Efficiency Assessment of Shock Wave Therapy in Patients with Pelvic Pain Employing Harmonic Analysis of Penile Bioimpedance

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In searching for novel objective methods to diagnosticate pelvic pain and assess efficiency of analgesic therapy, 37 male patients were examined prior to and after the course of extracorporeal shock wave therapy (5-10 sessions) with the waves directed to projections of prostate and/or crura and shaft of the penis. The repetition rate of mechanical pulses was 3-5 Hz. The range of energy pulse density was 0.09-0.45 mJ/mm^2. The overall number of pulses in a session was 1500-3000 in any treated zone with total energy smaller than 60 J. The applicator was relocated every other series of 300-500 pulses. Effect of the shock wave therapy was assessed according to subjective symptomatic scales: International Prostate Symptom Score, International Index of Erectile Function, Quality of Life, and nociceptive Visual Analog Scale. The objective assessment of shock wave therapy was performed with harmonic analysis of penile bioimpedance variability, which quantitatively evaluated the low-frequency rhythmic and asynchronous activities at rest as well as the total pulsatile activity of the penis. The magnitude of spectrum components of bioimpedance variations was assessed with a novel parameter, the effective impedance. The spectral parameters were measured in 16 patients prior to and after the treatment course. The corresponding control values were measured in the group of healthy patients. Prior to the shock wave therapy course, all spectrum parameters of penile bioimpedance significantly differed from the control ($p<0.05$). After this course, low-frequency rhythmic and the total pulsatile activity decreased to normal, while asynchronous activity remained significantly different from the normal. The novel objective physiological criteria of pelvic pain diagnostics and efficiency of its treatment reflecting the regional features of circulation and neural activity corresponded to the clinical symptom scaling prior to and after the shock wave course, and on the whole, these criteria corroborated improvement of the patient state after this therapy.

Key Words: *pelvic pain; extracorporeal shock wave therapy; bioimpedance harmonic analysis*

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The extracorporeal shock wave therapy (ESWT) based on non-invasive contact exposure of the affected area to the vibrational energy widely spread mostly for lithotripsy during urolithiasis [9]. In the following, low-intensity ESWT was also used in orthopedics [13]. In patients with Peyronie disease, ESWT eliminated pain syndrome and moderated penile deformations [1]. The defocused shock waves used to treat the patients with chronic pelvic pain syndrome (CPPS) produced a moderating effect and improved the quality of life [2]. The focused shock waves were also efficient in treatment of such patients [14].

The diagnostic method of parallel assessment of regional blood flow and ANS activity based on bioimpedance harmonic analysis (BHA) of an examined organ [3,4,11] can reveal the fine structure of the macroscopic pulsatile oscillations of bioimpedance and its microscopic variations related to ANS rhythmic activity.

The present paper assesses efficiency of focused ESWT in patients with CPPS employing the novel objective criteria yielded by BHA in comparison with the diagnostic data based on standard questionnaires. The bioimpedance variances data were analyzed by a novel method describing the intensity of rhythmic oscillations of a physiological parameter using the conception of efficient impedance. The need in this research is evident, since in contrast to the orthopedic and penile ESWT applications, the objective assessment of ESWT antinociceptive effect is problematic.

MATERIALS AND METHODS

ESWT was carried out with DUOLITH SD1 device (Storz Medical AG). During ESWT, elimination of pain syndrome in patients with CPPS (N=29) was accompanied by improvement of erectile function, which prompted us to treat an additional group of patients (N=8) with erectile dysfunctions. In all patients, the focused waves were directed to prostate projection area and/or to penile crura and shaft. The applicator was relocated every other series of 300-500 pulses. The overall number of pulses in a session was 1500-3000 in any treated zone, the repetition rate of mechanical pulses being 3-5 Hz. The range of energy pulse density was 0.09-0.45 mJ/mm^2, the total energy per a session being no greater than 60 J. The ESWT course comprised 5-10 sessions. Effect of ESWT was assessed according to the subjective symptomatic scales of prostatic symptoms: IPSS (International Prostate Symptom Score), IIEF (International Index of Erectile Function), QoL (Quality of Life), and nociceptive VAS (Visual Analog Scale). In addition, the effect of ESWT was assessed with the objective spectrum parameters of penile bioimpedance yielded by BHA, which reflected the neurogenic and circulatory penile statuses [4,7]. The rheophallogram was recorded during 5-6 min in supine position under the silence. The custom-made hardware–software system recorded the total (“basic”) bioimpedance and its microvariations with the resolving power of 50 mΩ in the range of 0-1000 Ω and 250 $\mu\Omega$ in the range of ±4 Ω in the channels of total and alternating impedance, respectively [4,6,11].

