REVIEW ARTICLE

A Review of the Effects and Mechanisms of Shockwave Therapy on Enthesopathy

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ABSTRACT

Extracorporeal shockwave therapy (ESWT) for the treatment of musculoskeletal diseases is a field that is developing rapidly and attracting increasing attention. Studies exploring the effects of shockwave therapy on enthesopathy have resulted in equivocal findings. Therefore, the purpose of this review article is to collectively review and analyze published literature on the effects of shockwave therapy on enthesopathy in human studies. This is a literature review study however, systematic search was performed on Scopus, EBSCOhost (Medline, CINAHL, and Sport Discus), and Google Scholar databases. The search resulted in 112 articles, nine relevant articles that met the inclusion criteria were selected for analysis in this review. Shockwave therapy can be safe and effective to reduce pain, improve functions and activities as it accelerates the entheses healing. The exact mechanisms of shockwave therapy on enthesopathy are still debatable. Further investigation is needed to confirm and validate the findings of previous related studies.

Keywords: Shockwave therapy, Enthesopathy, Musculoskeletal diseases

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INTRODUCTION

Injuries related to tendon-bone junction became an interest among researchers due to the delay in healing following conservative and surgical procedures (1,2). The complexity of tendon and bone to blend is attributed to the non-homogenous structure in both types of tissues (3). From the current literature, shockwave therapy is one of the rehabilitation modalities that has potential to be applied to the entheses to accelerate the healing process (4-12). As a mechanical stimulus, ESWT promotes biological healing processes through mechanotransduction (13). The mechanical stimuli can induce physiological responses at the cellular level (14-15). Several studies have reported the effectiveness of shockwave therapy on bone structure (13,16-18) and tendon structure (19) alone. However, collective scientific evidences regarding the exact dosage of application and effectiveness of shockwave therapy on enthesopathy is still lacking. Thus, existing evidences from previous related research needed to be interpreted so that it can be implemented in a clinical setting. Then, shockwave therapy may become a new, valid, safe, and low-cost modality for treatment related to enthesopathy. Studies exploring the effects of shockwave therapy on enthesopathy have resulted in equivocal findings (4-12). Therefore, the purpose of this review article is to review published evidence on the effects of shockwave therapy on enthesopathy in human studies.

METHODS

This is a literature review study and we used systematic search to find the related published literature.

Literature search

A literature search was conducted for scientific articles published with no limit of years using available databases such as SCOPUS, EBSCOhost (MEDLINE, CINAHL, and SPORT DISCUS), and Google scholar in August 2019. The search keywords were 'shock wave' or 'shockwave', 'tendon-bone' or 'bone-tendon', 'insertion' or 'insertional', 'enthesis' or 'osteotendinous', and 'junction' or 'ACL'. The keywords may appear in article title, abstract or the article keywords itself. The flow of literature search is illustrated in Fig. 1.

