTRACT

Introduction. There is no current consensus as to the most effective nonsurgical therapy for Peyronie's disease (PD).
Aim. This study aims to assess the benefit of penile traction therapy (PTT) when added to intralesional verapamil injections (IVIs) combined with oral L-arginine 1 g b.i.d. and pentoxifylline 400 mg t.i.d. in men with PD.
Methods. Seventy-four men with PD completed 12 IVIs. Patients electing to add PTT were advised to wear the device for 2–8 hours daily and no longer than 2 hours per session. Subjective responses were measured using patient questionnaires. Stretched penile length (SPL) and erect penile curvature (EPC) using penile duplex ultrasound were measured. Response to therapy was defined as at least a 10-degree reduction in EPC.
Main Outcome Measures. Change in SPL (cm) and change in EPC (degrees).
Results. Thirty-five patients in group I vs. 39 patients in the PTT group II completed the protocol. Fifty-four percent of men in group II responded to therapy vs. 46% in group I ($P = 0.75$). Responders in group II had a mean EPC improvement of 26.9 degrees vs. 20.9 degrees in group I ($P = 0.22$). Mean PTT use was 3.3 hours per day, and men with >3 hours per day use gained 0.6 cm in SPL vs. 0.07 cm using less than or equal to 3 hours per day ($P = 0.09$), while men in group I lost 0.74 cm of SPL on average. Multivariate analysis revealed that duration of PTT use significantly predicts length gain (0.38 cm gain for every additional hour per day of PTT use, $P = 0.007$).
Conclusions. There was a trend toward measured curvature improvement and a significant gain in SPL in men using the combination therapy protocol. Length improvement is related to duration of use of the traction device. **Abern MR, Larsen S, and Levine LA. Combination of penile traction, intralesional verapamil, and oral therapies for Peyronie's disease. J Sex Med 2012;9:288–295.**

Key Words. Peyronie's Disease; Penile Traction Therapy; Nonsurgical Treatment; Mechanotransduction

Introduction

Peyronie's disease (PD) is currently theorized to result from abnormal wound healing after repetitive penile trauma [1]. Men present with a variety of signs and symptoms including pain, erectile dysfunction, perceived penile length loss, and hourglass or curvature deformities. No reliable and effective nonsurgical therapy has emerged, likely in part because of the incomplete understanding of the disorder's pathophysiology [2].

Placing tissues under tension has been done in a number of fields. Much work has gone into elucidating the mechanisms through which mechanical strain can yield a biological response. Mechanotransduction is the process of converting mechanical stimuli into chemical responses in the cell [3]. Several signaling cascades are activated by tension on the cytoskeleton, which leads to a proliferative response as well as activation of various genes [4]. While it has yet to be studied in the penile model, proliferation in response to tension has been demonstrated in skin, skeletal muscle, and even bone [5–8]. On a histologic level, tension leads to a reorientation of tissues, including collagen fibrils parallel to the axis of stress [6,9].

Oral therapies for PD have shown very little benefit in human trials; however, they remain the

predominant initial treatment employed by urologists and primary care physicians because of their low cost, convenience, and low side effect profile [10]. A recent in vitro study has suggested that L-arginine, pentoxifylline, and phosphodiesterase type 5 inhibitors may exhibit an antifibrotic effect and may inhibit scar development; however, clinical data in humans is lacking [11].

Verapamil is a calcium channel blocker that has been shown in in vitro studies to inhibit local extracellular matrix production by fibroblasts, reduce fibroblast proliferation, increase local collagenase activity, and affect the cytokine milieu of fibroblasts [12,13]. Several published clinical trials have reported improvement in penile deformity and sexual function with intralesional verapamil injections (IVIs) [14–17].

The hypothesis of this study is that the combination of the mechanical effects of penile traction therapy (PTT) with the chemical effects of IVI and oral medications (pentoxyfilline and L-arginine) may have a synergistic effect on the tunica albuginea and Peyronie's plaque. We compare this treatment regimen to a matched cohort of men managed with IVI and the same oral therapy. Pretreatment characteristics including medical comorbidities, age, PD duration, tobacco use, International Index of Erectile Function-5 (IIEF-5) score, plaque calcification on duplex ultrasound (DU), stretched penile length (SPL), and erect penile curvature (EPC) were analyzed, and effects of treatment regimen on SPL, EPC, and a variety of patient-reported subjective measures were compared.

Aim

The main goal was to determine whether the addition of PTT to IVI and oral therapy for PD resulted in any additional benefit in SPL, EPC, or patient satisfaction. A secondary goal was to determine the effect of duration of traction therapy use on outcomes within the combination therapy group.

Methods

Protocol

Seventy-four consecutive men with PD treated between February 2005 and April 2010 were evaluated in this prospective, nonrandomized study. Patients receiving prior intralesional or surgical therapy for PD were excluded. Patients on oral therapy prior to our evaluation had these medications discontinued prior to enrollment in the protocol. Patients with PD symptoms deemed to be stable by the treating physician and with greater than 1 year of symptoms who desired immediate surgical therapy were excluded. SPL was measured with a ruler from pubis to corona dorsally with the penis on stretch by the treating physician (LAL), as this technique has been shown to most closely approximate erect penile length [18]. The technique of compression of the prepubic fat pad, firm stretch of the penis to the limit of elasticity, and measurement to the dorsal corona were performed in an attempt to minimize intraobserver variation. EPC was measured with a goniometer (Baseline, White Plains, NY, USA) during DU and after a combination of manual stimulation and intracavernosal injection of 30–90 mg of papaverine as needed to achieve rigidity better than or equal to the patient's home erections. A 500 mcg of intracavernosal phenylephrine was utilized for detumescence as needed for persistent or uncomfortable erections. Physical exam and biothesiometry (Bio-Medical, Newbury, OH, USA) were also performed as part of the initial evaluation. Biothesiometry was performed to document any preexisting penile sensory deficits at baseline to help monitor any sensory changes that may be caused by the penile traction device. Patients with evidence of PD plaque calcification on DU, using previously published criteria of acoustic shadowing of the plaque or heterogeneous hyperechoic plaque lesions [19], were excluded from this protocol. All patients had IVI of 10 mL of 1 mg/mL verapamil using the technique we previously reported [14]. IVIs were administered every other week for a total of 12 in 24 weeks. All patients were given oral L-arginine 1 g b.i.d. and pentoxifylline 400 mg t.i.d. Patients were all offered PTT. Those electing to add PTT obtained an external penile extender (US PhysioMED, Irvine, CA, USA), were instructed on proper application, and were advised to wear the device for 2–8 hours daily but no longer than 2-hour intervals with at least 15 minutes between sessions to prevent ischemic injury. Patients were advised to add a 0.5 cm spacer to the traction rods every 2–3 weeks as tolerated to maintain progressive traction forces on the penis. Patients were advised to use the PTT device throughout the 24-week protocol but not to wear the device while sleeping.

At each visit, patients completed a nonvalidated, author-generated questionnaire (Figure 1) indicating improvement, worsening, or no change with regard to perceived penile length, pain, girth, and rigidity as well as changes in EPC and sexual satisfaction. These were converted to binary variables