The amplitude spectra of bioimpedance oscillations were calculated with fast Fourier transform. To this end, a record of alternating bioimpedance component was filtered in the frequency band of 0.05-15.00 Hz and cut into the epochs of a certain duration. The epoch of 25.6 sec (4096 points, resolution 0.04 Hz) yielded the survey (overview) spectrum with particular emphasis on the low-frequency bioimpedance variations at the frequencies of Mayer wave and respiration. The epoch of 12.8 sec (2048 points, resolution 0.08 Hz) was employed to analyze the cardiac (pulsatile) bioimpedance harmonics. For analysis, the record fragments were selected, which did not contain the artifacts caused by involuntary movements or cough. Such fragments comprised 1-4 epochs of the above length. The amplitude spectra of several epochs in the selected fragment were averaged.

RESULTS

In CPPS patients, ESWT course decreased pain intensity from 5.2±2.4 to 2.8±1.1 VAS points (p<0.05). Simultaneously, IPSS decreased from 14.4±2.2 to 5.4±1.1 points (p<0.05). IIEF revealed as increase in total score of erectile function from 18.6±1.1 to 21.9±1.3 (p<0.05). Overall, the course of ESWT improved the quality of life reflected by a decrease in QoL index from 4.9±1.3 to 3.6±1.4 points (p<0.05).

In patients with erectile dysfunction (N=8), ESWT course insignificantly elevated IIEF from 17.4±1.6 to 19.9±1.7 points (p>0.2) and significantly decreased QoL index from 4.5±0.3 to 2.7±0.6 points (p<0.05). The positive trend and significant improvement corresponded to the data on therapeutic effect of low-intensity ESWT on erectile function [12]. Overall, the symptomatic scales showed that ESWT significantly improved the state of these patients.

The data on penile impedance were used to develop a method of obvious and demonstrative assessment of the rhythms in a variable physiological parameter, which measures the rhythm intensity with the help of “effective bioimpedance” of the same physical dimension as the analyzed parameter.

Variation of bioimpedance is a stochastic process including the rhythmic oscillations caused by circulatory (pulsatile) and neurogenic reasons [6,11]. The largest rhythmic oscillations represent a typical rheogram [8,10]. The low-amplitude bioimpedance oscillations are detected with BHA yielding a spectrum with a set of certain narrow peaks (Fig. 1, *c*). Penile BHA needs a peculiar technique to exclude the pronounced unstable fragments in the bioimpedance record.

A typical record of penile bioimpedance (Fig. 1, *a*) incorporates infrequent large oscillations (respiratory and motion artifacts) as well as the fragments with

