Evaluation of the efficacy of extracorporeal shock wave therapy (ESWT) on osteoarthritis and post-ESWT analgesia in animal models

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Evaluation of the efficacy of extracorporeal shock wave therapy (ESWT) on osteoarthritis and post-ESWT analgesia in animal models

by

Jessica Ann Dahlberg

A thesis submitted to the graduate faculty
In partial fulfillment of the requirements for the degree of
MASTER OF SCIENCE

Major: Veterinary Clinical Sciences (Veterinary Surgery)

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Iowa State University
Ames, Iowa
2006

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This is to certify that the master's thesis of

Jessica Ann Dahlberg

has met the thesis requirements of Iowa State University.
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CHAPTER 1. GENERAL INTRODUCTION

Thesis Organization

The literature review in Chapter 2 is intended to offer the reader a greater understanding and a comprehensive summary of the current knowledge that motivated this manuscript. The primary objectives of this thesis are included in two published manuscripts that are included in Chapters 3 and 4. The first publication is titled "The evaluation of extracorporeal shock wave therapy in naturally occurring osteoarthritis of the stifle joint in dogs". The second paper is titled, "Force plate evaluation of analgesia from focused extracorporeal shock wave therapy in unilateral forelimb lameness". Each study contains a separate summary, introduction, materials and methods, results, discussion, references, tables, and figures. The general conclusion in Chapter 5 discusses the results of each study and mentions the contribution they have made to the existing data involving extracorporeal shock wave therapy.

Introduction

Therapeutic use of extracorporeal shock wave therapy (ESWT) was first reported for the treatment of uroliths in humans in the 1970's and has been used in human orthopedics for over 10 years (1,2). ESWT has had promising results treating a wide variety of musculoskeletal diseases resulting in bone remodeling, neovascularization of bone-tendon interfaces, and orthopedic pain relief (2, 3). ESWT has been applied to musculoskeletal diseases in animals in the United States for over 7 years (4). Although, ESWT has been used extensively in human and veterinary medicine, questions regarding efficacy and mechanism of action remain.

Osteoarthritis is a significant cause of lameness in humans and animals (5, 6). Interestingly, studies evaluating the ESWT for osteoarthritis are lacking in literature and further trials are necessary. In Chapter 3, we have evaluated the effect of ESWT on naturally occurring osteoarthritis in the stifle joints of dogs.
Analgesia has recently been identified as a potential side effect of ESWT. There are no studies that objectively evaluate analgesia following ESWT. In Chapter 4, we have evaluated the analgesic effect of ESWT in horses.

There remains much to be learned about ESWT, as it becomes a widely accepted treatment for musculoskeletal disorders. This manuscript explores the efficacy of ESWT on osteoarthritis and characterizes post treatment analgesia effects.
CHAPTER 2. LITERATURE REVIEW

Pressure wave generation and focusing

Shock waves are acoustic pressure pulses that may reach very high pressures up to 1000 times atmospheric pressure (100 MPa). These pulses reach maximum pressure in nanoseconds while the entire pulse lasts 5-6 microseconds (7). Shock waves used in clinical situations are single-pulse mechanical pressure waves focused on target tissue (8, 9). The pulses are delivered relatively slowly with up to 4 pulses per second.

To date, three types of focused shock wave generators have been used to perform these functions (8, 9). All generators use a fluid media in which the shock wave is generated. With electrohydraulic devices, a spark is discharged through a converting medium and generates the pressure or shock wave, which is focused by a parabolic reflector. With electromagnetic shock wave devices, electric current induce magnetic fields that cause membranes to repel each other, resulting in compression of the converting medium and ultimately, focused shock waves. Using piezoelectric shock wave devices, focused shock waves result from oscillating quartz crystals in an electrical field. As a pressure wave moves through tissue, there is compression in front of and tension behind the wave. As the wave travels, a negative component on the trailing edge creates tension. This can create cavitation bubbles at interfaces of free gas or solid particles (10). The moving bubbles collapse asymmetrically creating a water jet onto the surface (11). A surface pit, created by the collapse of the bubble, has the same diameter as the water jet and is believed to disrupt the contacted tissue (12). Studies have shown that the interaction of lithotripter-generated shock waves with gas bubbles generate water jets with speeds up to 700 m/sec or nearly the speed of a rifle bullet (13).