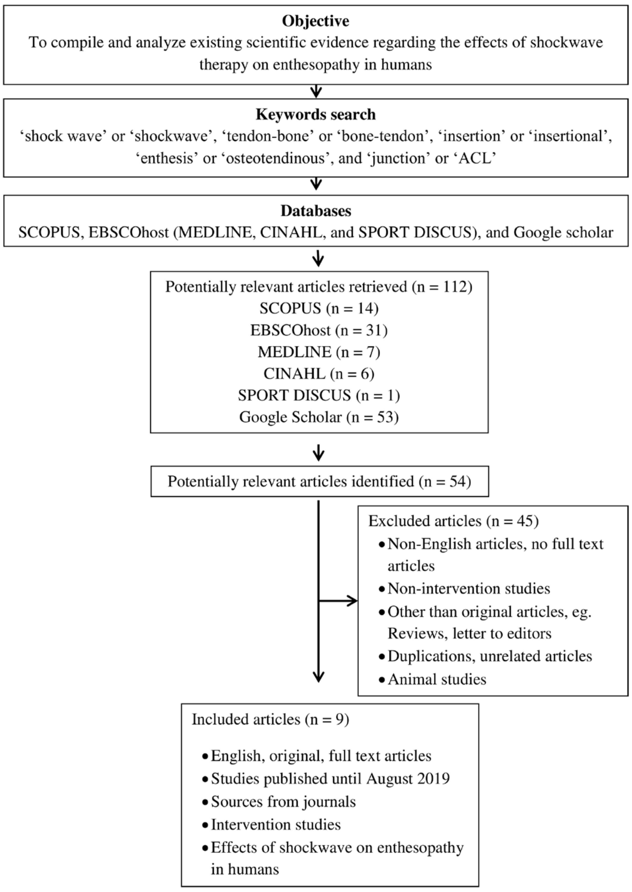

Figure 1: The flow of literature search

Inclusion criteria

The article must be a free full-length article in English language with an intervention study design investigating the effectiveness of shockwave on enthesopathy in humans. The sources were from journals.

Exclusion criteria

Articles were excluded if they were duplications and published as reviews, letters to editors, and without full-text.

Data extraction and analysis

Data on the methodology and findings for each study were extracted manually in an Excel database for manual analysis. The titles of the identified articles were screened to eliminate duplicates. The abstracts and full articles of the identified titles were reviewed manually to eliminate unrelated articles.

RESULTS

Articles retrieved

The search generated 112 articles related to the keywords. However, after the final selection, a total of 9 relevant articles that met the inclusion criteria were included for analysis in this review article.

Socio-demographic characteristics of previous human studies

Based on the literature search, nine studies involved humans (4-12) as their subjects. In human studies, the conditions involved were insertional Achilles tendinopathy (4,5,7-11), anterior cruciate ligament (ACL) (6) and insertional plantar fasciitis (12). Across the studies, 683 participants were included with the range of 40 to 198 participants in each study and comprised both gender with two main age range, i.e. 20 to 40 years old and 40 to 55 years old. There was only one article investigating the effects of shockwave therapy on enthesis after surgery (6). Meanwhile, others reported the effects of shockwave therapy on chronic injuries (Table I).

Table I: Socio-demographic characteristics of the participants enrolled from previous human studies (n = 9)

Authors / Year	Age in years; Mean ± SD (Range)	Gender		Participants
		Male	Female	
Furia (2006) (4)	ESWT group: 50.0 ± 9.2 (30-67) Control group: 52.6 ± 15.9 (21-80)	44	24	Individuals with IAT (n = 68)
Notarnicola et al. (2012) (5)	55.8±13.2	34	30	Individuals with IAT (n = 64)
Wang et al. (2014) (6)	28.0±7.55 (15-53)	42	11	Individuals with ACL reconstruction (n = 53)
Pavone et al. (2016) (7)	41.0 (32-56)	28	12	Individuals with IAT (n = 40)
Wu et al. (2016) (8)	Non-deformity group: 37.6 ± 9.2 Deformity group: 35.8 ± 7.4	39	28	Individuals with IAT (n = 67)
Wei et al. (2017) (9)	Eccentric exercise group: 36.8 ± 8.1 ESWT group: 34.9 ± 7.1 Endoscopy group: 34.5 ± 8.9	53	15	Individuals with IAT (n = 68)
Erroi et al. (2017) (10)	Platelet-rich plasma group: 47.7 ± 9.3 ESWT group: 53.2 ± 13.1	30	15	Individuals with IAT (n = 45)
Maffulli et al. (2018a) (11)	53.41 (20-81)	51	29	Individuals with IAT (n = 80)
Maffulli et al. (2018b) (12)	48.17±17.61 (20-82)	96	102	Individuals with IPF (n = 198)

ACL = Anterior cruciate ligament
ESWT = Extracorporeal shockwave therapy
IAT = Insertional Achilles tendinopathy
IPF = Insertional plantar fasciitis

Research methodology and main findings of previous human studies

Out of the nine studies, only three studies had a control group as one of their study groups (4-6), while the others only included intervention group/s, i.e. one intervention group (7,11,12), two intervention groups (8,10), and three intervention groups (9).

All researchers used various brands of shockwave therapy modalities however, there were two types of shockwave therapy modalities used, i.e. focus and radial types. Based on intensity classification cited by Rompe et al. (20) and Speed (21), two of the studies used focus type with high energy (4,6), three used focus type with medium energy (10-12), one used focus type with low energy (5), and three of the studies used radial type of shockwave therapy (7-9). Generally, the participants were sedated when the focus type shockwave therapy with high energy was applied during the treatment. Although more than half of the previous studies did not report the onset of the treatment given, it could be assumed as 'treatment for chronic condition' based on the common duration of symptoms experienced by the participants.

