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Shockwave Therapy as First-Line Treatment for Peyronie's Disease: A Prospective Study

A. SKOLARIKOS, M.D.,[1] E. ALARGOF, M.D.,[2] A. RIGAS, M.D.,[2] CH. DELIVELIOTIS, M.D.,[1] and E. KONSTANTINIDIS, M.D.[2]

ABSTRACT

***Background and Purpose*: To assess in a prospective study whether shockwave therapy (SWT) is effective as a first-line treatment for Peyronie's disease.**

***Patients and Methods*: Forty patients with previously untreated Peyronie's disease underwent SWT with the Epos overhead-module device (Dornier). The pain severity (visual analog pain scale [VAS] 0–5), the degree of penile angulation after vasoactive drug injection, plaque size by ultrasound measurement, and erectile dysfunction (IIEF score) were assessed prior to and after treatment. Of the 40 patients, 7 underwent two sessions and the rest three sessions. The time interval between treatments was 2 weeks. At a power level of 2 to 5 (mean 4), a maximum of 3000 shockwaves per plaque per treatment were applied. The mean follow-up was 12 months.**

***Results*: All patients completed the protocol. The tolerance and safety were excellent. Of the 25 patients with pain on erection, 12 (48%) noticed relief after the first session, while 9 more were pain free at the end of the treatment (VAS reduction 2.8; $P < 0.0001$, and 2; $P < 0.001$, respectively). For 25 patients (62.5%), an improvement in penile angulation >20° was observed, with a mean reduction of 35° (range 20°–60°) ($P < 0.001$). No significant change in plaque size was noted. Among 28 patients with erectile dysfunction, 18 (64.2%) had a marked increase in erection quality (IIEF score change: +4 for 10 patients, +6 for 4 patients, +8 for 2 patients, +9 for 2 patients).**

***Conclusion*: Our results support SWT as an effective and safe first-line treatment for Peyronie's disease.**

INTRODUCTION

PEYRONIE'S DISEASE was named after François de la Peyronie, who described the disease in detail in 1743.[1] Despite the long time that has elapsed since this description, the etiopathology of the disease remains unclear.[2] Consequently, definitive causal treatment is lacking, with all treatment options being symptom related.[2]

Bellorofonte and associates[3] and Butz[4] presented the first results of extracorporeal shockwave therapy (SWT) for Peyronie's disease. Subsequent studies were conducted with different types of lithotripters having variable effectiveness regarding pain alleviation, decrease of penile curvature, or improvement of sexual function.[5–18]

In the majority of these trials, various types of conservative treatment with limited or suboptimal results had preceded SWT. Although it is generally accepted that medical therapy is required in the early inflammatory, painful stage of the disease, there is no clear indication as to when other noninvasive or semi-invasive procedures have to be initiated. Furthermore, the question of whether conservative therapy is needed for nonresponders to drug therapy and for patients with calcified plaques who do not want surgery remains unanswered.

We present the results of a pilot study using SWT as a first-line treatment for patients with previously untreated Peyronie's disease.

PATIENTS AND METHODS

Forty patients with a mean age of 58.7 years (range 43–76 years) having previously untreated Peyronie's disease present for

[1]2nd Department of Urology, Sismanoglio Hospital, University of Athens, Athens, Greece.
[2]Andrological Institute, Athens, Greece.

a mean of 8 months (range 3–16 months) received SWT in a prospective study. Disease diagnosis was made from the patient's symptoms and physical examination. All patients were informed in detail about the therapeutic options for Peyronie's disease, and a signed consent form for SWT was obtained in every case.

The initial assessment involved administering the International Index of Erectile Function (IIEF) (Table 1) and a pain symptom score with a visual analog scale (VAS) on which 0 equaled no pain and 5 severe pain. Of these patients, 25 reported painful erections with a mean score of 3.29, and 28 had an IIEF score <18. Erection was achieved in all patients with an intracavernously injected angiodilating agent (alprostadil; Caverject, Pharmacia & Upjohn). The dose was titrated for each patient from 2.5 μg in 2.5-μg increments until a normal erection was achieved. The penis was then photographed and the penile angle measured with a goniometer by a urologist different from the one applying the treatment. The mean measurement was 45° (range 20°–68°). The size and site of the plaque were measured, the size being confirmed by ultrasonography.

