Annals of Physical and Rehabilitation Medicine 64 (2021) 101545

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Original article

Extracorporeal shock wave therapy for treating dyspareunia: A prospective, randomized, double-blind, placebo-controlled study

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ARTICLE INFO

Article history:
Received 4 February 2020
Accepted 9 March 2021

Keywords:
Dyspareunia
ESWT
Extracorporeal shock wave therapy
Pain
Sexual dysfunction
Vaginism

ABSTRACT

Background: Dyspareunia is a genital pain during or after penile-vaginal sexual intercourse. It is a painful spasm of the pelvic muscles that partly or entirely disables vaginal penetration.
Objectives: We examined the effect of extracorporeal shock wave therapy (ESWT) on idiopathic non-organic dyspareunia in women. A prospective, randomized, double-blind, placebo-controlled study was conducted.
Methods: The study included 62 women who reported dyspareunia. Patients in the treatment and placebo groups received ESWT perineally weekly for 4 consecutive weeks; placebo patients received placebo stand-off treatment. The grade of dyspareunia was estimated by using the Marinoff Dyspareunia Scale and subjective pain intensity on a visual analog scale (VAS) before and after treatment. Follow-ups were conducted 1, 4 and 12 weeks after the final ESWT session.
Results: The study included 61 women. The treatment but not placebo group differed by the Marinoff Dyspareunia Scale and VAS. Differences before and after treatment within groups were all $P < 0.001$ and between groups, $P < 0.001$. Pain reduction was always $> 30\%$. The effect sizes were both large: Marinoff 0.825 and VAS 0.883.
Conclusions: ESWT significantly reduced subjective pain in our women treated for dyspareunia.

1. Introduction

Dyspareunia is defined as a genital pain that takes place during or after penile-vaginal sexual intercourse. Although this term is used for both sexes, it occurs more frequently in women than men [1]. This dysfunction was first described in ancient Egypt in the Ramesseum Papyrus, the oldest surviving illustrated Papyrus roll [2]. The frequency of this dysfunction varies depending on the period in a women's lifetime. According to the World Health Organization [3], the frequency of this dysfunction ranges from 8% to 22%, but some authors claim that it is approximately 7.8% in women $\geq$ 40 years of age [4].

Sexual intercourse concomitant with a pelvic organic lesion leads to pain in many cases. Pelvic pain could be present naturally at the site of the pelvic inflammation, vaginal mucous inflammation, endometriosis, mucous atrophy, or pelvic surgery or due to many other conditions. Here, the pain depends not just on penile-vaginal intercourse [5–7]. In its essential definition, dyspareunia in women presents as an idiopathic dysfunction without a typical organic constitution, (i.e., only present with penile-vaginal penetration [1,8]). Dysfunction is often associated with painful spasms of the pelvic muscles. Perhaps for this reason, "vaginism" is included in this group. This dysfunction is defined as a painful spasm of the pelvic muscles that entirely disables vaginal penetration [6]. This whole complex is called genito-pelvic pain or penetration disorder [9]. The intensity of dyspareunia was not defined until Marinoff et al. [10] created a 4-point scale, with scores ranging from 0–3. The Marinoff Dyspareunia Scale describes the pain limitations to practice sexual intercourse: 0, no limitations in sexual intercourse; 1, causes discomfort, but does not prevent sexual intercourse; 2, frequently prevents sexual intercourse; 3, completely prevents sexual intercourse.

Because of the problem in searching for a suitable method of treatment for dyspareunia, we aimed to find a simple, modern

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https://doi.org/10.1016/j.rehab.2021.101545

approach that could provide pain alleviation during sexual intercourse. Extracorporeal shock wave therapy (ESWT) is a simple, safe, modern and promising painkilling option. It is a non-surgical and non-invasive procedure that seems a viable treatment option for some physical disorders. The use of extracorporeally generated electromagnetic, electrohydraulic, or piezoelectric shock waves for treating calculi in the kidneys or other parts of the urinary tract changed how these disorders are treated. A weaker, non-invasive energy source of ESWT has been used successfully to treat degenerative and painful joint disorders, plantar fasciitis and muscle disorders [11–13]. Good results have also been achieved in healing fractures, injuries and poorly healing wounds [14,15]. ESWT has been successful in treating muscle spasticity and hypertonia in apoplectic patients [16–19]. Good results have particularly been achieved in treating pain. It has been used in several studies for treating chronic pelvic pain in men [20]. These good results and our previous experience suggested that ESWT could be a promising treatment for women with pelvic disorders, particularly to attenuate the pain linked to dyspareunia. Ideally, the aim would be the complete relief of dyspareunia pain in patients. However, even a clinically relevant pain reduction would be an acceptable outcome.

The aim of this study was to determine whether ESWT is effective for treating dyspareunia in women.

