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Extracorporal Shock Wave Therapy in the Treatment of Peyronie's Disease

First Results of a Case-Controlled Approach

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Key Words

Peyronie's disease · Extracorporal shock wave therapy · Case control

Abstract

Objective: To test whether extracorporal shock wave therapy (ESWT) has an effect in the treatment of Peyronie's disease.

Methods: 22 patients with Peyronie's disease and previous unsuccessful oral drug therapy were treated with ESWT in a prospective design with a follow-up of at least 3 months; 23 agematched patients without previous therapy received oral placebo drug for 6 months daily as control. The standard follow-up included palpation, ultrasound, autophotography and evaluation of symptomatology based on a symptom score. The shock waves were applied under ultrasound guidance using the 'Storz Minilith SL1' lithotripter.

Results: The results show a significant decrease in penile curvature in the patients treated with ESWT. Concerning the decrease in pain, subjective improvement and improvement in the quality of sexual intercourse, there was no significant difference to the case-control group. The inhomogeneity of the 2 groups may influence these results due to the questionable varying natural history.

Conclusions: A prospective, controlled multicenter study with standardized parameters (concerning technique and patients) is urgently required to test the effect of ESWT.

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Introduction

Peyronie's disease is a connective tissue disorder. The tunica albuginea and the adjacent erectile tissue are affected by localized plaque. Early inflammatory stages show thickening of the tunica, while later on fibrotic, often calcified

plaque is typical [1]. The plaque is mostly unifocal and located in the penile dorsum, covering an area of about 1.5–3 cm [2].

In the acute inflammatory phase, patients suffer from pain during flaccidity and/or during erection and sexual intercourse. Besides pain, a predominantly dorsal deviation is

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the main symptom, in later stages it can be combined with erectile dysfunction or distal flaccidity [2].

Although Peyronie's disease was already described in 1743 by François de la Peyronie [3], the etiopathology still remains unclear. A number of different theories, such as penile trauma, various forms of medication as well as genetic, autoimmunological and infectious reasons are being discussed [4].

Due to this lack of concrete knowledge, no causal therapy is available, and therefore all therapeutic trials remain symptom-directed and are of questionable efficacy in most cases because of the lack of a double-blind placebo trial [5]. Only potassium p-aminobenzoate (Potaba®) was proved in a double-blind randomized study [6] to have an effect in noncalcified plagues. For intralesional therapy, none of the substances used so far (e.g. verapamil, interferon-α2b, dexamethasone, superoxide dismutase and collagenase) has shown a long-term effect in a similar controlled approach [5]. Furthermore, there is no clear indication as to when (i.e. in which stage of the disease) semi-invasive and surgical procedures have to be initiated. It seems to be generally accepted that conservative therapy is required in the earlier inflammatory, painful stages [5]. The question of whether conservative therapy is needed for nonresponders to drug therapy and for patients with calcified plagues who do not want surgery remains unanswered. On the other hand, surgery (e.g. penile straightening with or without plaque resection) can be performed in case of severe angulation without loss of erection [7]. If Peyronie's disease is combined with erectile dysfunction, usually the insertion of a penile prosthesis is the first-line therapy [7]. Nevertheless, in these cases as well, many patients ask for other therapeutic modalities following disappointing results of drug and intralesional therapy.

Extracorporal shock wave therapy (ESWT) is the gold standard in the urological treatment of urolithiasis [8]. Occasionally, stones in other organs such as salivary glands have also been treated successfully [9]. ESWT was likewise introduced in the treatment of calcified and noncalcified orthopedic diseases [10–12]. Currently, ESWT is used in the treatment of tennis and golfer's elbow, calcaneal spur and a complex called 'periarthritis humeroscapularis' [12]. Furthermore, ESWT is carried out in pseudoarthrosis due to a proven osteogenetic effect [12]. Apart from its obvious clinical effect, the action mechanisms are unclear. An improvement in vascularization with consecutive resorption of calcification has been discussed as one possible mechanism of ESWT [13]. With regard to non-calcified diseases, a change in the milieu of the free radicals or a direct disturbance of the pain receptors could be the reason for the pain-relieving effect [11, 12].