Once generated, shock waves are then focused by an ellipsoid or lens and directed at a treatment site in the body. If all material parameters are the same, the smaller the focus of the shock wave, the higher the positive pressure targeted at a smaller area. Shock waves may be dispersed over a larger area by increasing the focus size. The focusing devices mentioned
previously concentrate acoustic (mechanical) energy into focal areas and thus, increase desired tissue changes at the target area while avoiding effects in surrounding tissues (8).

This concentrated shock wave energy per unit area is referred to as Energy Flux Density (EFD) measured in millijoules per square millimeter (mJ/mm$^2$). The size of the ellipsoid and strength of the initiating current determine the EFD produced by the source (8). Total energy of therapeutic shock waves also depends on the number of pulses delivered to the target tissue (14). Human ESWT treatment typically uses 0.0001 to 0.6 mJ/mm$^2$ and EFD and pulse parameters are similar in veterinary ESWT (15, 16). Energy flux densities up to 0.89 mJ/mm$^2$ have been used in horses (17).

Kinetic energy is released when shock waves encounter a difference in acoustic impedance between 2 tissues such as muscle and bone. Shock waves can travel through tissues of similar acoustic impedance without losing a significant amount of energy. The acoustic impedance of fat, muscle, and water are similar (1380, 1650-1740, 1480 x 10$^3$ Ns/m$^3$ respectively). Conversely, there is a large difference in the acoustic impedance of air (429), lung tissue (260-480), bone (3200-7400), and uroliths (5600-14,400 x 10$^3$ Ns/m$^3$) (8). Shock waves are reflected, refracted, or absorbed at the interface of 2 tissues with unlike acoustic impedances and kinetic energy is released. Then, through unknown mechanisms, the shock waves cause tissue alterations and responses that have been useful in clinical applications.

Radial Pressure Wave Therapy (RPWT)

RPWT differs from ESWT in that radial pressure waves have different pressure profiles than shock waves. Extracorporeal shock waves are generated in fluid by the conversion of electricity into fast-moving high pressure waves. Conversely, radial pressure waves are created by discharges of compressed air that cause acceleration and collision of a projectile with a probe in the hand piece (8). Mechanical concussion generates waves of pressure, which decline in an inverse square proportion to the distance from the source. Maximum pressures of radial pressure waves are 100 times lower than ESWT and pulse durations are 1000 times longer. In contrast to ESWT, which delivers energy to deeper tissues, RPWT delivers maximal energy to the skin surface.
Cleveland et al compared ESWT and RPWT and found that the ESWT device produced cavitation, which lasted for 110 to 140 µs while the RPWT generator produced no detectable cavitation (18). This study highlights the physical differences of RPWT and ESWT. Much less information on RPWT than ESWT exists in literature.

**ESWT effects in vitro**

**Cell membrane alteration**

Low energy shock waves (0.12 mJ/mm$^2$) applied to cell cultures resulted in alteration of cell membranes (19). Gambihler et al thought that the cavitation effect of shock waves causes disruption of cell membranes and thus, increased permeability (20). The study applied 1000 pulses at 25 kV to a suspension of cells while a control cell suspension received sham treatment. After treatment, 15% of the ESWT cells remained undisturbed while 100% in sham treated controls remained undisturbed. Numerous researchers have utilized this shock wave-induced increase in cell membrane permeability in cellular studies. This transient increase in permeability allows for the passage of macromolecules such as oligonucleotides and small proteins into the cell cytoplasm (19). Gene therapy and photodynamic tumor treatment has utilized shock wave-induced fluorescein dye transfer into cells. Other experiments have delivered ribosome-inactivating proteins into cells, thereby, reducing drug concentration used to alter cell proliferation by up to 40,000 times (21). The enhanced cellular permeability caused by ESWT has also increased the effects of chemotherapy by aiding in chemical transfer into cells to decrease tumor perfusion (22).

