Extracorporal shock wave induced mechanical transduction for the treatment of low back pain – a randomized controlled trial

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Abstract—

Context: *Selective application of extracorporal shock waves (ESW) is a well-known treatment for orthopedic diseases, but effects of a complete body application on pain intensity and postural control in low back pain patients have not yet been evaluated.*

Objective: *To evaluate the effect of a 23Hz extracorporal complete body shock wave (CBSW) therapy (EvoCell) for the treatment of low back pain in comparison to current therapies (Fango).*

Design: *We conducted a randomized controlled trial in 100 patients admitted to 4 different groups from March till November 2015. The subjects received 9 interventions (ESWT/Fango) within 3 weeks with follow-up measurements after 4 and 8 weeks.Primary outcomes include parameters of posture, assessed by a Lightrasterstereography (LRS), a sitting-stability-check (S3) and changes in pain experience due to a Visual Analogue Scale (VAS), Heart Rate (HF) and Blood Pressure (BP).*

Results: *Only Fango had a significant decreasing acute effect on pain or blood pressure, but the subjects treated with EvoCell showed a significant pain reduction after 4 sessions and a greater pain reducing effect after 3 weeks of treatment. EvoCell had a highly significant reducing effect on heart rate ($p<0.001$). Additionally, the CBSW seemed to influence the ability to stabilize the trunk in an upright sitting position in the lateral direction above other treatments.*

Conclusion: *Regarding to the individually different response of proteins and other structures on ESW frequencies, the specific underlying mechanisms remain unclear. But as we were able to show, it can be assumed that the periodic application of a CBSW stimulates mechanical transduction and therefore is advisable to be part of a treatment in low back pain patients.*

Keywords— back pain, longitudinal, shock wave, treatment.

I. INTRODUCTION

While extracorporal shock wave therapy (ESWT)has been integrated successfully into therapeutic issues regarding musculo-skeletal diseases and tissue healing for years now, there is still surprisingly little knowledge about the working and functioning of mechanical transduction. Since 1980 shock waves have been used to destroy nearly any kind of pathological calcification of the human body. Starting with the defragmentation of urinal stones known as*extracorporal Lithotripsy*, ESWT was also applied to decalcify painful calcaneal spur, frozen shoulder, lateral epicondylitis ("tennis elbow"), and tendinopathies in general. Other new perspectives of research discuss the use of extracorporal shock waves in disturbances in bone healing, spasticity, chronic skin ulcers and myocardial ischaemia[1]. While being considered an effective, safe and non-invasive treatment especially in the fields of regenerative medicine, ESWT was not used until now to relief unspecific low back pain. Chronic pain is described as a problem of the neuronal system without having a real anatomical disease[2]. Most ESWT in orthopedics resulted in significant reduction of pain even if the calcification could not be defragmented completely[2].

The transformation of mechanical force into biochemical signals of cells giving mechanosensitive feedback could be the underlying mechanism to understand how cell recovery and tissue healing take place. Basically every cell-structure showed to respond to mechanical-transduction; exogenous stimuli are transported through the extracellular matrix, affecting other biochemical - even intracellular - structures like proteins and therefore biopolymers. These effects seem to include reorganization and an increase in efficiency, communication and cooperation between cells. Even though not every mystery

about mechanical transduction is yet unraveled, it is known that shock waves are able to relief pain, positively regulate inflammation or induce neoangiogenesis and stem cells activities, thus improving tissue regeneration and healing[3].

II. MATERIALS & METHODS

2.1 Study design

During a period of 9 months in 2015 from March till November, we conducted a randomized, non-blinded controlled trial within the premises of the SchönKlinik München Harlaching. To assess the effect of ESW for the treatment of low back pain compared to the application of established mud pack(Fangos), participants were allocated to four parallel groups with a sample size of n=25 each. Every subject received 9 interventions (M1-M9, 3 sessions/week) plus two follow-up measurements after 4 and 8 weeks (N1/N2). On each session, subjects passed the test battery before and after receiving the intervention. For the treatment, all participants laid down backwards on a mechanical transduction couch (legs raised, head binned, IMP AG) and received either an ESWT for 10/15, or a Fango treatment for 15 minutes, or no treatment (control group, CG). This experimental protocol was conducted according to the declaration of Helsinki and was approved by the institutional review board of the ethical committee of the SchönKlinik München Harlaching.

