

·Clinical Experience·

Extracorporeal shockwave therapy for Peyronie's disease: an alternative treatment?

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Abstract

Aim: To determine retrospectively the safety and efficacy of extracorporeal shock wave therapy (ESWT) in patients with Peyronie's disease. **Methods:** Fifty-three patients with stable Peyronie's disease underwent ESWT (group 1). Fifteen patients matched with the baseline characteristic of the patients in group 1, who received no treatment, were used as the control (group 2). The patients' erectile function (International Index of Erectile Function [IIEF-5] score), pain severity (visual analog scale), plaque size and degree of penile angulation were assessed before and after the treatment in group 1 and during the follow-up in group 2. **Results:** The mean follow-up time was 32 months (range: 6–64 months) in group 1 and 35 months (range: 9–48 months) in group 2. All the patients were available for the follow-up. Considering erectile function and plaque size, no significant changes ($P > 0.05$) were observed in group 1 before or after the ESWT. A total of 39 patients (74%) reported a significant effect in pain relief in group 1 after ESWT. However, regarding improvement in pain, IIEF-5 score and plaque size, no significant differences were observed between the two groups. In 21 patients (40%) of group 1, the deviation angle was decreased more than 10° with a mean reduction in all patients of 11° (range: 6–20°). No serious complications were noted considering ESWT procedure. **Conclusion:** ESWT is a minimally invasive and safe alternative procedure for the treatment of Peyronie's disease. However, the effect of ESWT on penile pain, sexual function and plaque size remains questionable. (*Asian J Androl* 2006 May; 8: 361–366)

Keywords: erectile dysfunction; extracorporeal shockwave therapy; Peyronie's disease; penile curvature

1 Introduction

Peyronie's disease is a connective tissue disorder and

the most frequent cause of penile curvature. In addition, it affects the quality of life of patients, often resulting in penile pain, penile curvature and impotence. The etiopathology of the disease remains unclear, and the prevalence of the disease is 1–4%. It seems to be more common in white men aged over 40 years [1]. Despite the innovative investigations in cell culture with identification of potential biomarkers [2], no causal therapy is yet available. Surgical treatment (e.g. penile straightening with

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or without plaque resection and vein graft implantation) is the standard choice of treatment in cases of severe symptomatic angulation [3, 4].

Although a large-scale randomized clinical trial comparing treatments for Peyronie's disease is not yet available, several studies have reported that extracorporeal shock wave therapy (ESWT) is a useful alternative to relieve painful erections [5–15]. Almost all the abovementioned studies considered that ESWT is a non-invasive modality and appears to be a safe and effective procedure. Nevertheless, the mode of action of ESWT in Peyronie's disease remains unclear. Taking into account the fact that in most cases pain associated with Peyronie's disease is self-limiting [16], the vast majority of these studies suffer from methodological bias, because no control arm was used, and it is not possible to attribute treatment success to the treatment itself as opposed to a placebo effect [5–15].

The aim of our study was to evaluate the efficacy and the safety of ESWT as an alternative treatment in patients with Peyronie's disease. The treatment results were compared with a case-matched control group receiving no treatment.

2 Materials and methods

From January 2001 to March 2005, 53 patients (group 1) with Peyronie's disease were treated by ESWT. Patients with stable disease, palpable plaque, penile deviation and/or painful erections, for whom at least 6 weeks had elapsed since last failed medical therapy, and patients with at least 6 months of follow-up were included in the study. Patients with the disease in the active phase, who were younger than 20 years and had blood clot disorders, chronic aspirin intake or aspirin intake in the last 6 days were excluded. A signed consent form was obtained from each patient and the patients were informed in detail about the therapeutic options of Peyronie's disease. Detailed medical and sexual histories were obtained before ESWT. As a control, 15 patients (group 2) without previous therapy for the disease were found in our computerized patient data from the last 8 years and were evaluated retrospectively. All patients in group 2 were matched with the patients of the ESWT group regarding the baseline characteristics (Table 1).

Patients in group 1 with only minimal or without calcification of the plaque ($n = 21$, 40%) had undergone previous drug therapy. Nine patients (17%) previously re-

Table 1. Baseline patient characteristics. ESWT: extracorporeal shockwave therapy; NS: not significant.