**Osteogenesis**

Studies performed *in vitro* on bone marrow stromal cells have resulted in enhanced stromal cell growth, production of Transforming Growth Factor-beta 1 (TGF-β1), and differentiation of stromal cells into osteogenic cells (23). TGF-β1 is a growth factor with chemotactic and mitogenic effect on osteoblastic cells. Shock wave stimulation of TGF-β1 is dose related with no effect at low levels and adverse effects such as stromal and bone cell damage at excessive levels. Increases in concentrations of osteogenic TGF-β1 occur as
superoxide radicals, such as nitric oxide, increase. Studies suggest that nitric oxide may be important secondary messenger in biologic fracture repair (24). Shock waves generate free radicals and, therefore, may play an important role in biological processes such as fracture repair. Another investigation involving substance P, a neurokinin involved in osteoblast proliferation, had higher levels in shock wave treated rabbit femurs (25). Additionally, studies using cell cultures found that ESWT increases both osteoprogenitor cell division and bone morphogenetic protein concentration. Bone morphogens proteins are growth factors belonging to the TGF-β super family involved in new bone and cartilage formation (23, 26).

The osteoblastic and cell-altering capabilities shock waves have displayed _in vitro_ have resulted in further _in vivo_ research and applications of shock waves on musculoskeletal disorders such as delayed and nonunion fractures, periarticular, and intra-articular diseases. Multiple ESWT studies have described ESWT to stimulate remodeling of bone, increase blood flow to bone-tendon interfaces, stimulate healing of ligaments, and alleviate pain associated with musculoskeletal disorders (3). ESWT has become the preferred treatment for hypertrophic pseudoarthrosis in humans and is considered a superior noninvasive treatment for calcific tendonitis, tendinopathies, and periarthritis.

**Bone microdamage**

In 2004, Da Costa Gomez evaluated the effect of ESWT and RPWT _in vitro_ on microcracks in equine bone (27). Mid-diaphyseal third metacarpals and third metatarsals were collected from 11 Thoroughbred racehorses with a unilateral catastrophic injury from 5 non-racing horses. ESWT (9,000 pulses 0.15 mJ/mm², 4 Hz) and RPWT (9,000 shock waves, 0.175 mJ/mm², 4 Hz) treatments were randomized to the proximal and distal segments of the long bones. The middle segment was used as a treatment control for pre-existing microcracks. After ESWT, bone specimens were stained and sectioned. Microcrack density and microcrack surface density were increased after focused ESWT. Microcrack length was increased after RPWT. These preliminary data suggest that ESWT and RPWT have the potential to increase bone microcracking in equine distal limb bone _in vivo_.

However, contrasting results were found in another microcrack study (28). Eight dorsal cortical bone specimens were treated with 2000 pulses of ESWT at 0.15 mJ/mm² and
8 specimens were treated with 2000 pulses of RPWT at 0.16 mJ/mm$^2$. The ultrasound velocity was determined in each bone specimen before and after each of the 4, 500 pulse treatments. The research team found that velocity, and therefore the modulus elasticity, was not affected by ESWT or RPWT and there was no formation of microcracks.

**ESWT effects in vivo**

A major benefit of ESWT use in clinical applications since its inaugural use with uroliths has been to avoid surgery. This advantage continues to validate and motivate the use of ESWT in various clinical applications today. The success of ESWT in *in vitro* studies has prompted extensive research from numerous *in vivo* trials to clinical application in human and veterinary hospitals. The ensuing review will discuss *in vivo* explorations and clinical applications of ESWT on musculoskeletal disorders including bone, tendon, ligament, and joint diseases. Additional clinical applications and potential complications are also discussed.