The reporting of the study adheres to the Consort statement for non-pharmaceutical trials.

2. Material and methods

2.1. Study design

The present study was a prospective, randomized, double-blind, placebo-controlled study conducted between 2017 and 2019. The protocol of the study was approved by the ethics committee of Charles University teaching hospital, Prague, Czech Republic. All patients gave their informed consent and confirmed their participation by signing a consent form. The patients were recruited in departments of the teaching hospital. The principles of treatment, application and evaluation were done by the authors as described in the author's list.

2.2. Participants

Patients were included if they had painful penile-vaginal penetration without pelvic organic reasons primarily connected to pain, a score of > 0 on the Marinoff Dyspareunia Scale, and a score > 0 on a visual analog scale (VAS); were 20 to 75 years old; and the duration of dyspareunia was > 3 months during the past 6 months. Reduction of pain was unobtainable by other therapeutic approaches. Patients were excluded if they had acute pelvic inflammation during the past 6 months, oncological disease within the past 5 years, a clinically significant haematologic disease (e.g., haemophilia or other bleeding disorder), myocardial infarction or cardiac arrhythmia within the past 6 months, any serious metabolic disorder (e.g., diabetes with organic changes) and affection in an intended application area.

2.3. Pain assessment

The patient quantified pain during the penile-vaginal sexual intercourse by using the Marinoff Dyspareunia Scale. The intensity of the vulvo-perineal pain was further evaluated by using a 10-cm VAS (0, no pain and 10, maximal pain).

Fig. 1. The focused shock wave handpiece unit.

2.4. Randomization

Participants were randomized to one of 2 groups by using IBM SPSS 23. The leading parameter for randomization was the patients' level of reported intercourse pain (Marinoff). IBM Sample Power 3 was used to calculate a sufficient sample size. Our estimations were based on our previous feasibility study in which the standard deviation difference was 0.868. We expected a mean difference of at least 0.5. With a power of at least 80%, we needed 26 patients for each group. With an expected dropout of approximately 10%, we estimated 58 patients (29 in each group).

2.5. Treatment

The patients in the treatment group received perineally applied ESWT weekly (4000 pulses per week for 4 consecutive weeks). The device used was a standard electromagnetic shock wave unit with a focused shock wave handpiece unit (DUOLITH SD1, Storz Medical, Tägerwilen, Switzerland) (Fig. 1). The energy flux density was set at 0.35 mJ/mm^2, frequency 4 Hz, focus zone 0–30 mm, therapeutic efficiency 0–90 mm and stand-off II. The position of the shock wave transducer was changed after every 500 pulses. Eight areas, covering the entire vulva and perineum, were treated (Fig. 2).

The placebo group underwent the same treatment procedure as the treatment group except that the handpiece was fitted with a placebo stand-off containing shockwave-absorbing material, a layer of air and air-filled microspheres, which disabled the energy transmission but enabled the generation of the sound and shaking that mimicked the treatment device [20,21]. Moreover, because none of our patients had ESWT before this study, the blinding seemed adequate.

2.6. Treatment assessment

Treatment effect (i.e., pain relief) was measured by assessing differences between the treatment and placebo groups with both the Marinoff Dyspareunia Scale and VAS. These parameters were measured before treatment and at 1, 4 and 12 weeks after the last ESWT. Post-hoc tests were performed within the treatment and placebo groups. During the treatment and follow-up periods, concomitant therapy for dyspareunia was prohibited. According to clinical practice, we assumed changes $> 30\%$ as clinically relevant [22].

2.7. Statistical analysis

We performed both between- and within-group tests. For the between-group test, we assessed the treatment and placebo

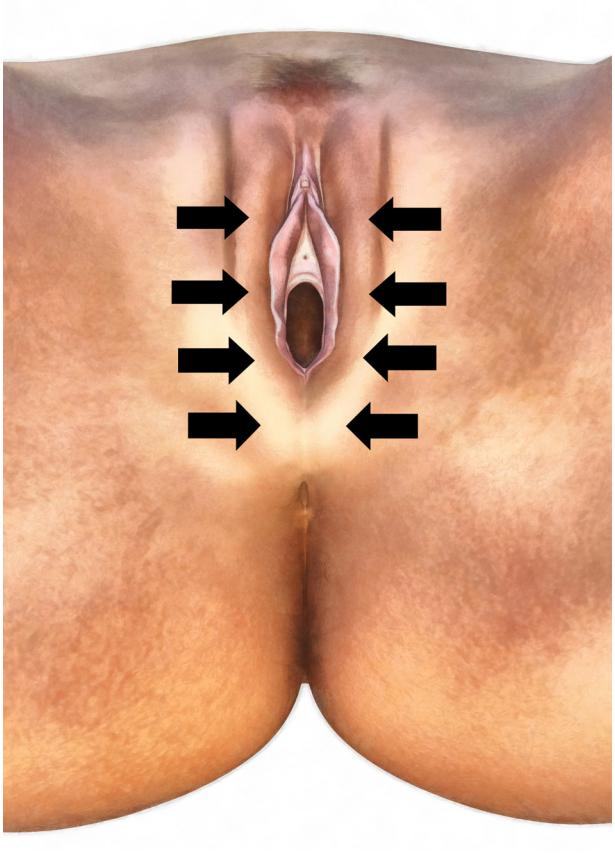

Fig. 2. Application areas on the vulva and perineum.

