External shock waves therapy in dystonia: preliminary results

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Keywords:
basal ganglia, dystonia, extracorporeal shock wave therapy, writer's cramp

Received 18 August 2008
Accepted 10 December 2008

Background and purpose: Extracorporeal shock wave therapy (ESWT) has been shown to reduce hypertonia in patients with upper motor neuron syndrome without any side effect. The aim of the present study is to investigate whether ESWT could be useful also in patients with dystonia.

Methods: We evaluated three patients with secondary dystonia and three patients with idiopathic writer's cramp. Placebo treatment was performed in each patient. ESWT was administered during four sessions (once weekly) to the target muscles of hand and forearm using an electromagnetic lithotripter (Modulith SLK – Storz Medical). Clinical evaluation was performed using the Unified Dystonia Rating Scale in patients with secondary dystonia and the Arm Dystonia Disability Scale in patients with writer's cramp.

Results: After treatment, the three patients with secondary dystonia showed a marked improvement which lasted at least until 1 month after the last session. In the patients with writer's cramp, the improvement after ESWT was less consistent being effective only in two subjects. There were no associated adverse effects.

Conclusions: Extracorporeal shock wave therapy is probably an effective and safe treatment for upper limb dystonia, particularly for the secondary forms. Larger randomized studies are needed to confirm these preliminary results.

Introduction

Focal limb dystonia, either idiopathic (occupational hand dystonia) or secondary to basal ganglia lesions, is often disabling and poorly responsive to pharmacological therapy [1,2]. Botulinum toxin (BoNT) is regarded as the most effective treatment designed to eliminate or reduce the abnormal muscle contractions [2,3]. However, transient weakness of the injected muscles is a common consequence of successful treatments [3,4].

Beside dystonia, another standard indication for the use of BoNT is focal spasticity due to stroke [3,5]. However, in patients with spasticity it has been suggested that also extracorporeal shock wave therapy (ESWT) was able to reduce muscle hypertonia without inducing weakness, thus providing a valid alternative to BoNT treatment [6]. Shock waves are characterized by high positive pressure (*c*. 1000 Bar), a rapid rise time (30 to 120 ns) and short pulse duration (5–10 μs) [7]. Although the exact mechanism of shock waves remains to be defined, a direct action on intrinsic components of the chronically hyperactivated muscles has been suggested [6]. Hypothetically, such unspecific mechanism of action could make shock waves a valid therapy for all the forms of muscle hypertonia, including dystonia. To evaluate the efficacy of ESWT in the management of limb dystonia, we treated three patients with secondary limb dystonia due to a lesion in the basal ganglia and three patients with idiopathic writer's cramp.

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Methods

Patients

All the patients were clinically evaluated at the time of their enrollment in the study, at least 3 weeks before ESWT (baseline clinical examination). Three patients (1–3) were affected by secondary dystonia, mainly involving the upper limb, due to a lesion in the basal ganglia. They had severe rest dystonia and the abnormal postures were further aggravated by the attempt to move. In all the patients the involved upper limb was

stiff, painful and non-functional. Patient 1 (a 49-year-old woman) was reported in detail previously [8]. She was affected by delayed-onset post-hemiplegic dystonia involving the left upper limb, due to vascular lesion in the right putamen that occurred at the age of 41 years. Baseline clinical examination revealed dystonic contractions of hand and forearm muscles causing abnormal posturing of the hand and wrist. The thumb was opposed to the fingers IV and V, which were deviated towards the ulnar side, whilst there was a radial deviation and extension of the other two fingers (II and III). Most of the time, the wrist was flexed. Patient 2 (a 25-year-old man) was affected by right hemi-dystonia at least from the age of 6 months. CT scan revealed a hypodense lesion in the left hemisphere, involving the head of caudate and putamen. Baseline clinical examination showed a marked dystonic posture of the right upper limb. The wrist was extended and deviated toward the ulnar side. Most of the time, the fingers were flexed into the palm with marked thumb adduction. Patient 3 (a 76-year-old man) was affected by delayed-onset post-hemiplegic dystonia of the left upper limb, due to a vascular lesion involving the right putamen, thalamus and internal capsule. Baseline clinical examination (4 years after the stroke) revealed, at rest, recurrent flexions of the wrist and fingers, often spreading to the elbow.