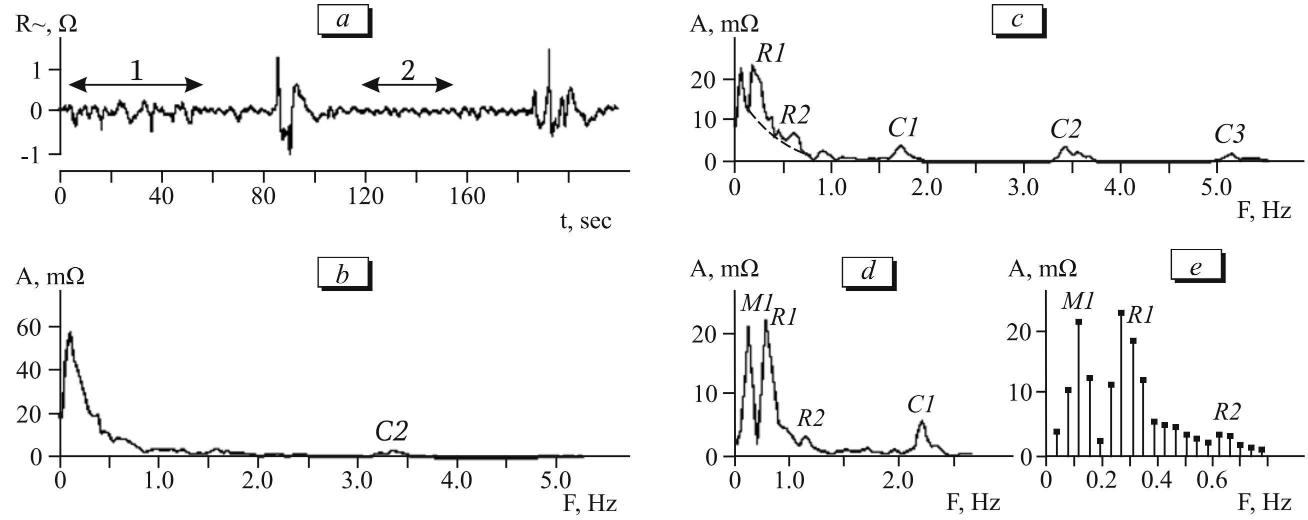


Fig. 1. Implementation of BHA method. *a*) a part of bioimpedance variation trace showing the fragment with AA (*1*) and a stationary fragment (*2*); *b*) bioimpedance spectrum calculated for fragment *1* in trace *a* with characteristic wide elevation in the low-frequency band of 0.1-1.0 Hz; *c*) bioimpedance spectrum corresponding to the period of 486-526 sec of the same trace demonstrating the narrow peaks of rhythmic variations *M1*, *R1*, and *R2* partially masked by a wide elevation of the spectrum plot reflecting the asynchronous variations of bioimpedance accompanied by unmasked pulsatile harmonics *C1-C3*; *d*) bioimpedance spectrum calculated for the stationary fragment *2* in trace *a*, where all the basic spectrum peaks of penile bioimpedance are resolved; *e*) the same spectrum as in *d*, initially calculated by the program as a set of spectrum amplitudes shaping the individual peaks. All the amplitudes composing a spectrum peak are taken into account during calculation of effective impedance characterizing the particular peak. Epoch 25.4 sec, frequency band 0.05-35.0 Hz. Patient *m2*, examination A110929, record 0.

relatively stable deviation range. The stable fragments lengthening 30-60 sec were selected for the primary scanning of a record with BHA revealing the fragments with characteristic amplitude spectra. Figure 1 (*b-d*) shows the typical spectrum samples obtained for various fragments of the record presented in Fig. 1, *a*. Of them, only the spectrum shown in Fig. 1, *d* revealed the characteristic narrow peaks at Mayer's frequency (*M1*, about 0.1 Hz) and at respiration rate (*R1*, 0.3 Hz in this particular case). In contrast, in other plots these peaks were partially or completely masked with a wide "hump" (the dash line in Fig. 1, *c*) related to asynchronous (non-rhythmic, non-stationary) character of variations in the corresponding fragment of bioimpedance trace. Really, such asynchronous variations can be viewed directly in the fragment *1* (Fig. 1, *a*) corresponding to the spectrum shown in Fig. 1, *b*. At the initial stage of analysis, a fragment was selected with no overt asynchronous activity (fragment *2* in Fig. 1, *a*). Then the amplitude spectrum of this fragment was calculated (Fig. 1, *d*, *e*). The Fourier transform of a digitalized (discrete) sinusoidal signal is known to yield a "diffused" spectrum peak composed of several components with the close frequencies. The widening of spectrum peaks results also from the non-stable frequency of the physiological rhythms. To take into account all the components A_i of a "diffused" peak (Fig. 1, *e*), we introduced the parameter of "effective impedance R_{eff}":

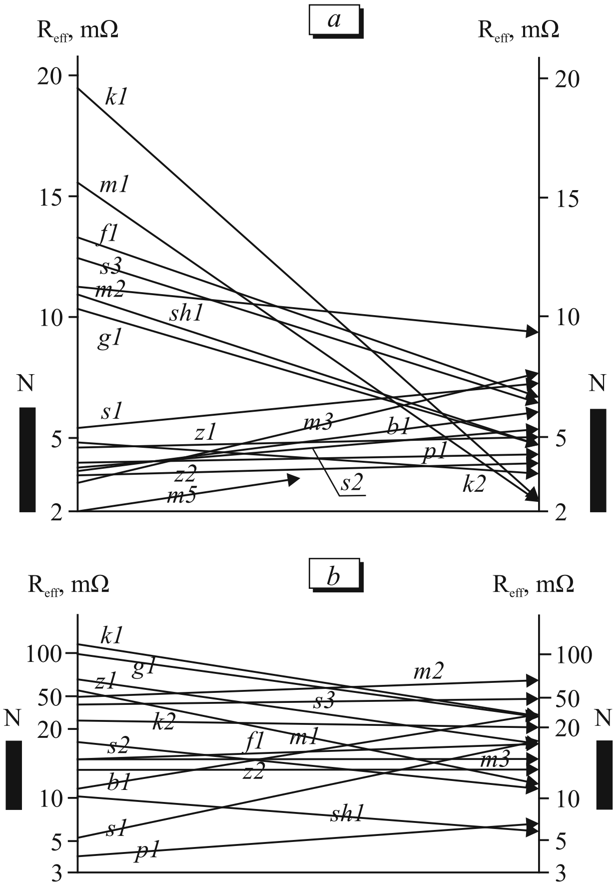
$$R_{eff}=0.71\times\sqrt{\sum A_i^2} \qquad \textbf{(1)}.$$

For a sinusoidal signal, the changes in the epoch length produce no effect on all the amplitudes (A_i) of its spectrum peak and on the value of R_{eff}. For a signal with several rhythms, an increase in the epoch length splits the initially unitary peak into several ones without significant changes in the value of R_{eff} calculated within the same frequency band.