Shockwaves were applied with a Dornier Epos Ultra Device having a joint arm for the therapy head that made it easy to move. The ultrasound system was equipped with a 7.5-MHz scanner for detecting the plaques and an isocentric-locating arm mounted on the therapy head. Palpation and ultrasonography were combined to locate the plaque. Of the 40 patients, 7 underwent two sessions and the rest three sessions. The time interval between treatments was 2 weeks. At a power level of 2 to 5 (mean 4), a maximum of 3000 shockwaves were applied per plaque per treatment.

The effect of SWT was evaluated by comparing the pain scores, IIEF scores, physical examination, and angle measurement on the photographs prior to and after treatment completion. Statistical analysis was performed with Student's *t*-test. Significance was set at $P < 0.05$

RESULTS

All patients completed the protocol. The follow-up was at least 3 months (mean 12 months).

Patient tolerance during the session was excellent. The mean VAS for pain during SWT was 0.65 (range 0–2). No significant side effects were observed. Two patients experienced penile bruising at the entry point of the shockwaves that disappeared within 48 hours. One patient had minor urethral bleeding.

Immediately after the first session, 12 patients (48%) with previous erectile pain noted a marked improvement, the mean reduction of the VAS being 2.8 ($P < 0.0001$) (Table 2). Nine more patients (36%) showed remission after the last treatment (score reduction 2; $P < 0.001$). This effect was sustained during follow-up. Eight patients (20%) showed complete remission of penile deviation. The deviation angle decreased >20° in 17 patients (42.5%), with a mean reduction of 35° (range 20°–60°) ($P < 0.001$). Nine patients (22.5%) without a decrease in penile deviation subjectively thought that the plaque was smoother. No penile-angle deterioration was noted among the patients throughout the follow-up.

TABLE 1. INTERNATIONAL INDEX OF ERECTILE FUNCTION (IIEF-5) QUESTIONNAIRE AND RESPONSE OPTIONS[a]

Over the past six months:					
1 How do your rate your confidence that you would get and keep an erection?	Very low	Low	Moderate	High	Very High
	1	2	3	4	5
2 When you had erections with sexual stimulation, how often were your erections hard enough for penetration?	Almost never/never	A few times (much less than half a time)	Sometimes (about half the time)	Most times (much more than half the time)	Almost always/always
	1	2	3	4	5
3 During sexual intercouse, how often were you able to maintain your erections after you had penetrated (entered) your partner?	Almost never/never	A few times (much less than half a time)	Sometimes (about half the time)	Most times (much more than half the time)	Almost always/always
	1	2	3	4	5
4 During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?	Extremely difficult	Very difficult	Difficult	Slightly difficult	Not difficult
	1	2	3	4	5
5 When you attempted sexual intercouse, how often was it satisfactory for you?	Almost never/never	A few times (much less than half a time)	Sometimes (about half the time)	Most times (much more than half the time)	Almost always/always
	1	2	3	4	5

[a]The IIEF-5 score is the sum of the ordinal responses to the five items; the score can range from 5 to 25.

TABLE 2. PATIENT CHARACTERISTICS AND OBJECTIVE CHANGES FOLLOWING SWT FOR PEYRONIE'S DISEASE

Variable	*Mean (range)*	P *value*
Age (years)	58.7 (43–76)	
Disease duration (months)	8 (3–16)	
Follow-up (months)	12 (3–18)	
Pain (VAS score)		
Before treatment	3.29 (2.5–4.3)	<0.001
After treatment	0.49 (0–2.3)	
Pain (VAS score) during treatment	0.65 (0–2)	
Penile angulation (degrees)		
Before treatment	45 (20–68)	<0.001
After treatment	10 (0–37)	
Plaque size		
Before treatment	1.5 (0.8–2.6)	0.65
After treatment	1.3 (0.7–2.1)	
IIEF		
Before treatment	16.5 (10–1)	0.06
After treatment	18.3 (14–22)	

Among the 28 patients with erectile dysfunction, 18 (64.2%) had a marked increase in erection quality. This was confirmed by a significant increase in the IIEF score (+4 for 10 patients, +6 for 4 patients, +8 for 2 patients, +9 for 2 patients). All of these 18 patients had received three sessions of SWT. For the overall population, the benefit to erection was marginally significant statistically ($P = 0.06$). After this SWT protocol, 9 of the 40 patients reported that the results were not what they desired and requested another type of treatment.