First results of ESWT in Peyronie's disease were presented by Butz and Teichert [14] who used a 'Storz Minilith SL1' to treat 52 patients. They achieved an improvement in symptoms of pain (83%), deviation (40%) and sexual intercourse (40%). Further studies, conducted with different lithotripters, resulted in an alleviation of pain in 83–100%, a decrease in deviation in 25–68% and an improvement in the quality of sexual intercourse in 43 to 62% of the cases [15–19].

In all the above-mentioned studies, different types of lithotripters, different numbers of settings and different intervals between the settings were obvious. Moreover, the number of impulses and the energy rate was different, thus demonstrating that ESWT in Peyronie's disease is still not standardized and must be considered as an interesting, but clinically experimental, form of therapy [20].

These conflicting results from the first studies using ESWT in the treatment of Peyronie's disease [14, 15, 21] prompted us to treat patients with ESWT in a case-controlled manner [22], because treatment of Peyronie's disease has to be correlated with the natural history of the disease which demonstrates spontaneous changes including improvement and deterioration of the known symptoms [23–25].

Patients and Methods

22 patients with Peyronie's disease were treated with ESWT in a prospective design. The follow-up, for which 20 patients were available, was at least 3 months after the start of therapy. As controls, 23 age-matched patients without previous therapy were evaluated. The basic data before treatment of both groups are given in table 1. The data for average age, average deviation, average plaque size, pain during flaccidity and erection and the score for tumescence and rigidity were similar. Significantly different were the median case history with 12 versus 6 months (p<0.001), the rate of calcification with 12/20 patients versus 0/23 patients (p<0.001), and the quality of sexual intercourse (p = 0.019). All ESWT patients had undergone previous unsuccessful drug therapy. 18 patients previously received potassium p-aminobenzoate (Potaba®), and 2 patients vitamin E. The casecontrol group had not been treated before.

Technically, the clinical evaluation followed the standardized proposal of our Peyronie's disease study group [2]. Plaque size was determined as the product of length and width (mm²), following measurement with a caliper or ruler [2]. The curvature (degree of angulation) was documented before and after treatment by means of self-photography by the patient with an erection using the Kelâmi [26] technique and/or during an intracavernous pharmacon injection test. A successful outcome of therapy (i.e. decrease in curvature) was only assumed if the deviation angle showed a reduction of >30% to the state before therapy. The calcification, shown as a hyperechogenic dot with shadowing, was evaluated by high-frequency ultrasound (Kretz Combison 420, 7.5 and 10 MHz). Concerning symptomatology, the

Table 1. Basic pretreatment data: ESWT versus case-control group

	ESWT group	Case-control group
Patients, n	20	23
Average age, years	50.9 (38-59)	52.9 (27-70)
Average history, months*	12 (3–93)	6 (1–12)
Average plaque size, mm ²		
$(length \times width)$	182.9 (42–750)	243.7 (15-869)
Patients with deviation, n	20/20 (100%)	14/23 (61%)
Average deviation, degree	41.8 (10-90)	45.9 (15-90)
Calcification*	12/20 (60%)	0
Pain during flaccidity, n	3/20 (15%)	2/23 (9%)
Pain during erection, n	9/20 (45%)	11/23 (48%)
Quality of sexual intercourse, n*		
Possible	1/20 (5%)	9/23 (39%)
Moderately restricted	9/20 (45%)	4/23 (17%)
Severely restricted	5/20 (25%)	8/23 (35%)
Impossible	5/20 (25%)	2/23 (9%)
*Significantly different finding	gs.	



Fig. 1. Lithotripter 'Storz Minilith SL1'.

patients were asked about the presence or absence of pain during flaccidity and erection. The subjective quality of sexual intercourse was evaluated with the help of a score by asking the patient if coitus was possible, moderately restricted, severely restricted or impossible. This subjective score does not differentiate between impaired sexual intercourse due to a mechanical difficulty resulting from altered penile geometry or a rigidity deficit. Additionally, we asked the patients about the quality of tumescence and rigidity during erection according to the score suggested by Bähren and Stief [27]: E0 = no tumescence, no rigidity; E1 = little tumescence, no rigidity; E2 = moderate tumescence, no rigidity; E3 = full tumescence, no rigidity; E4 = full tumescence, moderate rigidity, and E5 = full tumescence, full rigidity.