	ESWT (group 1)	Control (group 2)	<i>P</i>
No. patients	53	15	–
Age (years; mean \pm SD)	55.4 \pm 6.5	56.7 \pm 7.7	NS
Mean duration of disease (months, range)	11.4 (6.5–15.4)	9.7 (7.2–17.6)	NS
Painful erections (<i>n</i> , %)	48 (91)	11 (79)	NS
Prior therapy (<i>n</i> , %)	21 (40)		
Vitamin E	12 (23)	0	–
Potassium aminobenzoate	9 (17)		

ceived potassium p-aminobenzoate (Potaba-Glenwood®, Kapsel 500 mg, [Glenwood GmbH, Starnberg, Germany]; 12 g daily), and 12 patients (23%) had received vitamin E. Subsequently deterioration or no potential benefit of medical drug therapy was mentioned. Thus, these patients were included in the protocol for ESWT treatment. The group 2 had never been treated before.

Patients were asked about the duration of the disease, pain during erection and the quality of erection. The initial assessment involved administering the International Index of Erectile Function (IIEF-5) score. Patients estimated the severity of their pain during erection with a visual analog scale (VAS) score ranging from 0 to 10, with 0 being no pain and 10 being severe pain. The diagnosis was made from patient history and physical examination. The stable phase of the disease was defined the painless palpation of the plaque in the non-erect penis, the presence of the disease for longer than 6 months and unchanged symptoms during an additional 3 months, and the disappearance of pain during flaccidity [5].

The angle of penile curvature was documented before and after treatment using objective photographic pictures (not self-made, using a Polaroid camera device) from three different angles (frontal, lateral and above) during artificial erection. In all patients, erection was achieved using an intracavernosal injection with alprostadil (Caverject, Pharmacia & Upjohn, Karlsruhe, Germany) starting with 10 μ g and titrated up to 20 μ g until full erection. The penile angle was measured with a goniometer by a urologist during artificial erection. Plaque size and site were determined by palpation and ultrasound. A 7.5 MHz Siemens linear transducer (Siemens Sonoline Sienna, Germany) was used to confirm the calcifications.

Shock waves were applied with the Piezason 100

lithotripter (Richard Wolf, Knittlingen, Germany). Each patient completed a minimum of three sessions and most of the patients underwent five treatment sessions at weekly intervals. A dose of at least 2 000 shock waves was delivered in each patient at an energy density of 0.07–0.17 mJ/mm² at each treatment session. The procedure started with a low energy flow density of 0.07 mJ/mm² up to 0.17 mJ/mm² during the first 200 impulses. ESWT was performed without sedation or anesthesia and during the procedure the penis was fixed between the legs of the patient.

At 1, 3 and 6 month during the follow-up, the objective penile status was re-evaluated with an artificial erection and patient symptoms documented with the aforementioned standardized questionnaires.

The measurements of penile angulation and plaque dimensions were performed by two experienced independent examiners. Every measurement was repeated by either examiner blinded for the previously determined result in order to calculate the inter- and intra-observer variability. We evaluated the inter- and intra-observer agreement with the cronbach coefficient alpha (α), where $\alpha > 0.80$ was considered to be consistent with excellent agreement, and values of 0.70–0.80 or 0.50–0.80 to represent good or moderate agreement, respectively. The final value was a consensus value between the two examiners. For continuous variables, the paired *t*-test was used and for categorical variables, the χ^2 or the Fisher's exact test was applied. Commercial statistical software (SPSS 12.0, Chicago, IL, USA) was used. $P < 0.05$ was considered statistically significant.

3 Results

Patient characteristics are summarized in Table 1. In both groups, all patients completed the protocol. The mean follow-up time was 32 months (range: 6–64 months) in the ESWT group and 35 months (range: 9–48 months) in the control group.

In the ESWT group, 21 patients (40%) had an unsuccessful (deterioration or no potential benefit) previous drug therapy for Peyronie's disease. During the procedures, the mean VAS for pain was 1 (range: 0–2). Seven patients (13%) complained of mild pain at the entry point of the shock waves. The pain disappeared after the first 5 min. No significant side-effects of ESWT were observed and all patients tolerated the treatment well. Sixteen patients (30%) developed superficial penile bruising but for a period shorter than 48 h. In all of our patients, the plaques

were located on the dorsal penile surface. No plaque was found on the ventral penile surface or near to the urethra.