The intensity or dosages of shockwave therapy, i.e. number of shocks/impulses, pressures, total energy flux density (EFD), and the number of sessions differed across the studies. It was also found that focus type shockwave therapy with high energy was applied only once throughout the treatment session. The pain score i.e. visual analogue scale (VAS) was significantly improved in the intervention groups after one (4), two (10), three (4,11,12), four (10), six (5,10-12), twelve (4,7,11,12), eighteen (9) and twenty four months (11,12) of post-shockwave treatment. The research methodology and the main findings of the shockwave therapy effectiveness on enthesopathy in previous human studies are summarized in Table II.

DISCUSSION

It has been reported that shockwave therapy was effective to reduce pain experienced by the patients starting from 1-month post-intervention and persistent up to 24 months post-therapy. The pain scale was significantly lower in the intervention group when shockwave therapy was applied together with other types of local anaesthesia (regional block) compared to shockwave therapy with local anaesthesia as observed by Furia (2006) (4). It was mentioned that local anaesthesia reduced the effect of shockwave on the pain level. The reason is that infiltration of a local anesthesia before an ESWT procedure interferes with the focusing and targeting of the shock waves on the area of maximal discomfort (4).

High energy shockwave may require anaesthesia as the patients will experience pain during the treatment, whereas for low energy focal shockwave therapy, local anaesthesia is not recommended as it will reduce the therapeutic effect of shockwave therapy. Nevertheless, the dosage prescribed must be tolerable and within the patient's pain threshold limit.

It has been reported that a greater reduction of pain and limitation of activities among individuals with insertional Achilles tendinopathy was seen generally at 2 to 12 months of post-shockwave therapy. Previous studies showed significantly higher Roles and Maudsley Scores in the intervention group compared to the control group at 2nd and 6th months of post-shockwave therapy (5). Roles and Maudsley Scores are a four-point patient self-assessment scale of pain and limitations of activity. It indicates patients' satisfaction towards the result of the treatment. In other studies, although no significant value was found, the score was greater in the intervention group compared to the control group at 12 months (4), and it was 70% higher compared to baseline after 6 months of follow up (10).

Regarding the Victorian Institute of Sports Assessment-Achilles (VISA-A) score among the literature, a consistent results were reported. VISA-A is a set of questionnaires that measure the domains of pain, function in daily living, and sporting activity among individuals with insertional Achilles tendinopathy (22). It also predicts the clinical severity of Achilles tendinopathy. VISA-A score was significantly higher in the intervention group after two (10), four (10), six (10), twelve (11), eighteen (9) and twenty four months (11) post-treatment. Besides, Wu et al. (8) found the effectiveness of shockwave therapy for both insertional Achilles tendinopathy with and without Haglund's deformity at 14 to 15 months post-intervention. These findings showed that shockwave produced chronic therapeutic effects for reducing pain, improving individuals' functional and sporting activities starting at 2 months post shockwave therapy, and the effects were sustained until 24 months post-shockwave therapy regardless of the energy level applied.

American Orthopaedic Foot and Ankle Society Score (AOFAS) is used to measure pain, functions, and alignment among individuals with insertional Achilles tendinopathy. Generally, it measures the functional recovery after a hindfoot injury. Based on previous studies, in the 2nd and 6th months, the scores were significantly higher in the intervention group compared to the control group (5) and notably higher at 18 months after therapy compared to baseline scores (9). Like other types of questionnaires used, the effects of shockwave therapy can be seen after 2 months of post-intervention and continued until 18 months of follow-up period.

The shockwave therapy was interpreted as a successful intervention for insertional Achilles tendinopathy when the participants rated themselves with 1 or 2 in the 6-points Likert scales (8). However, for individuals with insertional plantar fasciitis, foot function index (FFI) has been used to assess foot pain and disability (12). This previous study reported that there was a significant decrement over time, i.e. at 3, 6, 12 and 24 months post-shockwave therapy in the intervention group.