2.2 Materials

ESW were applicated through a full-length treatment couch (170x82x66cm, EvoCell®) with an adjustable frequency ranging from 15Hz (900 SW/Min) to 30Hz (1800 SW/Min). One central actuator transmits a stroke of 1mm to the surface plate (wooden plate, cylinder at height of lumbar vertebrae L4/L5) providing a radial proliferation. Experimental guidelines from the manufacturer advice a usage of 23Hz for the duration of 10 to 15 minutes.

2.3 Population

Eligibility criteria covered the existence of nonspecific low back pain, age between 18 to 65 and no participation in other studies. A research assistant (RA) assessed the eligibility of every possible participant in a pre-study information call. Prior to measuring the subjects, an additional information interview gave them the opportunity to ask questions. Participants were allowed to cancel their attendance at any time without giving reasons. All interventions, the data collection and analysis took place in the rooms of our medical analysis department.

2.4 Study Interventions

Subjects were assigned randomly to either ESWT duration of 10 or 15 minutes, a 15 minutes Fango treatment or a control group. To encourage members of the CG not to interrupt their participation, an alternative treatment (ESW/Fango) after completing their 11 necessary assessment-sessions was guaranteed. The interpretation and analysis of the data was not provided by the administrating head of the study, which was involved in any of the measurements nor had any contact to the participants.

2.5 Randomization

The RA enrolled the participants for the study. Depending on the pre-study information calls, he gathered and blinded the VAS values for back pain of every subject. Afterwards the research coordinator used a randomized block design (2 blocks of variable length), dividing the blinded VAS values for back pain <=5 and >5 respectively, to generate the allocation sequence. After block-building, the RA assigned the participants to interventions. This method should guarantee homogenous starting conditions for all 4 treatment groups. Blinding the participants was not possible, because the treatments obviously differed from each other.

2.6 Outcomes

The primary outcome low back pain was defined as ‘current intensity of unspecific pain along the lumbar spine’, and was assessed at the beginning and the end of every session as well as immediately before and after the treatment via a VAS (0-10). Secondary outcomes included the postural sway defined as the ability to stabilize the trunk to an upright sitting position seated on a wobble board. First of all in lateral, and afterwards in ventral direction using the S3-check from proxomed® over a period of 15s on every session. Stabilizing-indices evaluate the percentage of time a participant was able to stabilize his trunk depending on 3 sections (red=poor/high amplitude, yellow=ok/middle amplitude, green=good/low amplitude). Low values indicate good posture. Additionally we assessed changes in the spine curvature with the help of a lightrasterstereography immediately before and after the interventions. Reflecting markers were used to assign the vertebrae

prominens and the lumbar dimples at S2. As tertiary outcomes we assessed the vascular relaxation defined by blood pressure and heart rate with an electronic blood pressure cuff.

2.7 Sample Size and Statistical Analysis

Power analysis was conducted with G-Power regarding a repeated measures ANOVA model within factors with α=0.05, β=0.90 and an estimated middle effect size of 0.25, leading to a sample size of at least n=20 for each group. All statistical analyses were conducted using the open source software 'R studio' in combination with its' GUI 'R commander'. The descriptive statistics/distributions were based on measures of dispersion and central tendency. Decision over normal distribution included graphical analysis as well as the shapiro-wilk-tests.Chi²-Test was used to determine distribution discrepancies between the groups; the repeated ANOVA model described the variance of the outcome variables within the four different treatments.

III. RESULTS

100 participants were recruited and split into 4 treatment groups with n=25 each. 16 Participants left the study after allocating them to a special group or simply did not appear to the appointment. Further 14 subjects discontinued the intervention due to missing time (10) or indisposition (2xEvo10, 1xEvo15, 1xFango) and one participant was excluded from the analysis because of a missing session; therefore 69 subjects finished all 11 measurements in total (Figure 1).