In the ESWT group, the disease duration of 21 patients (40%) was shorter than 12 months. Forty-eight patients (91%) reported painful erections before ESWT. Patients with disease longer than 12 months reported pain scores that were not statistically ($P = 0.09$) different from those with a duration shorter than 12 months. All but nine patients (17%) with painful erections reported a reduction in pain at the end of the treatment. Thus, in 74% of the total patients ($n = 39$) a significant effect in pain relief was achieved. With regard to pain, with the completion of treatment 33 patients (62%) were completely pain free. Overall, the pain disappeared after the first two therapy sessions in 28 patients (53%). In the control group, 57% of patients ($n = 8$) had no pain at the end of the follow-up period. Thus, no significant difference in pain disappearance was seen between the two groups ($P = 0.214$).

In the ESWT group, the overall improvement in penile angulation was 57% ($n = 30$, Table 2). In 21 patients (40%), the deviation angle was decreased more than 10°. The mean angulation reduction was 11° (range: 6–20°). The duration of the disease did not affect the reduction of penile angulation ($P = 0.113$). The improvement in angulation was verified by photographs taken after the treatment. In four patients (8%) the penis was almost straight at the early follow-up period (at 1 month). During the follow-up no penile angle deterioration was noted among the patients in ESWT group. In the control group, no significant difference regarding penile angulation was observed during the follow-up.

In group 1, the IIEF-5 scores before and after ESWT remained almost unchanged ($P = 0.205$, Table 2). Concerning tumescence and rigidity, there were no significant differences before or after ESWT ($P > 0.1$). Similarly, in group 2, no significant changes were seen during the follow-up period (Table 2). Among the 18 patients (34%) of the ESWT group with erectile dysfunction, the IIEF-5 score increased significantly only in five patients (28%). At the end of treatment, 32 (60%) of the 53 patients in ESWT group reported that the results were not what they desired and requested another type of treatment.

Concerning plaque size, there were no significant differences before or after ESWT in group 1 and during the follow-up period in the group 2 ($P = 0.064$ and $P = 0.28$, respectively, Table 2). In both groups, no patients de-

Table 2. Comparison of objective changes following ESWT and during the follow-up. *P*[†] of comparison objective changes after ESWT and during follow-up in control group; ESWT: extracorporeal shockwave therapy; IIEF-5: International Index of Erectile Function; NS: not significant; VAS: visual analog scale.

	ESWT (group 1)			Control (group 2)			<i>P</i> [†]
	Before ESWT	After ESWT	<i>P</i>	At baseline	After follow-up	<i>P</i>	
Pain (VAS; median, range)	6 (4-8)	1 (0-4)	< 0.001	6 (4-8)	2 (0-5)	<0.001	NS
Plaque size (mm ² ; median, range)	515 (80-900)	476 (50-850)	NS	489 (55-790)	470 (45-770)	NS	NS
Angulation (degrees; mean, range)	44° (25–64°)	35° (15–46°)	< 0.001	42° (22–58°)	40° (15–58°)	NS	<0.001
Intercourse (<i>n</i> , %)							
Possible	21 (40)	28 (48)		6 (43)	7 (50)		
Moderate	14 (26)	14 (26)	NS	5 (36)	4 (29)	NS	NS
Impossible	18 (34)	14 (26)		3 (21)	3 (21)		
IIEF-5 (mean, range)	11 (8–19)	12 (8–18)	NS	10 (7–20)	12 (9–17)	NS	NS

veloped any new plaque calcification or progression of it during the follow-up. In the ESWT group, the plaque size decreased in 38% (*n* = 20) of the total patients. Overall, in only five patients (9%), the plaque was not palpable after ESWT. In addition, there was no correlation between the change in plaque size and any symptomatic improvement (*P* = 0.106). In general, the ultrasonographic measurements of the plaque were inaccurate. In the ESWT group, the ultrasound did not detect six plaques (sensitivity of ultrasound in diagnosis of plaques: 89%) that were easily palpable even by the patients.

There was an excellent inter- and intra-observer agreement in the measurement of penile angulation (α = 0.88 and 0.85, respectively) and plaque dimensions (α = 0.84 and 0.81, respectively).

4 Discussion

Similar to other cases, our results suggest that the use of ESWT is safe [6–8]. No major ESWT-related complications occurred in any of the patients and no serious side-effects have been reported. In 74% of the total patients (*n* = 39) a significant effect in pain relief was achieved. In regard to pain, with the completion of treatment, 62% of the patients were completely pain free. Overall, the pain disappeared after the first two therapy sessions in 53% of the patients. Although in Peyronie's disease it is generally accepted that pain diminishes with time, an effect of the natural disease course [16], it seems that ESWT did reduce pain on erection and it has an immediate therapeutic effect [5, 6]. However, all these published studies should be evaluated with great caution because none of them was a case-matched control study.