Ultrasonographic measurements of the plaque were unreliable: there was no correlation between the change in plaque size and any symptomatic improvement. In addition, ultrasonography did not detect seven plaques that remained easily palpable.

DISCUSSION

Various treatment methods, both medical and surgical, have been described for Peyronie's disease, but none has been entirely satisfactory.[2] Shockwave therapy for this purpose was first described in the 1980s, and several studies have evaluated its efficacy.[3–18] In all these studies, SWT followed the use of different types of conservative treatments; i.e., it was a second-line treatment option for medically refractory disease. Lebret and colleagues[5] proposed SWT as a first-line treatment, but as only 64% of their patients had had no previous treatment, and their results were mixed with those from the rest of the patients, only inferences could be drawn about SWT as a first-line treatment.

We have been using SWT as a first-line option for patients who present with Peyronie's disease and have received no prior treatment. Our results suggest that such use of SWT is safe and effective. During the follow-up, 84% of patients remained pain free, 62.5% experienced reduction of the penile curvature, and 64.2% had their sexual function improve.

Although minor trauma and an altered immune response to it is thought to be the underlying pathophysiologic mechanism of Peyronie's disease, the true etiopathology remains unclear.[2] As a consequence, causal treatment does not exist. In addition, the natural history of the disease is difficult to evaluate. Peyronie's disease traditionally has been characterized as a process with gradual spontaneous resolution. However, it seems that in most cases, it remains unchanged or has a progressive course.[19] Disease duration at presentation >2 years is associated with a lack of spontaneous resolution.[19]

The symptoms and signs of Peyronie's disease can be summarized into an early and a late phase. A patient in an early phase typically presents with a nodule or plaque, painful erection, penile deformity during erection, or some combination thereof. Late signs include a harder plaque, a stable penile deformity during erection, and erectile dysfunction. The cut-off point between these two phases remains unclear. Spontaneous improvement in pain usually occurs within 1 year, as the inflammation of the early acute phase is believed to settle.

Although it is generally accepted that conservative drug therapy is required in the early inflammatory, painful stage of the disease, there is no clear indication of when other noninvasive or semi-invasive procedures have to be initiated. Overall, medical therapies for Peyronie's disease have not resulted in a reliable cure rate, especially for penile deformity, which probably underlines the difficulty in restoring the elasticity of the tunica albuginea.[2] Local penile SWT has been proposed as topical therapy for Peyronie's disease. However, the rationale for this approach is not known. Experiments with SWT on pigskin have shown that shockwaves delivered at low energies stimulate wound healing.[20]

The overall success rate for SWT has been 54% to 76%.[3–18] The pain disappears in all patients once the disease process stabilizes, but this happens at variable time intervals after presentation. The disappearance of pain almost immediately after the start of treatment in 56%[18] to 100%[6] of patients in various studies is quite encouraging. In our study, the pain resolved in 84% of the patients with the completion of treatment, and all of these men remained pain-free during the follow-up period.

Various authors have reported that 0[6] to 75%[7] of patients have had improvement in their penile angulation. Our success rate is among the highest reported in the literature. Furthermore, 20% of our patients experienced complete remission of penile deviation. This may indicate an anti-inflammatory action or a supportive role in the wound healing process of the shockwave energy. Overall, we noted no significant decrease in plaque size. In the literature, plaque size decreased in 0[17] to 58%[11] of cases. Data on the extent of the plaque size decrease and on the significance of this finding are lacking. Subjective and objective evidence of sexual function improvement are presented for 12%[16] to 62%[7] of patients treated with SWT in various studies. Factors such as severe penile deformity preventing intercourse, a flail penis, psychological distress, and impaired penile vascular function contribute to erectile dysfunction. Whether SWT is acting in all these factors needs further investigation.