ESWT was only applied to those patients who did not respond to previous therapy because we did not want to carry out first-line therapy at the clinical experimental level. Patients with and without calcified plaques were accepted. For the case-control group, we only included patients without previous therapy and without calcification.

The shock waves were applied under ultrasound guidance using a 'Storz Minilith SL1' lithotripter (Storz Medical AG, Kreuzlingen, Switzerland; fig. 1). The treatment consisted of two sessions within 3 days. If an improvement in the symptoms was observed, ESWT was repeated after 3 months. Per session, 2,000 high energetic shock waves were applied with a maximum energy level of 7. This is equivalent to an energy flow density of 0.35 mJ/mm². The emission frequency was 120 shocks/min. Generally, a catheter (16 french) was inserted during treatment for better fixation in the optimal position. The first 10 patients were treated as inpatients under analgesicsedation. With growing experience and because the ESWT was well tolerated, we switched to an outpatient modus without sedation.

For the follow-up, the patients of both groups presented at 3 months. Concerning ESWT, we lost 2 patients to follow-up. This means that we obtained data on 20 of 22 treated patients. In the case-

control group, no dropouts were noted during the follow-up period of 6 months.

The effect was evaluated by measuring the plaque size, the deviation by photodocumentation using the Kelâmi technique, and the calcification by high-frequency ultrasound. The subjective symptoms, e.g. pain during flaccidity/erection and quality of sexual intercourse, were assessed using the above-mentioned symptom evaluation scheme.

A statistical analysis was carried out, using nonparametric tests for descriptive analysis, based on the Mann-Whitney U test and the Kruskal-Wallis test. The effect of ESWT and in the case-control group on the change in plaque size and change in deviation was evaluated by comparing the data before and after treatment.

Results

20 of 22 patients treated with ESWT were available for follow-up. Of the case-control group, all 23 patients could be evaluated. The average follow-up was 8.5 months in the ESWT group and exactly 6 months in the case-control group.

There were no severe side effects under ESWT. Skin hemorrhage was seen in 4 of 57 sessions (7%), and slight urethral bleeding in 12 of 57 sessions (21%).

In the ESWT group, the plaque disappeared in 2 of 20 patients (10%) versus 3 of 23 patients (13%) in the case-control group. After ESWT, the calcification was no longer

Table 2. Development of plaque size and deviation under ESWT versus case-control group (mean, range)

	ESWT group (n = 20)	Case-control group (n = 23)
Plaque size, mm ² Before treatment After treatment	182.9 (42–750) 205.6 (0–746)	243.7 (15–869) 205.7 (0–605)
Deviation, degree Before treatment After treatment	(n = 20/20) 41.8 (10–90) 30.8 (0–60)	(n = 14/23) 45.9 (15–90) 45.0 (0–90)

Table 3. Development of pain under ESWT versus case-control group

	ESWT group (n = 20)	Case-control group (n = 23)
Penile pain during flaccidity Before treatment After treatment	3/20 (15%) 1/20 (5%)	2/23 (9%) 3/23 (13%)
Penile pain during erection Before treatment After treatment	9/20 (45%) 4/20 (20%)	11/23 (48%) 6/23 (26%)

evaluable by ultrasound in 1 of 12 patients (8.3%) with calcified plaques at the end of the observation period. In the case-control group after 6 months, 1 of 23 patients (4.3%) with primary noncalcified plaques had developed a new calcification.

The average plaque size (table 2) in the ESWT group increased from 182.9 mm^2 before treatment to 205.6 mm^2 after treatment; this change was not significant (p = 0.907). In the case-control group, there was a nonsignificant (p = 0.136) decrease in the average plaque size from $243.7 \text{ to } 205.7 \text{ mm}^2$.

In the ESWT group, 10 of 20 patients showed a decrease in curvature of >30% of the previous deviation angle versus 3 of 14 patients (21%) in the case-control group (table 2). The average dorsal deviation decreased in the ESWT group from 41.8 to 30.8° with a borderline statistical effect (p = 0.052). There was also a change in the average dorsal deviation in the case-control group from 45.9° before treatment to 45.0° after treatment without statistical relevance (p = 0.513).