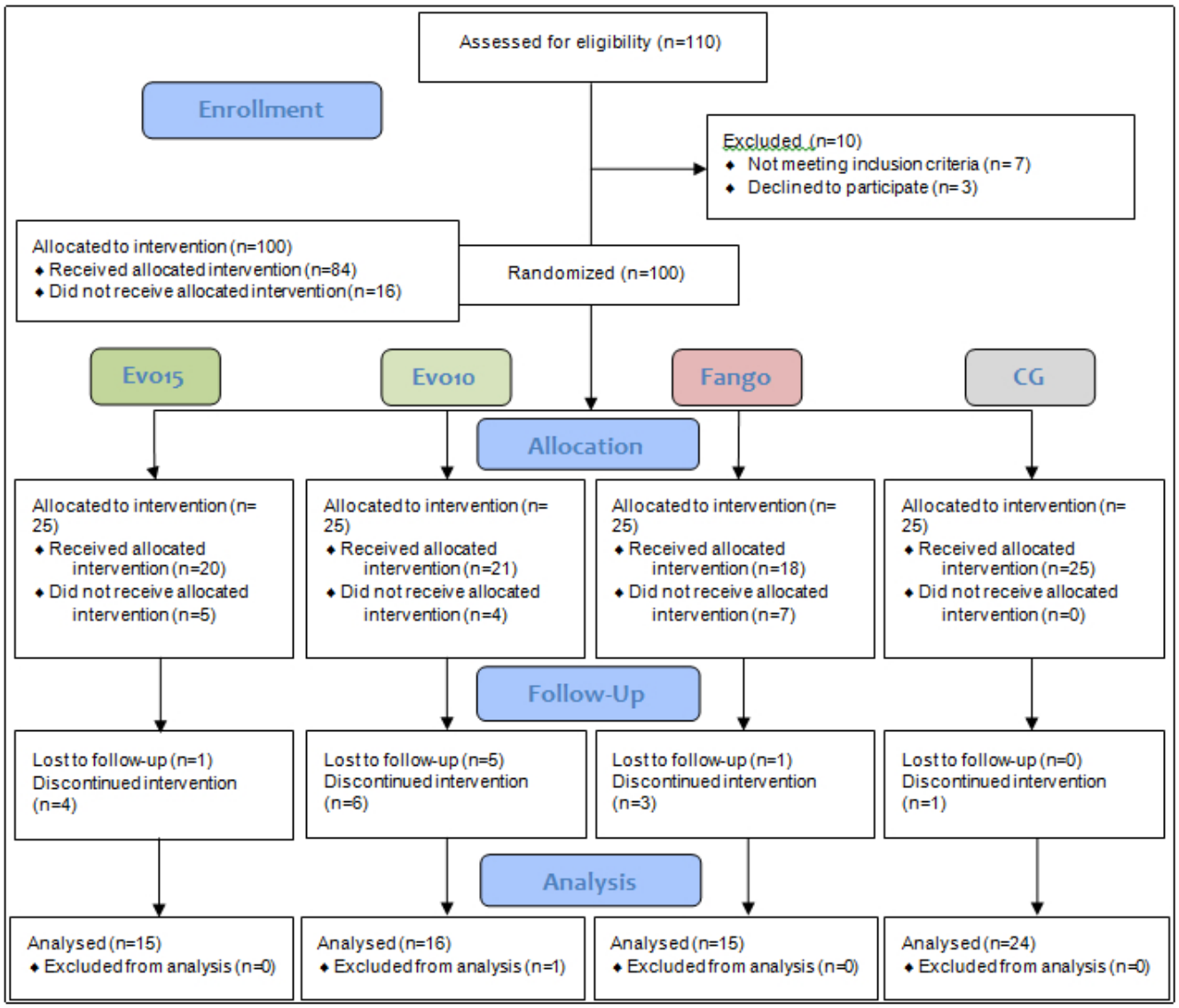

FIGURE 1: CONSORT 2010 FLOW DIAGRAM OF THE STUDY SAMPLE

Baseline characteristics of the sample are shown in Table 1.

TABLE 1
BASELINE CHARACTERISTICS OF THE SAMPLE

	Mean age	Gender (m/w)	Mean weight	VAS mean M1	VAS mean M4	VAS mean N2
Fango	38.8	7/8	81.7	3,2	2,1	2,1
Evo15	41.1	4/11	75.2	4,1	2,7	1,8
Evo10	35.5	6/9	72.3	2,9	2,2	2,1
CG	37.6	8/16	74.2	4,0	4,1	3,9

Neither mean age, nor weight nor VAS mean score at startup significantly differed between the four intervention groups.

3.1 Pain Intensity

Only subjects treated with Fango showed a significant decreasing acute effect on pain intensity, comparing the mean values for each session before and after intervention. But superior effects of the shock wave therapy could be identified in the mid- to long-term course. While the pain intensity in the Fango group before intervention just slightly reduced over time (n. sig. after 4 sessions, sig. decrease after 9 sessions, $p<0.05$), the EvoCell treatment showed sig. pain reduction after 3 sessions (compared to the starting VAS, $p<0.05$) and highly significant decrease in pain intensity ($p<0.001$) over the whole period of time (*Figure 2*).