The other three patients (4–6) were affected by simple writer's cramp according to Sheehy and Marsden [9]. They were all right-handed females, aged 41 (patient 4), 47 (patient 5) and 25 years (patient 6). In all these subjects, baseline clinical examination revealed excessive pen pressure during writing; in patient 4 an excessive wrist flexion was seen during writing, whilst in the other two an excessive wrist extension was noticed. All the patients referred tension or discomfort during writing in the fingers and forearm. Mirror dystonia (i.e. the abnormal posture of dominant hand induced by writing with the opposite, non-dominant, hand) was not seen in any of the three patients. Patients 3 and 6 were never injected with BoNT. In the remaining patients, the last BoNT injection was performed at least 6 months before the enrollment in the study. All patients gave their written informed consent and the study was conducted in accordance with the Declaration of Helsinki.

ESWT protocol

The treatment protocol consisted of a course of four sessions (once weekly) with 800–3000 pulses being delivered to each selected muscle during each session, at an average of 0.030 mJ/mm^2. When the selected muscle was an intrinsic hand muscle, we delivered 800 shots (thenar muscles were considered as a single muscle). When the selected muscle was a forearm muscle, 2000 shots were delivered. We used an electromagnetic lithotripter (Modulith SLK – Storz Medical) with cylindrical coil and ultrasound in-line scanning. Different points of application were used to treat several areas of the target muscles. In the three patients with secondary dystonia, ESWT was delivered to the muscles responsible for the most prominent dystonic movements: thenar muscles and all dorsal interosseous muscles in patient 1; thenar muscles, flexor carpi ulnaris and extensor carpi ulnaris muscles in patient 2; flexor carpi ulnaris and radialis and flexor digitorum superficialis muscles in patient 3. In the three patients with writer's cramp, ESWT was widely distributed to the volar surface of the forearm (3000 shots) in order to treat wrist and fingers flexor muscles; ESWT was also widely delivered to the dorsal surface of the forearm in order to treat wrist and fingers extensor muscles (3000 shots).

At the low energy adopted in the present protocol, ESWT is painless and the main sensation experienced by the subjects is a 4-Hz click. However, they may feel a faint sensation of light touch or prickle or itch near the stimulating coil, making more difficult the possibility to obtain a reliable placebo treatment. To overcome this problem, ESWT was associated with a continuous stimulation of the skin near the coil by randomly alternating taps with the sharp or dull end of a safety pin. Such stimulation can induce a sensation very similar to that induced by ESWT at low energy.

Placebo treatment

Each patient was treated with a single placebo session, which was performed 2 weeks before the first ESWT session. Four additional sessions (once weekly) of the placebo treatment were repeated after ESWT in subjects 3-5-6. The placebo session was similar to ESWT session; however, shock waves were prevented from reaching the target muscles by a foam cushion placed on the surface of the cylindrical coil connected with the patient's body. Skin stimulation (see above, ESWT protocol) was associated with both ESWT protocol and placebo treatment in order to create a similar sensation.

Evaluation of efficacy

Clinical assessments were made before the first ESWT session (T0); after each of the four sessions (T1-T2-T3-T4); 1 and 2 months after the last session (T5-T6). The same clinical assessment was also made before placebo treatment, immediately and 1 and 2 weeks after placebo treatment. Dystonic movements of patients 1–3 were clinically rated according to the Unified Dystonia

Rating Scale (UDRS) for the distal arm and hand [10]. Furthermore, in these three subjects the severity of pain was evaluated using a four-point intensity of pain score (0 = no pain; 1 = mild; 2 = moderate; 3 = severe). Dystonic movements of patients 4–6 were rated according to the Arm Dystonia Disability Scale (ADDS) [11] for upper limb dystonia.

Electrophysiological evaluation

It was performed at the time of patients' enrollment in the study, after the first placebo session and after the last ESWT session (T4). The following parameters were assessed in the affected arm: parietal component (N20) of somatosensory evoked potentials (SEPs) obtained by median nerve stimulation at the wrist; compound motor action potential (CMAP) and F wave from abductor digiti minimi by ulnar nerve stimulation at the wrist. Statistical analysis of electrophysiological values was performed with ANOVA with repeated measures.