We realize the difficulty in drawing conclusions from stud-

ies such as ours. Although our protocol used objective measurements of change, the number of patients was small. In addition, given that a cohort of patients with Peyronie's disease will naturally see improvement in their pain and curvature during the course of the disease, the absence of a control group limits the ability to interpret data. The mean follow-up period in our study was slightly longer than in the reported studies, where it ranged from 1 to 9 months.[5–18] This time is considered by many experts to be too short to come to a definitive conclusion regarding SWT in Peyronie's disease or to offer it as a first-line treatment.

CONCLUSION

Shockwave therapy is a useful alternative to relieve painful erections and penile deviation in patients with otherwise-untreated Peyronie's disease. The impact on erectile function should be individually discussed with every patient. However, we believe that additional multicenter randomized studies with long-term follow-up are needed before SWT becomes accepted as one of the standard first-line treatments for Peyronie's disease.

REFERENCES

1. Peyronie F de la. Sur quelques obstacles qui s'opposent à l'éjaculation naturelle de la semence. Mém Acad R Chir 1743;1:425.
2. Gholami S, Gonzalez-Cadavid N, Lin Ch, Rajfer J, Lue TF. Peyronie's disease: A review. J Urol 2003;169:1234.
3. Bellorofonte C, Ruoppolo M, Tura M, et al. Possibilita di impiego del litotritore piezoelettrico nel trattamento delle fibrosi caverbosi gravi. Arch Ital Urol 1989;61:417.
4. Butz M. Treatment of Peyronie's disease by extracorporeal shock wave (ESW) [abstract]. J Endourol 1995;9(suppl):S-165.
5. Lebret T, Loison G, Herve J-M, et al. Extracorporeal shock wave therapy in the treatment of Peyronie's disease: Experience with standard lithotriptor (Siemens-Multiline). Urology 2002;59:657.
6. Kiyota H, Ohishi Y, Asano K, et al. Extracorporeal shock wave treatment for Peyronie's disease using EDAP LT-02: Preliminary results. Int J Urol 2002;9:110.
7. Mirone V, Imbimbo C, Palmieri A, et al. Our experience on the association of a new physical and medical therapy in patients suffering from induratio penis plastica. Eur Urol 1999;36:327.
8. Colombo F, Baroni P, Serrago M, et al. Shock waves in La Peyronie's disease: Two years' experience. Eur Urol 1997;35(suppl 2):124.
9. Colombo F, Serrago M, Esposito N, et al. Shock waves in La Peyronie's disease: Preliminary report. J Urol 1998;159(suppl):119.
10. Gianneo E, Nespoli R, Conti G, et al. La Peyronie's disease (PD) and extracorporeal shock wave therapy: Our experience [abstract]. J Urol 1999;161(suppl):205.
11. Abdel-Salam Y, Budair Z, Renner C, et al. Treatment of Peyronie's disease by extracorporeal shockwave therapy: Evaluation of our preliminary results. J Endourol 1999;13:549.
12. Hussain J, Lynn NNK, Jones DK, et al. Extracorporeal shock wave therapy in the management of Peyronie's disease: Initial experience. Br J Urol 2000;86:466.
13. Lebret T, Herve JM, Lugagne PM, et al. [Extracorporeal lithotripsy in the treatment of Peyronie's disease: Use of a standard lithotriptor (Multiline Siemens) on young (less than six months old) plaques] (Fre). Prog Urol 2000;10:65.
14. Hamm R, McLarty E, Ashdown J, et al. Peyronie's disease: The Plymouth experience of extracorporeal shock wave treatment. Br J Urol 2001;87:849.
15. Neururer R, Studen M, Maneschg C, et al. ESWT for the treatment of induratio penis plastica: Clinical outcome [abstract]. J Urol 2002;167(suppl):204.
16. Manikandan R, Islam W, Srinivasan V, et al. Evaluation of extracorporeal shock wave therapy in Peyronie's disease. Urology 2002:60:795.
17. Mitchel M-S, Ptaschuyk T, Musial A, et al. Objective and subjective changes in patients with the Peyronie's disease after management with shock wave therapy. J Endourol 2003;17:41.
18. Hauck EW, Hauptmann A, Bschleipfer T, et al. Questionable efficacy of extracorporeal shock wave therapy for Peyronie's disease: Results of a prospective approach. J Urol 2004;171:296.
19. Gelbard MK, Dorey F, James K. The natural history of Peyronie's disease. J Urol 1990;144:1376.
20. Haupt G, Chvapil M. Effect of shock waves on the healing of partial thickness wounds in piglets. J Surg Res 1990;49:45.