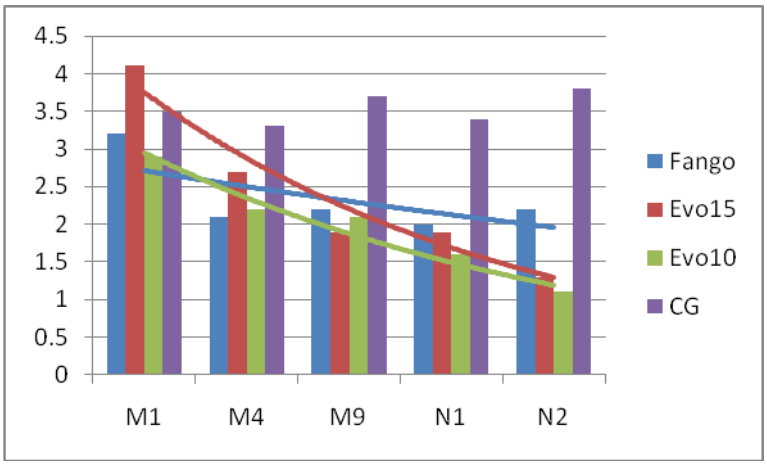

FIGURE 2: CHANGES IN MEAN VAS-SCORE AFTER 3 AND 9 INTERVENTIONS AND DURING THE FOLLOW-UP

3.2 Postural Control

EvoCell groups significantly improved their ability to stabilize sitting on a wobble board in the sagittal and frontal plain during the intervention period (M1 to M9). This trend did not recover completely over the follow-up period for Evo15 (M1-N2*, $p<0.05$, *Figure 3*).Statistical significance is shown in *Table 2*.

TABLE 2
P-VALUES FOR THE CHANGES OVER TIME OF THE STABILITY INDICES FOR ALL GROUPS

Axis	ventral		lateral	
Session	M1 to M9	M1 to M12	M1 to M9	M1 to M12
Fango	0.10	0.40	0.24	0.06
Evo15	0.03*	0.61	0.04*	0.02*
Evo10	0.04*	0.44	0.02*	0.76

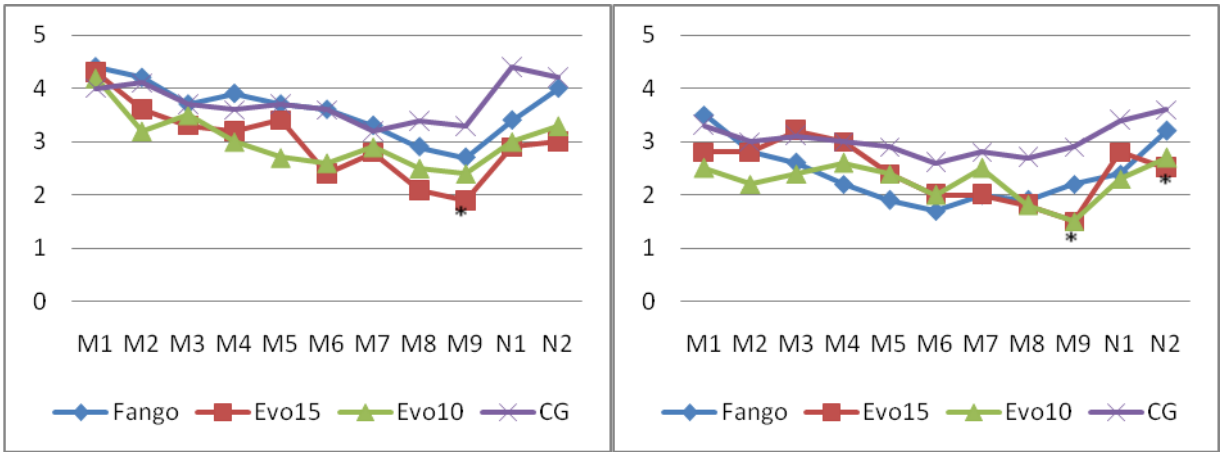

FIGURE 3: MEAN OF THE STABILITY INDICES FROM THE S3-CHECK (PROXOMED®) FOR ALL GROUPS (L.: LATERAL, R.: VENTRAL/DORSAL)

Regarding the static posture assessed by the LRS, no changes in any of the collected parameters could be identified. Neither geometrical variables influenced by muscular exertion like lordosis/kyphosis angle, hip rotation or torsion, nor trunk shape (e.g. length, surface characteristics).