Based on the statements of the patients, an overall subjective improvement was evident in 13 of 20 (65%) due to ESWT versus 12 of 23 (52%) in the case-control group. Theses data were not significantly different (p = 0.610). The data concerning pain during flaccidity and erection are given in table 3. There was no significant effect on pain during flaccidity and erection in either the ESWT or the case-control group. The data concerning the development of quality of sexual intercourse are given in table 4. The changes in both groups compared before and after treatment were not significant. Concerning tumescence and rigidity there were no significant differences according to the score mentioned [27] between the ESWT group (average at start E4.7 vs. E4.5 after treatment) and the case-control group (E4.6 vs. E4.7).

Table 4. Development of the quality of sexual intercourse under ESWT versus case-control group

	ESWT group (n = 20)	Case-control group (n = 23)
Quality of sexual intercourse		
before treatment		
Possible	1/20 (5%)	9/23 (39%)
Moderately restricted	9/20 (45%)	4/23 (17%)
Severely restricted	5/20 (25%)	8/23 (35%)
Impossible	5/20 (25%)	2/23 (9%)
Quality of sexual intercourse		
after treatment		
Possible	4/20 (20%)	13/23 (56%)
Moderately restricted	9/20 (45%)	3/23 (13%)
Severely restricted	2/20 (10%)	5/23 (22%)
Impossible	5/20 (25%)	2/23 (9%)

Discussion

Peyronie's disease is an inflammatory condition characterized in the early stage by fibrosis and in progressive disease by calcification. It is similar to orthopedic soft tissue diseases like golfer's elbow or 'periarthritis humeroscapularis' [12]. As in orthopedic administrations [10–12], the indication for ESWT in Peyronie's disease may be the presence of noncalcified and calcified plaques [12] with an effect on pain relief [11, 12]. Since Peyronie's disease leads to varying complaints, the goal of ESWT therapy has to be defined before treatment. Hypothetically, therapy could focus on a reduction in plaque size with a consecutive decrease in the deviation angle and improvement in the ability to have sexual intercourse. A decrease in pain could be discussed as a further target of therapy, but this subjective

Table 5. Results of previous studies concerning treatment of Peyronie's disease with ESWT

	Baumann and Tauber [15]	Butz and Teichert [14]	Colombo et al. [16]	Gianneo et al. [17]	Michel et al. [18]	Sautter et al. [19]
ESWT	Wolf Piezolith 2500	Storz Minilith SL1	Storz Minilith SL1	Storz Minilith SL1	Storz Minilith SL1	Dornier Epos Ultra Device
Number of patients	18	52	86	153	25	15
Age, years	54 (39–64)	55 (24–74)	? (34–74)	? (31–76)	54 (?)	57 (?)
Average history, months	18.1 (12–60)	?	?	?	30.9 (?)	?
Mean follow-up, months	14 (3–29)	9 (?)	?	?	1	?
Plaque calcification	17/18 (94%)	?	32/86 (37%)	136/153 (89%)	?	?
Plaque size Decrease No change Increase	5/18 (28%) 8/18 (44%) 5/18 (28%)	? ? ?	? ? ?	82/153 (54%) ? ?	5 (20%) 13 (65%) ?	? ? ?
Deviation decrease	5/18 (28%)	21/52 (40%)	18/72 (25%)	102/151 (68%)	19/25 (76%)	?
Pain intensity, no more pain	10/10 (100%)	15/18 (83%)	32/34 (94%)	48/50 (96%)	14/15 (93%)	7/9 (77%)
Quality of sexual intercourse improved	6/14 (43%)	10/21 (48%)	?	46/74 (62%)	5/25 (20%)	6/14 (43%)
General improvement (subjective opinion)	8/18 (44%)	28/52 (54%)	62/86 (72%)	103/153 (67%)	?	9/15 (60%)
Side effects Skin hematoma/hemorrhage Urethral bleeding	2/18 (11%) ?	? (75%) ? (6 %)	9/86 (10%) 1/86 (1%)	1 (?) 1 (?)	? (90%) ? (30%)	?

symptom needs special evaluation with careful monitoring due to the high degree of spontaneous relief in the early stage [23, 24]. Typically, remission of Peyronie's disease in the early stage has been reported in nearly 40% [23, 25], overall spontaneous regression has been seen in 13%, stable disease in 47%, and progression in 40% of the cases [24]. Therefore, every treatment success for this special condition raises the question of whether the effect is within the natural range or actually due to the efficacy of the trial [5].