In some patients, the *M1* и *R1* peaks merged due to a low respiration rate (less than 0.3 Hz). In such cases, formula **(1)** was employed to calculate the total low-frequency rhythmic activity (LFRA) with all the spectrum amplitudes located in the frequency band of 0.05-0.4 Hz encompassing *M1* and *R1* peaks. Similarly, the total pulsatile activity (TPA) was calculated for all pulsatile harmonics. In the same stationary fragment of bioimpedance record, the first root mean square of bioimpedance variations (RMS_1) was calculated, which approximated the square root of the sum of squares of LFRA and TPA attesting to compliance of examined variances with Parseval's theorem and correctness of assessment of the analyzed fragment as the stationary one.

To continue the analysis, we selected an artifact-free non-stationary fragment of bioimpedance record (fragment *1* in Fig. 1, *a*). Here, the second root mean square value RMS_2 was calculated, which included both rhythmic and asynchronous bioimpedance changes. The asynchronous activity (AA) was calculated by the following formula:

$$AA=\sqrt{RMS_2^2-RMS_1^2} \qquad \textbf{(2)}.$$



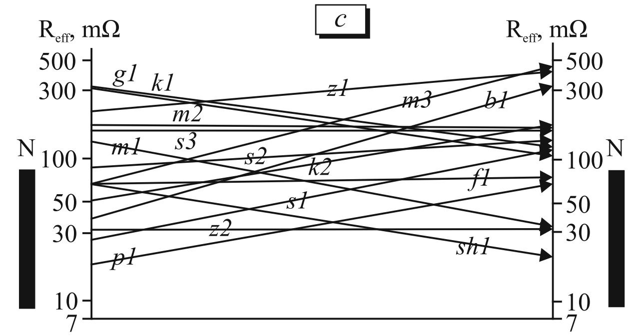


Fig. 2. Effect of ESWT course on TPA (*a*), LFRA (*b*), and AA (*c*) of penile bioimpedance in patients with chronic pelvic pain syndrome and erectile dysfunctions. The spectrum parameters are shown prior to (left ordinate) and after (right ordinate) the ESWT course. Each line corresponds to individual patient with its code. The solid bars show the normal range (N) of the spectrum parameters.

The above technique was employed to examine the control group of healthy men aging 18-76 years (*N*=18). To delineate the normal range of TPA, LFRA, and AA, the extreme deciles (two points at the boundaries of every parameter range) were discarded, which yielded the following normal values: TPA=2~6 mΩ, LFRA=8~26 mΩ, and AA=8~86 mΩ (solid bars in Fig. 2). Averaging over the entire group of healthy men resulted in the following values (*m*±*SEM*): TPA=4.6±0.8 mΩ, LFRA=18.2±2.7 mΩ, and AA=49.1±18.8 mΩ (Table 1). The greatest scattering was characteristic of AA, which probably reflected the individual psychophysical peculiarities of the examined persons. Pronounced scattering in AA measured prior and after the treatment indicates the need in additional clinical criteria to form the subgroups of patients in order to enhance the accuracy of BHA-based diagnostics.

Table 1 shows the data of 16 patients treated with ESWT. The objective results were assessed in 5-7 days after the end of ESWT course, because every a ses-