Participants' quality of life showed significant improvement in mobility, pain, and discomfort including

Table II: Summary of the research methodology and main findings of the effectiveness of shockwave therapy on enthesopathy in previous human studies

Authors / (Year) (Sample size)	Aims/ Purposes	Study groups	Type of shock-wave machine	Sedat-ed	Treatment onset	Dosage / sessions	Parameters	Findings
Furia (2006) (4) (n = 68)	To determine the efficacy of high energy ESWT for the treatment of adults with chronic IAT and to determine if the use of a LA field block had an adverse effect on outcome	Controls, ESWT group; interven-tion + LA subgroup, intervention + other type of anesthesia subgroup (NLA)	Dornier (MedTech Inc, Kennesaw, Ga)	Yes	6-60 months after the onset of symptoms.	3000 shocks, 0.21 mJ/mm², EFD=604 mJ/mm² (once)	VAS, Roles & Maudsley Scores	1. 12 months after treatment, the number of patients with successful Roles and Maudsley scores was statistically higher in the ESWT group compared with the control group. 2. Compared to control group, the VAS score was significantly higher in the intervention group at 1, 3 and 12 months post shockwave therapy. 3. The mean VAS score in NLA subgroup was signifi-cantly lower than LA subgroup.
Notar-nicola et al. (2012) (5) (n = 64)	To assess the clinical efficacy and perfusion effects of oral dietary supplements in association with ESWT for IAT	Intervention and control	Minilith SL1 (Storz Medical Tagerwilen, Switzerland)	No	Not men-tioned	0.05-0.07 mJ/ mm², 1600 impulses (3 sessions, 3-4 days intervals)	VAS, An-kle-hindfoot scale score, the Roles and Maudsley, tis-sue oximetry values	1. The VAS score was significantly lower at 6 months in the experimental group compared to the control group. 2. The ankle hindfoot and the Roles and Maudsley scores were significantly higher in experimental group compared to control group at 2 and 6 months. 3. There was a statistically significant reduction in tissue oximetry values compared to baseline in both treatment groups at 2 and 6 months of follow up.
Wang et al. (2014) (6) (n = 53)	To evaluate the effect of ESWT on ACL reconstruction in human	Intervention, control group	OssaTron (High Medical Tech-nology, Lengwil, Switzerland)	Yes	Immediate-ly after ACL reconstruc-tion	0.298mJ/mm² = 20kV, 1500 impulses (once)	Lysholm score, KT1000, IKDC, Radio-graph-X-Ray, BMD, MRI	1. Significant better Lysholm score in ESWT group than control group at 1 and 2 year postoperatively. 2. Significant better KT-1000 values in ESWT group than control group at 2 year postoperatively. 3. Tibia tunnel on X-Ray was significantly smaller in ESWT group compared with control group at 2 year postoperatively. 4. On MRI, ESWT group showed significant decrease in tibia tunnel enlargement at 6 month and 2 years compared with the control group.
Pavone et al. (2016) (7) (n = 40)	To investigate the effect of com-bination of ESWT and eccentric exercise program on chronic IAT	Intervention group only	Electromedical device OssaTron	No	3 months post previous treatment	14kV, 4Hz, 800 shocks (4 sessions, with 2 week interval)	VAS, AOFAS (alignment and functional outcome of ankle)	1. Significantly improved VAS and AOFAS scores at 12 months.