groups, which resulted in 4 measurements (one measurement before treatment and one each at 1, 4 and 12 weeks after the last ESWT. For the within-group analysis, the evaluations were performed between before treatment and always one of 1, 4 and 12 weeks after the last ESWT, to assess the course of the treatment (3 paired tests). The descriptive numerical method of skewness and kurtosis was used to test for normality of the concerned data sets. The normality of the variables was also assessed with the Shapiro-Wilk and Kolmogorov-Smirnov tests. Because the data did not follow a Gaussian distribution, we used non-parametric statistics. Medians were calculated for all variables. To calculate differences between the treatment and placebo groups, we used the Mann–Whitney U test for non-parametric samples. Four tests were performed. Wilcoxon signed-ranks test for paired samples was used to evaluate within-group differences. Three tests were performed. We interpreted effect sizes as small ($d = 0.2$), medium ($d = 0.5$), and large ($d = 0.8$) based on benchmarks suggested by Cohen (1988). The data were analysed with IBM SPSS 23. Two-sided $P < 0.05$ was considered statistically significant.

3. Results

We included 62 women, aged 20 to 51 years, with objective dyspareunia for at least 3 months during the past 6 months. The flow of participants is in Fig. 3. We generated 2 groups of patients (treatment and placebo groups). The treatment group included 31 patients aged 24 to 51 years (mean age 40) and the placebo group 31 patients aged 20 to 50 years (mean age 39). The groups did not differ in parity or body mass index. Both groups were comparable on all demographic variables.

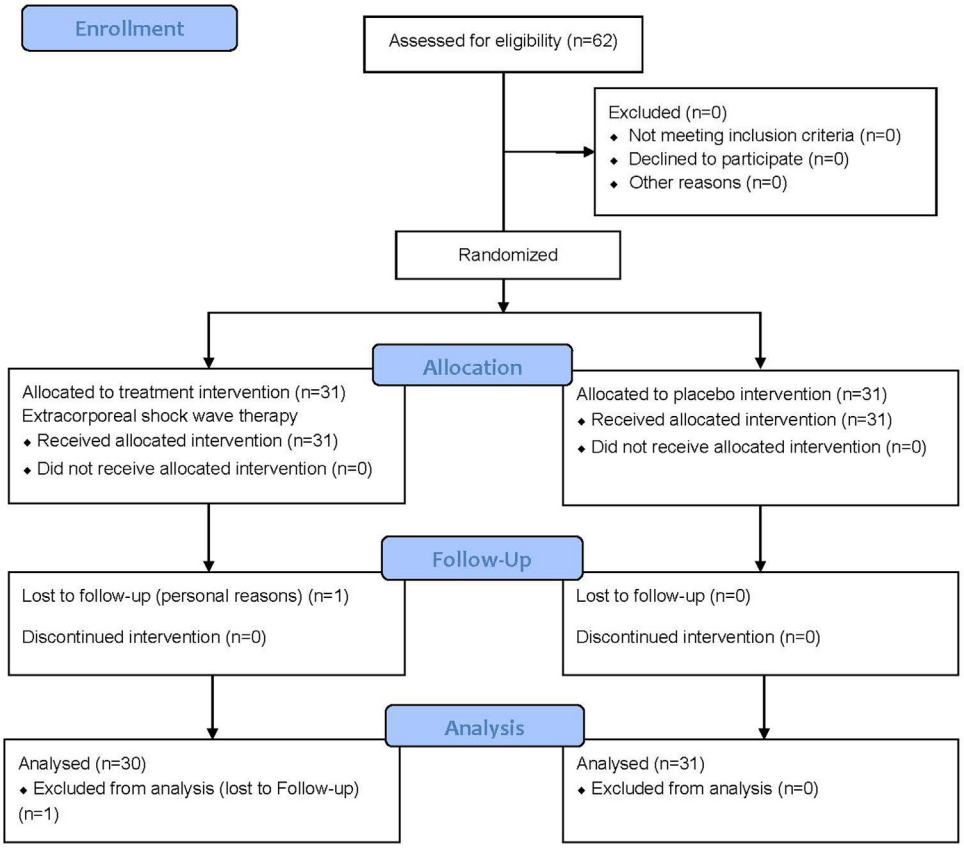

Fig. 3. Flow of participants in the study.