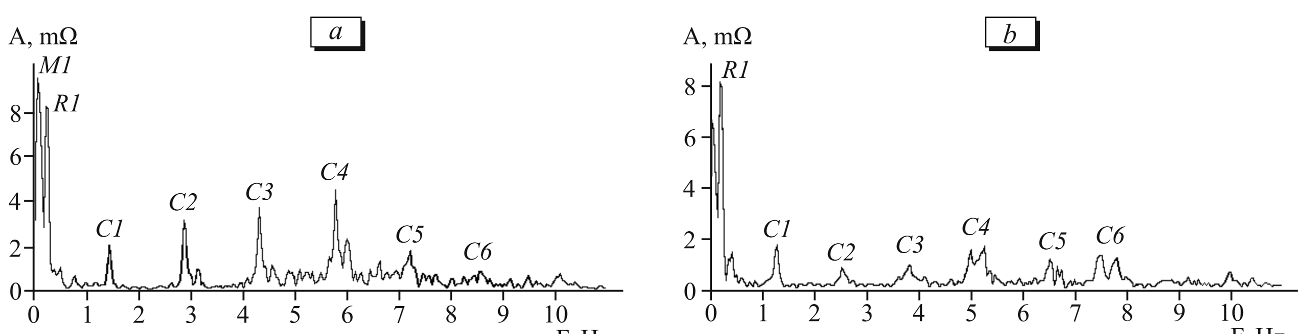


Fig. 3. Effect of ESWT course on spectrum parameters of a typical patient *f1* with initially abnormally high TPA caused by the near resonances C2-C6 (*a*). Normalization of TPA after ESWT (*b*) course resulted from the decrease in the amplitudes of these resonances. Epoch 25.4 sec, frequency band 0.05-35.0 Hz. *a*) Examination D110727, record 0, period 92-128 sec; *b*) Examination D110901, record 1, period 380-410 sec.

TABLE 1. Spectrum Parameters of Penile Bioimpedance in Norm and in Patients with Chronic Pelvic Pain Syndrome and with Erectile Dysfunctions (*m*±*SEM*)

Stage of examination	LFRA, mΩ	AA, mΩ	TPA, mΩ
Norm	18.2±2.7 (*N*=18)	49.1±18.8 (*N*=18)	4.6±0.8 (*N*=18)
Prior ESWT	38.6±9.0* (*N*=15)	115.5±25.0* (*N*=15)	8.0±1.3* (*N*=16)
After ESWT	26.5±4.2 (*N*=15)	158.7±34.4* (*N*=15)	5.3±0.5 (*N*=16)

Note. *$p<0.05$ compared to the norm.

sion induced the transitory changes in all the parameters measured immediately after it. Prior to the ESWT course, all the spectrum parameters significantly differed from the control values (Table 1). After the treatment, LFRA and TPA approximated to the control values and did not significantly differ from them, although AA remained significantly greater than the norm and did not significantly differ from the initial level.

The results of ESWT course can be shown in a graphical way (Fig. 2) demonstrating not only normalization of LFRA and TPA, but also the decrease in their scattering. Thus, normalization of these parameters was the most pronounced in the patients that initially demonstrated the largest deviations from the norm. This trend was most clearly manifested with TPA, which in 6 patients was dramatically greater than the norm (Fig. 2, *a*). This "overshoot" resulted from pronouncedly high "near resonances" [4], *i.e.*, the high narrow pulsatile peaks *C2*, *C3,* and *C4*, which were greater than the fundamental pulsatile harmonic *C1* (Fig. 3). After ESWT course, the considered patients demonstrated significantly decreased and normalized TPA (Table 1) due to diminished height of the "near resonance" peaks (Fig. 3). In these patients, the initially large TPA did not probably attest to elevated blood supply to penis, but indicated an enhanced tone of penile arteries and the corresponding increase in their rigidity accompanied by an increase in the quality factor of the oscillating structures manifested by the narrowing of spectrum peaks and increase in their height. A decrease in TPA after ESWT course was paralleled by a decrease in *M1* peak reflecting the strength of sympathetic influences and by an increase in *R1* peak relating to activity of parasympathetic system [5]. Detection of the near resonances with BHA and their suppression with ESWT can be viewed as an example of objective graphical diagnostics of the regulatory abnormalities and treatment efficiency.

While depending on *M1* and *R1* peaks, the integral parameter LFRA does not reflect redistribution of the effective impedance in favor of any of them and hence, it cannot be used to assess the changes in vegetative balance. To reliably resolve the *M*- and *R*-peaks, standardization of respiration conditions should be provided with the respiratory rate of no smaller than 0.3 Hz. Nevertheless, LFRA can be employed as an index of total regional ANS activity. Probably, the decrease of this parameter in the treated patients is related to moderation or elimination of pain.

ESWT course produced the opposite changes in AA in various patients (Fig. 2, *c*). However, the positive clinical results of the treatment suggest that the changes of this parameter can reflect the state of erection, which was improved in most patients. Overall, BHA method can yield the objective parameters to characterize the state of regional circulation and neurogenic activity, which makes it possible to advance a novel method to diagnosticate vascular erectile dysfunction [7] and to assess efficiency of physical therapy. The reality of andrological applications of BHA and their objective assessment with BHA should be examined in further studies.

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