Address reprint requests to:
A. Skolarikos, M.D.
2nd Department of Urology
University of Athens.
6 Laskareos St.
Nea Zoi Peristeri
12137, Athens, Greece

E-mail: andskol@yahoo.com

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2. Grzegorz Lukasz Fojecki, Stefan Tiessen, Palle Jörn Sloth Osther. 2016. Extracorporeal shock wave therapy (ESWT) in urology: a systematic review of outcome in Peyronie's disease, erectile dysfunction and chronic pelvic pain. *World Journal of Urology* . [CrossRef]
3. P. Lukes, F. Fernández, J. Gutiérrez-Aceves, E. Fernández, U. M. Alvarez, P. Sunka, A. M. Loske. 2016. Tandem shock waves in medicine and biology: a review of potential applications and successes. *Shock Waves* **26**:1, 1-23. [CrossRef]
4. Michael Pan, Jason R. KovacThe Future of Erectile Dysfunction Therapy I: Implementation of Translational Research 99-107. [CrossRef]
5. James R. Craig, William O. Brant, James F. Smith, Tom F. LuePeyronie's Disease: Natural History, Diagnosis, and Medical Therapy 289-300. [CrossRef]
6. April Durant, Darryl MillisApplications of Extracorporeal Shockwave in Small Animal Rehabilitation 381-392. [CrossRef]
7. Karsten Knobloch. 2012. Die Operation ist nicht mehr die einzige therapeutische Option. *MMW - Fortschritte der Medizin* **154**:19, 36-37. [CrossRef]
8. Ege Can Serefoglu, Wayne J. G. Hellstrom. 2011. Treatment of Peyronie's Disease: 2012 Update. *Current Urology Reports* **12**:6, 444-452. [CrossRef]
9. Sentai Ding, Jiajü Lü, Hui Zhang, Lijing Wei, Kejia Ding. 2010. A novel modification of tunical plication by plaque thinning: long-term results in treating penile curvature of Peyronie's disease. *International Urology and Nephrology* **42**:3, 597-602. [CrossRef]
10. Alessandro Palmieri, Ciro Imbimbo, Nicola Longo, Ferdinando Fusco, Paolo Verze, Francesco Mangiapia, Massimiliano Creta, Vincenzo Mirone. 2009. A First Prospective, Randomized, Double-Blind, Placebo-Controlled Clinical Trial Evaluating Extracorporeal Shock Wave Therapy for the Treatment of Peyronie's Disease. *European Urology* **56**:2, 363-370. [CrossRef]
11. J HubbardPeyronie's disease 223-238. [CrossRef]
12. J F Smith, T J Walsh, T F Lue. 2008. Peyronie's disease: a critical appraisal of current diagnosis and treatment. *International Journal of Impotence Research* **20**:5, 445-459. [CrossRef]
13. Vassilis Poulakis, Konstantinos Skriapas, Rachelle Vries, Wolfgang Dillenburg, Nikolaos Ferakis, Ulrich Witzsch, Michael Melekos, Edward Becht. 2006. Extracorporeal shockwave therapy for Peyronie's disease: an alternative treatment?. *Asian Journal of Andrology* **8**:3, 361-366. [CrossRef]
14. 2005. LiteratureWatch. *Journal of Endourology* **19**:8, 1045-1062. [Citation] [Full Text PDF] [Full Text PDF with Links]