Table 1
Comparison of the placebo and treated groups before and after treatment (Mann–Whitney U test).

	Placebo median	Treated median	*P*-value for change
Marinoff Dyspareunia Scale score (0–3)			
Before treatment	2	2	0.982
1 week	2	0	<0.001
4 weeks	2	0	<0.001
12 weeks	2	0	<0.001
Visual analog scale score (0–10)			
Before treatment	4	4	0.871
1 week	4	1	<0.001
4 weeks	4	0.5	<0.001
12 weeks	4	0	<0.001

Table 2
Comparisons within the placebo and treated group before and after treatment (Wilcoxon signed-rank test).

	Placebo median	Significant changes after vs before treatment	Treated median	Significant changes after vs before treatment
Marinoff Dyspareunia Scale score (0–3)				
Before	2		2	
1 week	2	NS	0	$P<0.001$
4 weeks	2	NS	0	$P<0.001$
12 weeks	2	NS	0	$P<0.001$
Visual analog scale score (0–10)				
Before treatment	4		4	
1 week	4	NS	1	$P<0.001$
4 weeks	4	NS	0.5	$P<0.001$
12 weeks	4	NS	0	$P<0.001$

NS: not significant.

The study was completed by 30 patients in the treatment group and 31 in the placebo group (Fig. 3). One patient in the treatment group underwent treatment but did not participate in any of the follow-ups for personal reasons. This patient was excluded from further analysis.

3.1. Between-group comparisons

The treatment and placebo groups did not differ before treatment, but did differ at the three follow-up times for both the Marinoff Dyspareunia Scale and VAS (all $P < 0.001$) (Table 1).

3.2. Within-group comparisons

We found large, statistically significant differences in the treatment group for patient-reported pain before treatment and at the 3 follow-ups (all $P < 0.001$; Table 2) but no significant decrease in patient-reported pain in the placebo group at all three times. The effect size for the data between before and 12 weeks after the treatment for the Marinoff Dyspareunia Scale was 0.825 and for the VAS was 0.883, which agrees with the large effect size.

4. Discussion

To our knowledge, this is the first randomized controlled study of ESWT used to treat dyspareunia in women. ESWT-induced hyperstimulation of nociceptors and changes in brain patterns may play a vital role in dyspareunia treatment. After ESWT, the women reported a significant reduction in pain during sexual intercourse, which held over all 3 follow-ups.

Some authors suggest the possible interruption of nerve pulse conduction by ESWT. An autonomous nervous system and the coordination between smooth and cross-striated muscles are considered involved in a change in structures during shock wave treatment [23]. Clinical trials have reported the stimulation of growth factors and the promotion and formation of new blood vessels (angiogenesis) [14].

Several orthopedic and urological investigations reported no side effects of ESWT treatment [24,25]. The high tolerability of ESWT and the ability to apply shock waves without anesthesia permit evaluation without any risks to the patient [25]. Incidentally, anesthesia is not recommended before ESWT because of the significant killing of all positive outputs.

We found reliable pain reduction in the placebo group and did not see the previously noted placebo effect of ESWT in chronic pelvic pain syndrome in men [20,21], which is probably due to the specificity of the pain assessed in our study. Even knowing that the effect of ESWT treatment is dose-dependent, we did not exceed the 0.35 mJ/mm^2 level because of potential pain intolerance caused by the ESWT application. Still, the treatment effect seemed suitable [6,20,21,26]. Self-reported pain reduction was always $> 30\%$, which corresponds to a clinically relevant result in accordance with the relevant literature [22], so the improvement we achieved is relevant for daily life. Another positive finding was no side effects (e.g., bleeding, hematoma, bruising, blistering) associated with the ESWT treatment.

The strengths of this study are its relative simplicity and reproducibility in other settings and the large number of patients. A major weakness is that we did not have any objective measurements of pain severity, especially regarding sexual intercourse. Another limitation is the exclusion criteria enforced owing to safety concerns, which may reduce the generalizability of sample study findings to the target population.

5. Conclusions

ESWT seems a safe and effective treatment option for dyspareunia in women. Our study demonstrated an impact on pain perception. Dyspareunia could be reduced to an acceptable level with this modern, non-invasive approach. Also, use of

painkilling or muscle relaxant drugs may be reduced. ESWT is easily replicable and cost-effective (assuming that the device is present in the medical facility). Further discussion is needed for several parameters, including energy flow, the frequency of ESWT application, pain assessment and technique.

Protocol approval

Teaching hospital of Charles University Prague (3.8.2015/7770/EK-Z).

Disclosure of interest

The authors declare that they have no competing interest.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.rehab.2021.101545.

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