With regard to the use of ESWT in the treatment of Peyronie's disease, the results of most of the initial studies [14, 16, 17, 19] do not provide exact data about case history and stage of the disease. An exact history (18.1 months) is only given in the studies of Baumann and Tauber [15] and Michel et al. [18] (30.9 months). Information concerning calcification is missing in three series [14, 18, 19]. Data about previous therapy are not given in any of the other studies. On the basis of this rather complicated situation, we applied ESWT to treat 22 patients with Peyronie's disease and previous unsuccessful oral drug therapy, using 23 agematched patients as case controls. The most important dif-

ferences were that the patients of the ESWT group had received previous drug therapy and the case-controls had not. Thus, the patients undergoing ESWT had a longer case history with all the risks of chronification [24], which meant less favorable conditions for comparison. Nevertheless, there was no significant difference between the 2 groups concerning the main symptoms, e.g. plaque size and deviation angle.

With regard to possible risks, the first positive aspect of ESWT treatment is the lack of serious side effects. Urethral bleeding has been reported in 1% [16, 17], 5.7% [14] and 30% [18] of the patients. The observation of urethral bleeding in 21% of the patients in our series is explained by the insertion of a catheter at the beginning of our trial. After stopping this procedure, urethral bleeding was no longer observed. Due to the fact that urethral bleeding is a sign of urethral injury and can lead to strictures, we will carefully observe these patients during the next years using urodynamic studies.

Skin hemorrhage or hematoma have been reported with a frequency of between 1 and 90% [14, 16–18] (table 5).

We experienced the occurrence of small skin lesions in only 7%.

Complete disappearance of the plaque was seen in 10% of the ESWT patients versus 13% of the controls. This is not only comparable with the 9.1% reported by Gianneo et al. [17], but also with those patients who received no therapy [24]. This means that both figures are well within the range of the natural course of the disease [24]. Complete disappearance was neither observed [15] nor reported [14, 16, 18, 19] in any of the other studies. Complete disappearance of the plaque was reported in 39% of the patients in the natural follow-up [23].

The disappearance of calcification in 1 of 12 patients in the ESWT group and the appearance of new calcified formations in 1 of 23 men in the case-control group may reflect the natural history of the disease, although exact data concerning this problem are lacking [23–25]. No other study group has reported on a complete disappearance of the calcifications (table 5). Baumann and Tauber [15] demonstrated a decrease in calcifications in 4 cases and an increase in 4 further cases in their series of 17 men.

Concerning changes in plaque size, interestingly data are only given in three [15, 17, 18] of six previous studies (table 5). Gianneo et al. [17] report a decrease in 54%, Baumann and Tauber [15] in 28% and Michel et al. [18] in 20% of the patients, without giving exact data about the dimensions of plaque size diminution. Our results demonstrated an increase in the average plaque size in the ESWT group and a slight decrease in the case-control group, but these two findings were not significantly different. Of the studies dealing with the natural history of Peyronie's disease, only one [23] gives data on the development of plaque. A diminution of plaque was only seen in this study in 19% of the patients. Thus, all the above-mentioned alterations in plaque size could still be within the range of natural history.

Penile deviation decreased in 50%, of our ESWT patients with a decrease of >30% to the previous deviation angle, which is a borderline significant effect. In the control group, the average deviation angle did not change. A decrease in penile curvature of 25–76% has already been reported by other authors in 5 [14–18] of 6 studies (table 5). Quantifying this effect in a way similar to our approach, Baumann and Tauber [15] and Gianneo et al. [17] reported a decrease in penile curvature of more than 30° and more than 50% respectively. Unfortunately, the techniques of evaluating penile deviation are not standardized in all studies. They differ depending on interview results [16], measurement of deviation using photo documentation [17] and a routinely done intracavernosal pharmacon injection test with objectivation of deviation under maximal rigidity [18].