Results

At the end of the study, patients were requested to say if they experienced any differences amongst the several sessions, including both placebo and ESWT treatments. The negative answer of all the subjects proved that placebo treatment was valid.

Placebo treatment left unchanged the clinical scores in each of the six patients. On the contrary, immediately after the first ESWT session (T1), the UDRS scores decreased in each subject with secondary dystonia (Figs 1 and 2) and the ADDS scores decreased in each subject affected by writer's cramp (Fig. 1).

In all the three subjects with secondary dystonia, ESWT induced persistent effects (Figs 1 and 2). In

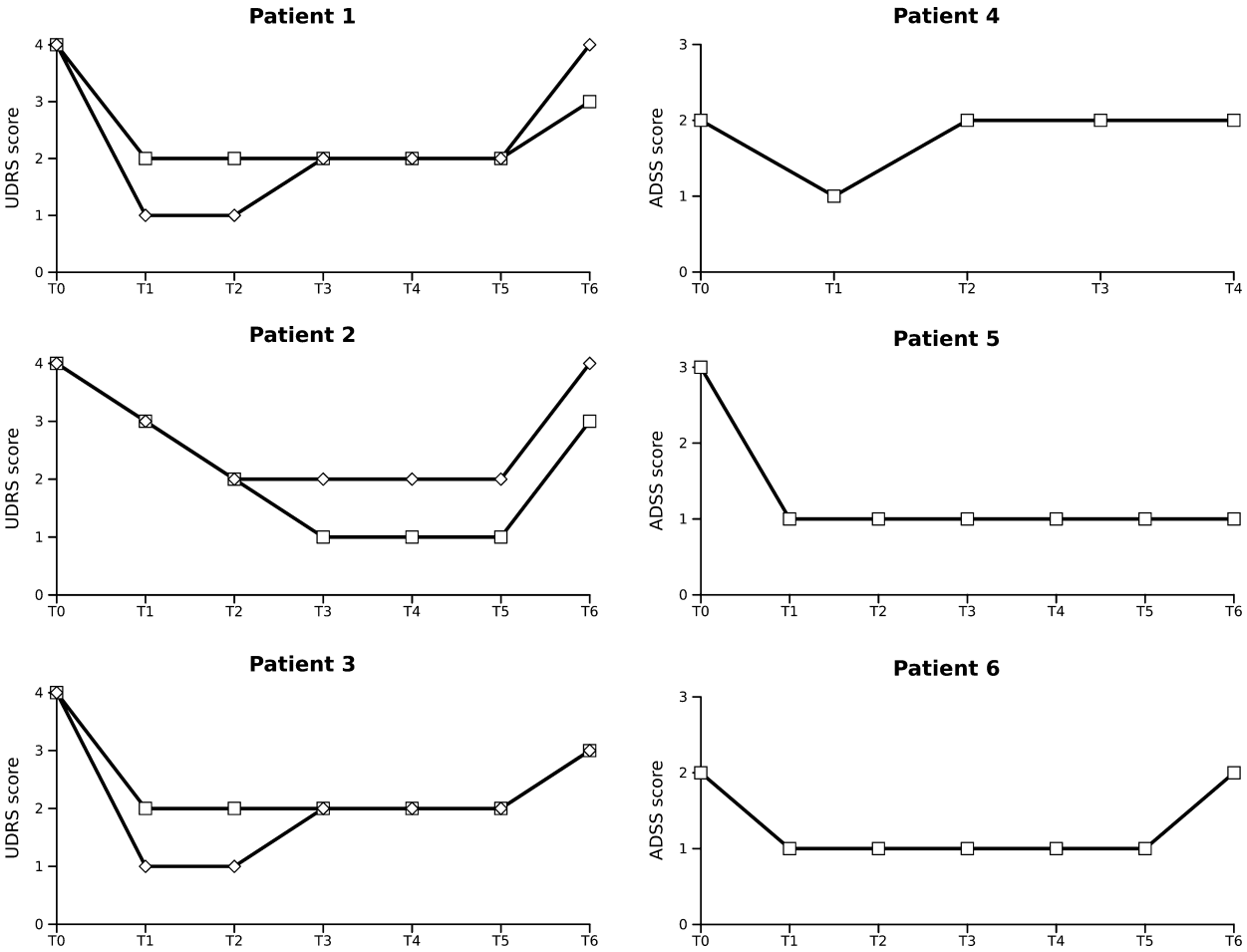

Figure 1 Rating of secondary dystonia (Unified Dystonia Rating Scale) for patients 1–3 and rating of writer's cramp (Arm Dystonia Disability Scale) for patients 4–6 before extracorporeal shock wave therapy (ESWT) (T0), after each session of ESWT (T1–T4), 1 month after the last session of ESWT (T5) and 2 months after the last session of ESWT (T6). In patient 1 the squares represent thumb opposition and diamond fingers deviation. In patient 2 squares represent thumb opposition and the diamonds indicate ulnar hand deviation. In patient 3 squares represents wrist flexion and diamond fingers flexion.

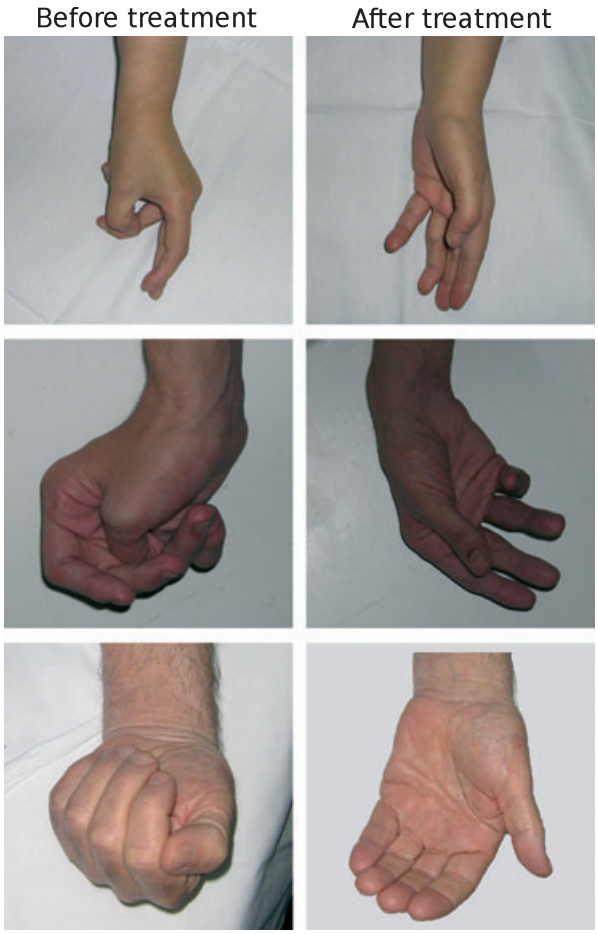

Figure 2 Hand pictures of patients with secondary dystonia (1, first row; 2, second row; 3 third row) before (T0) and after treatment (T1).

subjects 1 and 3, the maximum effect was obtained at T1, whilst in subject 2 it was obtained at T3. The effect was absolutely stable in all subjects from T3 to T5. Two months after the last session (T6), the effect was drastically reduced; amongst the six tested dystonic movements, two regained the pre-treatment values, whilst the effect was still present in the remaining four, though reduced in comparison to T3–T5 values. In all the three subjects, pain was reduced from score 3 before treatment to score 2 at T1. Such improvement persisted unchanged until up to T6 in patient 2 and up to T5 in the other two. In none of the subjects ESWT induced side effects, including weakness of the treated muscles.

Amongst the three writer's cramp patients (Fig. 1), subject 1 had only a slight and transient improvement in writing at T1, which disappeared at T2. This subject wanted to be injected with BoNT after the last session (T4); therefore data at T5 and T6 for this patient were not available. Patient 2 showed a very good improvement after the first session (T1), which lasted 2 months after the last session (T6). In patient 3 the improvement lasted only 1 month after the last session (T5). In none of the subjects ESWT induced side effects, including weakness in the treated muscles. No significant changes of electrophysiological values were found both after placebo stimulation and ESWT (Table 1).