**BONE - RESEARCH**

*Osteogenesis*

ESWT has been shown to induce osteogenesis in laboratory animals (29, 30, 31). First, the focused shock waves produce microfractures of trabecular bone resulting in release of osteoinductive growth fractures. Next, a “fracture hematoma” forms and neovascularization ensues attracting osteoprogenitor cells. Finally, osteoblasts proliferate and bone formation occurs. Delius *et al* performed an *in vivo* study applying very high-energy shock waves (1500 pulses at 27.5kV) to rabbit bone (29). Initially, bone disruption was evident by periosteal detachment and subperiosteal hemorrhaging. However, during the weeks following ESWT, intense apposition of new cortical bone lead to considerable cortical thickening.

*In vivo* osteogenic qualities of shock wave therapy were first detected in studies with rabbits. One thousand five hundred shockwaves at 27.5 kV were applied to the normal femurs of 19 rabbits divided into 5 groups. Periosteal elevation, cancellous bone disruption,
and osteonecrosis occurred following the shock wave treatment (29). Studies in rabbit radius defect models found that treated bones had greater callus formation than non-treated bones (32, 33). In bilateral 1 cm radius defects, ESWT was applied via fluoroscopy to 1 forelimb on days 7, 14, and 21 while the other forelimb served as a control. After 6 and 12 weeks, the subjects were sacrificed and the calluses were examined. The average callus area in the ESWT-treated radial defect was greater in both the 6 and 12-week groups and statistically significant in the 12-week group \( (p < 0.05) \). Uslu et al concluded that ESWT has a disorganizing and dispersing rather than a direct osteoinductive effect on callus formation (33). In 1991, Ekkercamp et al performed ESWT in vivo on sheep models and used fluorescent microscopy to confirm dose dependent osteogenesis (34). Tischer et al investigated the ability of shock waves of varying EFDs to cause osteogenesis outside of the focus zone (35). Eighteen adult Chinchilla-Bastard rabbits were assigned into 3 groups and 1 distal femur of each animal was treated with focused shock waves. Two EFDs \((1.2 \text{ mJ/mm}^2, 0.9 \text{ mJ/mm}^2)\) and a sham treatment group were used. New periosteal bone formation outside the shock wave focus was significantly increased in rabbits in the group treated with 1.2 mJ/mm\(^2\) compared to the 0.9 mJ/mm\(^2\) group \( (p = 0.007) \) or the sham group \( (p = 0.001) \).

The scenario of bone damage resulting from high-energy shock waves appears to be applicable only to laboratory animals and has not been reported in dogs or humans. The mechanism of bone stimulation seen in large animals is likely due to other mechanisms (28).

**Fracture healing**

One of first studies on fracture healing was performed in rats (36). Mid-diaphyseal humeral fractures were created in 40 rats. Thirteen rats were treated with 100 pulses (14 kV), 13 subjects were treated with 100 pulses (18 kV), and 14 rats served as controls. ESWT was performed on days 2, 5, 9, 14, and 19. Measuring breaking strength, the fracture site of the treated bones were 18% (14 kV) and 30% (18 kV) stronger than the control bones.

ESWT has had beneficial effects on in-vivo non-union canine models (37). Johannes et al performed radial ostectomies on 10 beagles, which resulted in hypertrophic non-unions. Twelve weeks later, 4,000 pulses \((0.54 \text{ mJ/mm}^2)\) were delivered to the ostectomy site of 5
dogs. Four of 5 treated dogs experienced osseous union in 12 weeks after treatment and only 1 of 5 control dogs developed osseous union.