Wu et al. (2016) (8) (n = 67)	To compare the result of ESWT for IAT with or without Haglund's deformity	Intervention group with and without deformity	Swiss Dolor-Clast, (Electro Medical System Munich, Germa-ny)	No	Not men-tioned	0.12 mJ/mm², 2000pulses, 8Hz (1/week, for 5 sessions)	VISA-A, 6 point Likert scale	1. The VISA-A score increased significantly in both groups post ESWT treatment. 2. There was greater improvement in VISA-A score for the non-deformity group compared with deformity group. 3. For the 6-point Likert scale, there were significant decreases in both groups at follow up time compared to baseline.
Wei et al. (2017) (9) (n = 68)	To investigate the effectiveness of endosco-py-assisted radio frequency ablation, ESWT and eccentric exercises in IAT	Three intervention groups only	Swiss DolorClast device (Electro Medical Systems SA, Nyon, Switzerland)	No	Not men-tioned	0.12 mJ/mm², 2000shocks, 10Hz (3 sessions, (1/week for 3 weeks), 1 week interval)	VAS, VISA-A, AOFAS	1. VAS, AOFAS ankle/hindfoot scales and VISA-A scale scores were significantly improved in endosco-py and ESWT groups after 18 months of treatment.
Erroi et al. (2017) (10) (n = 45)	To investigate the effectiveness of platelet-rich plasma and focused shock-wave therapy in IAT	Two intervention groups	Modulith SLK, (STORZ Medi-cal, Switzerland)	No	After 6 months of post diag-nosis and 12 weeks of wash out period from any non-operative therapy	2400 impulses, 0.17-0.25 mJ/ mm² (3 sessions, week-ly intervals)	VAS, VISA-A, patient satis-faction	1. Significant improvement of VISA-A and VAS scores in both groups (ESWT and PRP) at all-time points. (2, 4, 6, months follow up). 2. Patient satisfaction increased progressively >70% at 6 months for both groups.
Maffulli et al. (2018a) (11) (n = 80)	To determine the effectiveness of ESWT in patients suffering from IAT over a 24 months period	Intervention group only	Swiss DolorClast device (Electro Medical Systems SA, Nyon, Switzerland) and Stortz devices (Stortz Medical AG, Tagerwilen, Switzerland)	No	Not men-tioned	Initial 500, 1.5 bar, 2.5 or above, 2500 impulses (1/ week for 3 con-secutive weeks, max gap between 2 consecutive treatments of two weeks)	VAS, VISA-A (severity of TA), EQ-5D-3L (QOL)	There was significant amelioration over time in 5 of the 8 analyzed outcomes that were VAS, VISA-A and EQ-5D -3L domains (Mobility, pain/discomfort and usual activities scores).
Maffulli et al. (2018b) (12) (n = 198)	To determine the effectiveness of ESWT in patients suffering from plantar fasciitis in both the short and long term	Intervention group only	Swiss DolorClast device (Electro Medical Systems SA, Nyon, Switzerland) and Stortz devices (Stortz Medical AG, Tagerwilen, Switzerland)	No	Not men-tioned	Initial 500, 1.5 bar, 2.5 or above, 2500 impulses (1/ week for 3 con-secutive weeks, max gap between 2 consecutive treatments of two weeks)	VAS, Foot Function Index (FFI), EQ-5D (Quali-ty of life)	There were significant improvements over time in 6 of the 8 analyzed scores (VAS, FFI, and 4 scores of ED-5D (mobility, pain/discomfort, usual activities and thermometer scale)).