In the literature, only one prospective study with control group exists [15], and in concordance to our findings it showed no significant difference in pain relief between the ESWT and control group.

Concerning changes in plaque size and in accordance with previously published data [12, 13], in our study the plaque size decreased in 38% (20/53) of cases. Overall, in only five patients the plaque was not palpable after the treatment. In contrast to Bauman and Tauber [14], we did not find increase in calcification during the follow-up period in the present study. To our knowledge, only one study has reported a complete disappearance of the calcifications [15].

In the current study, the overall improvement in penile angulation was 57% (30/53). Furthermore, complete remission of penile deviation was experienced in four of the present patients (8%). In the literature, several authors have reported a decrease in penile curvature of more than 30% in their patients [6, 10, 13, 15]. In contrast to other studies [6, 8, 10], in the present study, a standardized protocol was followed, and the angle of penile curvature was documented in all patients after treatment using photographic documentation during artificial erection.

Unfortunately, the evaluation of quality of sexual intercourse after therapy for Peyronie's disease is very difficult. In the present study, we used a validated questionnaire (IIEF-5) for the quality of sexual intercourse. Many studies showed a significant improvement in this respect [6, 8, 12]. In the present study, the overall improvement was 9%. Interestingly, although most of the patients reported reduction in pain on erection, only five patients reported better results with their erection status

after the end of therapy. Furthermore, patients reported that the loss of distal rigidity was not improved after the treatment.

No protection was necessary from damage over the urethra because in all patients the plaque was located on the dorsal penile surface. In the present series no macroscopic urethral bleeding was seen. Except for the fact that no ESWT was applied ventrally, the main reason for the absence of any urethral bleeding in the present series may be the low energy of shock waves. Furthermore, according to the manufacturer instructions, the Lithotripter Piesozon 100 is specialized for the application of shock waves in only a superficial manner (according to the manufacturer, absorption of > 95% of energy occurred in < 1 cm). Contrarily, using another type of lithotripter and applying almost double energy of shock waves, Hauck *et al.* [15] observed 21% of urethral bleeding. However, these authors did not mention the location of penile plaque and the relation of plaque to the urethra.

Although, several authors have suggested that drug therapy should be the choice of treatment in the early phase of the disease [17], no conservative therapy has been found to be effective. For Peyronie's disease surgery remains the mainstay of treatment. However, surgical therapy has some disadvantages such as penile shortening, risk of de novo impotence, or formation of granuloma [18, 19]. Many patients found the excessive shortening of the penis unacceptable. Furthermore, due to formation of suture granuloma or discomfort from non-absorbable sutures, reoperation may be necessary in many patients [20]. From this point of view, surgery is not always the ideal solution for treating Peyronie's disease. Furthermore, many patients do not want to undergo an invasive procedure. Thus, an alternative procedure such as ESWT seems to be promising. The different outcomes in treatment groups from all studies can be explained by technical aspects, like the type of patient evaluation, the mean follow-up and the type of lithotripter.

The present study has several limitations. It is a retrospective, non-randomized case-control study. The numbers in the control group were small. However, the patients were well-matched between the two groups regarding the baseline characteristics. Furthermore, the mean follow up of 32–35 months (range: 6–64 months) is short for this chronic disease. We used a specialized ESWT device (with relative low-energy settings), which was not used in previous clinical study. Taking into ac-

count the natural history of Peyronie's disease and the fact that ESWT is becoming more popular for the treatment of this disease, a multicenter, prospective, randomized study in large patient groups using the same ESWT device with the same settings is mandatory.

5 Conclusion

ESWT seems to be a simple and safe alternative therapy for treating Peyronie's disease. The results of the present and previous studies clearly show that ESWT is well-tolerated without severe complications. However, in the present retrospective case-control study, after ESWT no significant changes in pain, plaque size or sexual function were observed. The improvement of penile angulation seems to be the potential effect of ESWT treatment. However, we suggest that, for the evaluation of penile curvature, an intracavernosal injection before and after therapy should be considered. Furthermore, prospective, randomized studies with longer follow-up and larger number of cases in this special group of patients are necessary.

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