The effect of shock wave therapy has been studied on acute fractures fixed internally with orthopedic implants (38). Bilateral tibial fractures with 3-mm gaps were created in 8 adult dogs and the metallic plates and screws were applied. Two thousand pulses (14 kV) were delivered to the fractures while the contralateral limbs served as controls. Serial radiographic examinations evaluating callus formation were taken at 1, 4, 8, and 12 weeks. Tissue histology was examined at 12 weeks. Radiographically, there was no statistically significant difference in the amount of callus formation between the treated and the control groups until 12 weeks after ESWT when the treated dogs showed significantly more callus formations than in the control group. Histologically, there was significantly more dense cortical bone formation in the treated group at 12 weeks. The researchers did not describe any disturbance to the bone plate or screws.

Orthopedic implants

A potential application of shock waves is to loosen bone cement (polymethylmethacrylate) used for prosthesis placement (39). Cement extraction contributes to morbidity associated with arthroplasty revisions. Using the same mechanism to fracture uroliths, ESWT may break apart the implant material and facilitate removal of the prosthesis. Weinstein et al suggest that ESWT may be useful adjunct in revision surgery necessitating extraction of polymethylmethacrylate before replacement of endoprosthesis. Shock waves were focused at the bone-cement interface in 1 femur of 6 pairs of canine femurs with femoral stem implants. The other femur served as a control. The results found that the ESWT-treated femurs had significantly less shear strength than the control femurs (P < 0.003). Additionally, microfractures were seen at the bone-cement interface. Stranne et al subjected canine femurs to either manual cement extraction or ESWT followed by manual cement extraction (40). The contralateral femurs served as controls. No statistical significance was demonstrated between the 2 groups in relation to mechanical properties (torque, angle, or energy capacity). ESWT exposure had a minimal and insignificant effect on bone strength at bone-cement interfaces. The inconsistent effects of ESWT on loosening
cemented orthopedic implants suggest that more research is warranted to define the role of ESWT in revision arthroplasty.

**BONE – HUMAN CLINICAL APPLICATIONS**

*Non-unions/pseudoarthrosis*

Osteosynthesis and bone grafting has been the gold standard for treatment of delayed or non-union fractures and pseudoarthrosis in humans. However, the low risk and non-invasive nature of high-energy shock wave therapy has proven to be a valid alternative to invasive surgical treatments of these diseases in humans (2, 3, 14, 16, 30, 31, 37, 41, 42, 43). Over the last decade, ESWT has become the preferred treatment for non-unions in humans according to the largest study to date (44). Seventy-six to 85% of treated non-unions in people have undergone fracture healing (45, 46). Encouraging results from ESWT occur with fracture gaps less than 5mm, whereas fracture gaps greater than 5mm do not respond favorably to ESWT (44). ESWT has proven to be successful on long bone diaphyseal pseudoarthrosis (31). Two thousand pulses (18 kV) were applied to diaphyseal pseudoarthrosis sites. Within 6 weeks, a callus formation was manually detected in the non-union soft tissue. The callus transformed into bony union in 3 of the 4 cases.

Human non-unions respond differently to ESWT depending on their location. Shaden *et al* conducted a study using ESWT to treat various bone fractures or delayed bony unions in 115 patients (42). The ESWT treatment lasted 20 to 60 minutes and the amount of EFD and number of pulses applied depended on the fracture site. Scaphoid fractures received an EFD of 0.25 to 0.35 mm/mJ² and 1000 to 2500 pulses. Tibia or femur fractures received an EFD of 0.4 mm/mJ² and 12,000 pulses. Eighty-seven (75.7%) of the patients achieved union. Those patients who failed to achieve union may not have healed due to defects greater than 5 mm or inadequate immobilization.

Another ESWT study was performed on 43 patients with pseudoarthrosis persisting for 9 months after trauma or selective osteotomies (47). All patients received a single session of 3000 impulses at an EFD of 0.6 mJ/mm² under regional anesthesia. Radiographs and bone scintigraphy were performed from 8 weeks to 9 months after ESWT. Thirty-one of 43
(72.1%) patients developed cortical bridging at their pseudoarthrosis site at approximately 4 months after ESWT. Twenty-five of 31 (80.6%) of the successfully treated patients showed active bone growth (positive scintigraphy) while 4 of the 12 (33.3%) unsuccessfully treated patients showed positive scintigraphy. Twenty-nine of the 35 (82.9%) patients with a positive bone scintigraphy displayed evidence of bony healing compared to 2 of 8 (25%) patients with a negative bone scintigraphy.