ACL = Anterior cruciate ligament
AOFAS = American Orthopedic Foot and Ankle Society Score
BMD = Bone mineral density
EFD = Energy flux density
IKDC = International Knee Documentation Committee
EQ-5D-3L = 3-level version of EuroQol 5 Dimensional
KT 1000 = a knee arthrometer
LA = Local anesthesia
MRI = Magnetic Resonance Imaging
NLA = Non local anesthesia
ESWT = Extracorporeal shockwave therapy
QOL = Quality of life
FFI = Foot function index
TA = Tendon Achilles
IAT = Insertional Achilles Tendinopathy
VAS = Visual analogue scale
PRP = Platelet-rich plasma
VISA-A = Victorian Institute of Sport Assessment-Achilles

usual activities scores three months after the last session of shockwave therapy in individuals with insertional plantar fasciitis. Meanwhile, the thermometer score was significantly better after 6 months of therapy compared to baseline level. This seems to indicate that the general perception of health status requires more time to improve (12). A similar questionnaire has been used to determine the quality of life among insertional Achilles tendinopathy participants (11). However, only pain and discomfort scores, including usual activity scores, were significantly improved after three months of shockwave therapy. It was reported that the mobility score began to improve at six months post-intervention.

To date, only one study investigated the effects of shockwave on tendon-bone junction after an Anterior Cruciate Ligament reconstruction in humans (6). The high energy shockwave was applied once immediately after the operation with the same anaesthesia by focus type shockwave. Their result showed that the knee function score was significantly greater in the intervention group compared to the control group at 1 and 2-years post-operatively. Furthermore, ligament laxity measurement revealed significant better values in the intervention group compared to the control group at 2-years post-operatively. Both diagnostic methods, i.e. X-ray and Magnetic Resonance Imaging (MRI) presented a smaller tibia tunnel after 2 years and significantly decreased in tibia tunnel enlargement after 6 months and 2 years post-operatively consecutively. Based on the outcome, high energy shockwave has the potential to improve knee function and knee joint laxity after ACL reconstruction and promote tendon-bone junction healing at 2 years post-operatively.

Most of the outcome measures in previous literature investigated the pain level, functional activities, and quality of life among the participants. The beneficial effects of shockwave therapy can be seen started at 2-months of post-therapy and continued for one to two years of the follow-up period. These findings reflected that few sessions of shockwave therapy might accelerate the entheses healing by reducing the pain level, improved functional activities, including the participants' quality of life for up to 2 years.

Shockwave produces mechanical stimulus that can propagate through tissue medium via mechanotransduction (13). Mechanotransduction was hypothesized as the working mechanism of ESWT (18). It was speculated that the propagation of the mechanical stimulus promotes biological healing such as tissue regeneration, wound healing, angiogenesis, bone remodelling and anti-inflammatory effects (13). Mantila et al. (14) mentioned that mechanical loading modulates gene expression and signaling pathways that may be associated with osteoblast differentiation and bone formation. The authors postulated that the presence of chemokines in the early response following mechanical loading is able to recruit osteoblasts and/or osteoblasts precursors to a site of bone formation, and chemokines are involved in bone remodelling and wound repair. Additionally, Schaden et al. (18) mentioned that growth factor release, cytokine expression and cellular events stimulated by ESWT result in bone repair. Meanwhile, Cheng at al. (16) reported that increased neovascularization scores following ESWT is related to the decrement of pain and improvement of function. The researchers speculated that neovascularization may improve blood supply, leading to tissue regeneration in tendinopathy. The potential mechanisms of shockwave therapy to accelerate the entheses healing are illustrated in Fig. 2. However, future study is warranted to validate these findings.

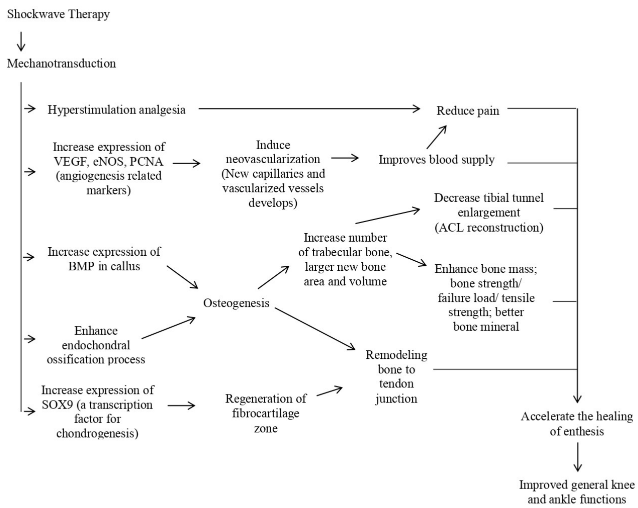

Figure 2: Potential mechanisms of shockwave therapy to accelerate the entheses healing

Comparisons of previous literature are difficult due to the limitation of studies with large scale variations. It includes variations in dosages, i.e. the amount of energy applied, the number of shocks or impulses, the number of sessions and interval between treatments. Besides, either extracorporeal shockwave therapy (ESWT) was applied alone or combined with other dietary supplementation, medication, or other therapeutic approaches such as exercises that might cause differences in the outcome measures. Additionally, the researcher needs to consider the type and brand of shockwave modality used, the intensity employed, i.e. high, low or moderate, and the differences between focused and radial type shockwave therapy that may contribute to the inconsistent effects on the treatment of enthesopathy.

CONCLUSION

Several previous studies have provided evidence that shockwave therapy can be safe and effective to reduce pain, improve functions and activities when applied on entheses structure. However, the exact mechanisms of shockwave therapy on enthesopathy are still unclear. Hence, further investigations are warranted to confirm and validate the findings of these previous studies.

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