3.3 Heart Rate and Blood Pressure

Fango significantly reduced BP in pre-post measurements ($p<0.05$), while neither the short nor the long duration ESWT showed any effects on pulmonary relaxation. By contrast,EvoCell groups appeared to have a significant reducing effect on HR ($p<0.001$).All acute effects regarding BP and HR were a matter of intervention based changes andvacated until the next session.

IV. DISCUSSION

Reviewing current and past literature dealing with cellular effects of mechanical transduction, it is becoming clear that a broad variety of structures take part in converting mechanical signals into biochemical responses, from ion channels to focal adhesions or cytoskeletal filaments[4][5]. Either by modifying opening and closing rates due to tensions of the membrane bilayers (through distorsion of integrins), or directly affecting the potential of proteins and enzymes, mechanical transduction is capable of modifying the extension and contraction of bioactive molecules. Especially the modification of biopolymers may be of higher interest for rehabilitation, being significant for metabolism, immunology, fibers or different hormones. With exogenous stimuli generating microscopically rearrangements, even stem cells commitment could be modified[6][7]. Besides the positive effects, grievance of inter-cellular mechanical transduction (e.g. due to mutation) showed to be a risk factor for many diseases as well (cardiomyopathies, cancer progression, etc.)[8].

Considering these aspects, it seems appropriate to ascribe therapeutic effects in cases of pain reduction and neuromuscular reorganization to mechanical transduction in the field of extracorporal shock waves. Therefore, in our longitudinal randomized controlled trial we were able to introduce CBSW to the field of low back pain treatment. Stimulation of healing processes on a cellular level has been published[3], but these effects were based on specific punctual application at the extracellular matrix. The microscopical mode of action generated by CBSW remains unclear and might be difficult to identify due to overlying effects. Especially against the background of individual response of cell structures to specific mechanical frequencies, the identification of responsible configurations for supportive effects seems impossible.

Besides lowering the pain intensity, ESWT appeared to improve postural control on a wobble board, too. Based on the knowledge of the structural diversity affected by mechanical stimulation, it seems eligible to assume that not only muscle fibers are influenced by ESWT, but afferent and efferent nerve tracts as well. Although a learning effect can't be denied, Fango and control group showed no significant changes in the stabilizing indicesand fully recovered to the base level until N2.

It seems that Fango treatment is more useful for acute effects, while for a long term therapy, shock waves might be a promising alternative [9]. Unfortunately, neither the specific mechanisms of pain reduction, nor the concept of forwarding extracorporal shock waves to a cellular level (frequency, amplitude, intensity) is currently clarified. Rubin and

McLeod[10]prefer loading at 20Hz instead of 30Hz and Warden and Turner[11] identified highest effects in cortical bone adaptation at an axial ulna loading frequency of 10Hz, while Rohringer et al.[12] postulate a 5Hz stimulus in the case of protein modification by treatment of Lymphatic Endothelial Cells. We used a frequency of 23Hz (recommended based on prior experiences of other institutes) with obviously good results for our primary outcome. Additionally, several high- and low-energized SW are used for the treatment of different diseases related to arthrosis, tendons and muscle fibers by doctors and physiotherapists. Although there is no evidence-based literature on the accurate effects of ESWT (less than ever for utilization frequencies), massive positive feedback has been published in the last decade in the field of mechanical transduction. Therefore we would plead for further clinical and experimental protocols under this topic, to benefit from the practical applications and to determine the scope of mechanical transduction by scientific investigations.

V. CONCLUSION

Regarding the individually different response of proteins and other structures on extracorporal shock wave frequencies, the specific underlying mechanisms remain unclear. Nevertheless the therapeutic use seems to be beyond all questions. As we were able to show in our randomized control trial, it can be assumed that the periodic application of a complete body shock wave stimulates mechanical transduction and therefore is advisable to be part of a treatment in low back pain patients. Further studies should focus on the comparison between a CBSW and evidence-based singular ESWT for the treatment of several diseases (e.g. in diabetes[13]). Based on the multiple positive effects combined with ESW, research should not be afraid of experimental clinical designs in future.

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