Table 1 Electrophysiological parameters.

	Baseline	After placebo	After ESWT (T4)
Latency CMAP (ms)	2.82 (0.76)	2.78 (0.80)	2.80 (0.71)
Amplitude CMAP (mV)	7.83 (3.06)	7.47 (3.19)	7.85 (3.32)
F wave latency (ms)	24.17 (1.17)	23.67 (2.42)	23.52 (1.24)
F wave amplitude (mV)	0.52 (0.33)	0.53 (0.31)	0.54 (0.32)
Parietal N20 latency (ms)	20.67 (2.34)	20.38 (2.61)	20.67 (3.56)
Parietal N20 amplitude (μV)	2.20 (0.71)	2.12 (0.95)	2.23 (0.92)

Values are expressed as mean (standard deviation).
CMAP indicates compound motor action potentials following ulnar nerve stimulation at the wrist.
Parietal N20 is the cortical component of the somatosensory evoked potential (SEP) obtained by stimulating the median nerve at the wrist.

Discussion

These preliminary results suggest that ESWT can be effective in patients affected by dystonia, particularly in those with dystonia secondary due to a lesion of the basal ganglia. In all these patients we obtained very consistent results, with an immediate and long-lasting benefit. On the contrary, the results in patients with writer's cramp were less homogenous: no effect was noticed in patient 1, fair results were observed in patient 2 and a good but short-lasting improvement was present in the remaining subject.

One possible explanation for the difference in the results observed in the two groups could be at least partially related to the identification of target muscles. The detection of the muscles responsible for dystonic contractions in patients with secondary dystonia is easier than that of muscles involved in writer's cramp. Secondary dystonia is present at rest and therefore the dystonic movements are not associated with voluntary movements, making the detection of muscles involved in dystonia easier and more precise. On the contrary, writer's cramp appears only during writing, which is a complex motor behaviour where the boundary between normal and abnormal movements may be unclear [12]. In this context, it could be difficult to differentiate between normal, dystonic and compensatory movements, particularly when mirror dystonia is absent. Therefore, we decided to treat all the forearm muscles, in order to deliver ESWT to the muscles involved in dystonic contraction. This strategy necessary made the treatment

less focalized on the muscles primarily involved in dystonia and this could be responsible for our partially non-consistent results.

After ESWT no adverse effects were observed in any patient. In particular, ESWT did not induce weakness in the treated muscles, confirming previous results in patients with spasticity [6]. Indeed, weakness is the major side-effect of BoNT injection, which often limits or even overwhelms the clinical benefit. In patients affected by dystonia, the ability to reduce abnormal muscle tone without inducing weakness would be of great importance. In patients with upper motor neuron syndrome muscle hypertonia is often associated with muscle weakness, which '*per se*' makes the affected limb non-functional; in this clinical situation the muscle weakness possibly induced by the toxin does not cause any further functional impairment [13]. On the contrary, patients with dystonia very often do not present muscle weakness. In these patients, the weakness induced by the toxin is probably a major clinical impact.

The mechanism underlying the benefit induced by ESWT in dystonic subiects is still uncertain. The absence of weakness after the treatment and the lack of any change in electrophyiological parameters evaluating motor function (CMAP, F wave) suggest that the effect is not obtained by altering motor conduction at the level of spinal motoneurons. In fact, if the reduction of the dystonic contraction was obtained by weakening the function of the 'final common pathway' in the motor system, then the clinical effect should be linked to the development of weakness in the treated muscles, as in the case of BoNT treatment. Similarly, the absence of sensory disturbances after the treatment, combined with the lack of SEPs changes, makes improbable a direct action of ESWT on sensory fibres. Therefore, we suggest that the most probable mechanism of action of ESWT in dystonia is a direct effect of shock waves on fibrosis and other intrinsic components of chronically overactivated muscles. This mechanism might modify muscle spindle excitability, inducing a modulation of the muscle input directed to the spinal cord [14].

Given its safety, efficacy and long-lasting effect, ESWT may be useful in dystonic patients, particularly in those with secondary forms due to lesions in the basal ganglia. Further trials should be performed before making more conclusive recommendations on the use of shock waves in dystonia.

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