The other authors did not give detailed information about their method of measuring changes in deviation [14, 15, 18]. Recently, Michel et al. [18] pointed out that the therapeutic effects of ESWT on deviation depend mainly on the technique of objective assessment, suggesting that artificial erection is the best method.

The subjective response was 65% in our ESWT group versus 52% in the case-control group. Both figures range between the 44% and 72% given by most other studies [14-17, 19]. Interestingly, the development of pain, which is the most important subjective symptom, was different in our study to other investigators. Our results concerning the reduction in pain during flaccidity revealed a minimal nonsignificant difference, with better results in the ESWT group. Pain during erection decreased in both groups in the same range. Our figures concerning the decrease in pain during flaccidity and erection are contradictory to the studies reported previously. These ESWT studies report a complete disappearance of pain of up to 100% (table 5). Clearly, 'pain' depends on the stage of the disease [24]. In the early, inflammatory, stage, pain is seen in 50-70 % of patients [2, 28] with a high percentage of spontaneous resolution [24]. Unfortunately, a clear evaluation of the activity of the disease, based on its duration was not possible in most of the studies [14, 16, 17, 19]. As mentioned before, only two other studies [15, 18] give exact data on case histories of more than 12 months. Baumann and Tauber [15] reported on the relief of pain under ESWT in 10 of 10 patients with painful erections, although these patients had a relatively long median history of 18.1 months and pain provides evidence of a more active process of shorter history [23, 24]. This observation is absolutely contradictory to our findings and cannot be explained by the natural history of the disease [23, 24].

In the therapy of Peyronie's disease it is most difficult to evaluate the quality of sexual intercourse as a subjective symptom. Remarkably, all studies show an improvement in this respect, with our results at the bottom of the scale. The problem is to interpret these data without objective evaluation of the quality of sexual intercourse with the help of modern questionnaires [29], nocturnal penile tumescence measurements, and the response to injection tests. In our study, the improvement in the ESWT group (35%) was not substantially different from that in the case-control group (30%) judged by the score asking the patient for his own impression. Concerning tumescence and rigidity, there was no significant difference before and after treatment between the ESWT group and the controls, and moreover within the groups themselves.

In conclusion, the above discussion elucidates major problems in objectively judging the effects of ESWT especially with regard to the natural history, the definition of clear indications, and the interpretation of the outcome. The situation is further complicated by the use of different lithotripters. Baumann and Tauber [15] used the 'Wolf Piezolith 2500', Sautter et al. [19] the 'Dornier Epos Ultra Device' and the other groups the 'Storz Minilith SL1' [14, 16–18]. If the same lithotripter ('Storz Minilth SL1') was used, most of the application parameters concerning the energy level, number of impulses, number of sessions and the intervals between the sessions were different [14, 16–18], additionally worsening any comparative judgement of outcome.

Conclusions

ESWT shows no significant effect in patients with a history of Peyronie's disease lasting >1 year and previous ineffective drug therapy in a case-controlled approach concerning plaque size, calcification, pain, quality of sexual intercourse, and general subjective improvement. Concerning the decrease in curvature, there might be an effect. Individual patients may also benefit with respect to pain or an improvement in the quality of sexual intercourse. Regarding the natural history of Peyronie's disease [23–25], the interpretation of successful results should be very critical. Since ESWT is becoming more and more widespread in the treatment of Peyronie's disease, a controlled, multicenter, prospective and randomized study using the same ESWT device in the same setting is suggested in order to clarify which patients benefit from ESWT or which do not.

References

- Brock G, Hsu GL, Nunes L, von Heyden B, Lue TF: The anatomy of the tunica albuginea in the normal penis and Peyronie's disease. J Urol 1997;157:276–281.
- 2 Weidner W, Schroeder-Printzen I, Weiske WH: Sexual dysfunction in Peyronie's disease: An analysis of 222 patients without previous local plaque therapy. J Urol 1997;157:325–328.
- 3 De la Peyronie F: Sur quelques obstacles qui s'opposent à l'éjaculation naturelle de la semence. Mém Acad R Chir 1743;1:425–434.
- 4 Somers KD, Dawson DM: Fibrin deposition in Peyronie's disease plaque. J Urol 1997;157: 311, 315
- 5 El-Sakka AI, Lue TF: Peyronie's disease. Curr Opin Urol 1998;8:203–209.
- 6 Weidner W, Schroeder-Printzen I, Rudnick J, Krause W, Weiske WH, Drawz B, Rebmann U, Pastermadjeff L, Kallerhoff M, Lenk S, Sperling H, Kliesch S, Schnittker J, Aulitzky W: Randomized prospective placebo-controlled therapy of Peyronie's disease (IPP) with Potaba® (aminobenzoate potassium). J Urol 1999;161(suppl):205.
- 7 Levine LA, Lenting EL: A surgical algorithm for the treatment of Peyronie's disease. J Urol 1997;158:2149–2152.
- 8 Chaussy C, Eisenberger F, Wanner K, Forssmann F, Hepp W, Schmiedt E, Brendel W: The use of shock waves for the destruction of renal calculi without direct contact. Urol Res 1976; 4:175–181.
- 9 Iro H, Schneider H, Födra C, Waitz G, Nitsche N, Heinritz HH, Benninger J, Ell C: Shockwave lithotripsy of salivary gland stones. Lancet 1992;339:1333–1336.

- 10 Dahmen GP, Haupt G, Haist J, Loew M, Lüssenhop S, Rompe JD, Schleberger R: Die Extrakorporale Stosswellentherapie in der Orthopädie. Indikationen, Techniken, bisherige Ergebnisse und Empfehlungen. Konsensus-Papier der Arbeitsgruppe Orthopädische Stosswellentherapie, 2. Konsensus-Workshop der Deutschen Gesellschaft für Stoßwellenlithotripsie, Schloss Weitenburg, 1995.
- 11 Haupt G: Stosswellen in der Orthopädie. Urologe A 1997;36:233–238.
- 12 Haupt G: Use of extracorporal shock waves in the treatment of the pseudarthrosis, tendinopathy and other orthopedic diseases. J Urol 1997; 158:4–22
- 13 Heist J, von Keitz-Steeger D: Stosswellentherapie knochennaher Weichteilschmerzen Ein neues Behandlungskonzept; in Chaussy C, Eisenberger D, Jocham D, Wilbert D (eds): Die Stosswelle Forschung und Klinik. Tübingen, Attempto, 1995, pp 162–168.
- 14 Butz M, Teichert HM: Treatment of Peyronie's disease (PD) by extracorporal shockwaves (ESW). J Urol 1998;159(suppl):118.
- 15 Baumann M, Tauber R: Induratio penis plastica – Extrakorporale piezoelektrische Stosswellentherapie als neuer Therapieansatz. Akt Urol 1998:29:1–5.
- 16 Colombo F, Mantovani F, Patelli E, Pozzoni F, Pisani E: Shock waves in la Peyronie's disease: Two years experience (abstract 494). Eur Urol 1999;35(suppl 2):124.
- 17 Gianneo E, Nespoli R, Conti G, Comeri G: La Peyronie's disease (IPP) and extracorporal shock waves therapy (ESWT): Our experience. J Urol 1999;161(suppl):205.
- 18 Michel MS, Braun P, Sazova O, Musial A, Köhrmannn KU, Alken P: Shock-wave therapy for the treatment of Peyronie's disease: First clinical investigation for the objective determination of deviation improvement by means of artificial erection. J Urol 1999;161(suppl):262.

- 19 Sautter T, Bangerter U, Tullio S, Hauri D: Extracorporal shockwave (ESW) as a new effective treatment in Peyronie's disease. Eur Urol 1999;35:(suppl 2):124.
- 20 Weidner W, Müller S: Stellungnahme zur ESWT bei Induratio penis plastica. Urologe A 1998;37:107.
- 21 Colombo F, Serrago M, Esposito N, Patelli E, Mantovani F, Pisani E: Shock waves in la Peyronie's disease: The preliminary report. J Urol 1998;159(suppl):119.
- 22 Hauck EW, Altinkilic BM, Schroeder-Printzen I, Ludwig M, Weidner W: The extracorporal shock-wave in treatment of Peyronie's disease

 First results of a case controlled approach. Eur Urol 1999;35(suppl 2):68.
- 23 Furlow WL, Swanson HE, Lee RE: Peyronie's disease: A study of its natural history and treatment with orthovoltage radiotherapy. J Urol 1975;114:69–71.
- 24 Gelbard MK, Dorey F, James K: The natural history of Peyronie's disease. J Urol 1990;144: 1376–1379.
- 25 Poutasse EF: Peyronie's disease. J Urol 1972; 107:419–422.
- 26 Kelâmi A: Autophotography in evaluation of functional penile disorders. Urology 1983;21: 628–629.
- 27 Bähren W, Stief CG: Intrakavernöse Pharmakontestung SKAT-Test; in Bähren W, Altenwein JE (eds): Impotenz. Stuttgart, Thieme 1988.
- 28 Byström J, Rubio C: Induratio penis plastica. Peyronie's disease. Clinical features and etiology. Scand J Urol 1975;10:12–20.
- Rosen RC, Riley A, Wagner G, Osterloh IH; Kirkpatrick J, Mishra A: The international index of erectile function (IIEF): A multidimensional scale for assessment of erectile dysfunction. Urology 1997;49:822–830.

Editorial Comment

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This well-presented and methodologically careful study shows the outcomes of extracorporeal Shock wave therapy (ESWT) in patients with induratio penis plastica.

I appreciate the effort made to standardize a clinical method that, however, must still be considered experimental, both in terms of therapeutic results and the number and intensity of applications.

The work shows clearly the main difficulty in evaluating the real efficiency of ESWT of induratio penis plastica: the two different techniques used in this article and the inclusion criteria are different from most of the studies already reported in the scientific literature.

I feel, however, that a consensus on treatment methodology has still not been reached because if, on the one hand, there is merit in using a control group, on the other hand this group is not exactly comparable to the study group. I believe, instead that the control group is not homogeneous, either in terms of its background (the study group is in an advanced disease phase, with a longer clinical history and higher calcification rate) or insofar as the absence of calcifications in the plaques of the control group is concerned, this is also a necessary requirement in the inclusion criteria for the control group.

Another point that makes the experimental study and the control groups nonhomogeneous is the different therapies previously undergone: the ESWT group received oral therapies and the control group none at all.

With regard to the technique, I feel that the methods used are open to scrutiny and are different from those used by other groups cited in the literature. In particular, a urethral catheter is no longer used before treatment, especially since the ESWT device already gives consistent support in that the penis is positioned at the beginning of treatment. In addition, the number of applications is generally 3 or 4, which can be repeated, and not the two applications proposed by the authors.

Finally, ESWT is considered the only type of therapy for Peyronie's disease. Recently we published [1] a study in which we compared patients undergoing ESWT alone with patients treated with both shockwaves and perilesional injection of verapamil.

Previous studies have shown the importance of calcium in the metabolism of fibroblasts and in the neosynthesis of collagen. Therefore, calcium antagonists such as verapamil were studied particularly for their antifibroblastic power. Furthermore, ESWT, successfully used in orthopedic or salivary stones because of its lithotriptic power, can be used to break the plagues in Peyronie's disease. The suggestion for a synergy between mechanical and biochemical plaquedisintegrating actions has been supported by our results.

Indeed, this controlled and nonrandomized study suggests that mixed therapies can improve the symptoms of disease. In particular, the fast resolution of pain might suggest the quick stabilization of plaque metabolism. The mechanism of interaction in the ESWT and post-ESWT verapamil injection cycle is not clear. Probably a softened and partially shattered plaque would be a better target for verapamil by offering a more extensive surface of action.

Furthermore, ESWT could facilitate the stretching effects of fluid injection. On the other hand, the verapamil injection cycle could consolidate the effects of ESWT and prevent a restart of collagen neosynthesis following therapeutic microtrauma. A better explanation of this mechanism should be founded on histological data.

References

Mirone V. Imbimbo C. Palmieri A. Fusco F: Our experience on the association of a new physical and medical therapy in patients suffering from induratio penis plastica. Eur Urol 1999;36:327-330.

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