Non-union fractures with hypertrophic biological activity have benefited from ESWT more than atrophic non-unions (48). Unstable, avascular, or hypoplastic non-unions in humans do not benefit from shock wave therapy (42). In a 2000 study in humans, 100% of hypertrophic non-unions developed bony union while only 34.6% of atrophic non-unions achieved bony union after ESWT (45). Duration of non-union healing also influences the onset of bony union regeneration. A recent human study found that those with non-unions lasting 6 months or less experienced a decreased fracture gap by 3 months post ESWT. Those subjects with non-union fractures lasting 9 months or more experienced a decrease in fracture gap by 4 months post ESWT. Those with shorter duration of non-union before ESWT also endured less pain and more callous formation post ESWT (42).

**Femoral head osteonecrosis**

ESWT has been investigated as a potential non-invasive alternative for osteonecrosis of the femoral head (49, 50). Twenty-two patients with femoral head necrosis confirmed with MRI results were treated with ESWT and evaluated 1 year post treatment (50). Visual Analog Scores (VAS) evaluating pain decreased from 8.5 before treatment to 1.2 one year after ESWT. Additionally, the Harris hip score increased from 43.3 to 92 points. The Harris Hip Score is a subjective analysis of degree of pain during and extent of ability to move the coxofemoral joint. Furthermore, patients who responded favorably to ESWT had an absence of a distinct zone of sclerosis around the necrotic area remaining after treatment. The study suggests that ESWT is valuable modality for the treatment of femoral head necrosis in the early stages of the disease process.
Non delayed-union fractures / pseudoarthrosis

As in human medicine, ESWT is more effective on non-union fractures with hypertrophic biological activity than on atrophic non-unions (48). Similarly, unstable, avascular, or hypoplastic non-unions do not benefit from ESWT (37, 43). The osteogenic and neovascular properties of ESWT may be useful for fractures with delayed healing such as those seen in the ulna or distal radius of toy breeds, multiple fractures, open fractures, fractures in older animals, and fractures in systemically ill animals (3, 51, 52, 53).

A case study utilized ESWT in horses with distal phalanx fractures refractory to conservative treatments such as nonsteroidal anti-inflammatory drugs and corrective shoeing (54). McClure performed 3 treatments at 2 week intervals targeting shock waves (EFD 0.15 mJ/mm²) through the frog. A bar shoe was maintained throughout the treatments. In this study, the horse treated with ESWT for a distal phalanx fracture was clinically sound and returned to race training 10 weeks after the first ESWT treatment.

Dorsal metacarpal disease

Bucked shins result from repetitive loading and consequent bone remodeling in the dorsal cortex of the third metacarpal bone. ESWT has shown to increase the number of activated osteons from the periosteum to the endosteum of the third metacarpal bone (55). A separate study suggests that ESWT may be a useful adjunctive therapy in addition to training modification in horses suffering from dorsal metacarpal disease. Fifty thoroughbred racehorses with clinically or radiographically evident dorsal metacarpal disease were treated with RPWT and a modified training program (56). After completion of treatment, 40 of the 50 horses returned to racing without recurrence of lameness. Twenty of the 50 horses with a single oblique dorsal cortical stress fracture returned to racing in a mean time of 5 months after the last ESWT treatment (56). A separate study had similar results. Eight hundred pulses at 0.14 mJ/mm² were delivered to the dorsal aspect of the third metacarpal bone at 1 to 2 week intervals for 3 treatments (54). A cycle of 1 week of walking and 2 weeks of training was repeated twice. When treated early in disease with this ESWT protocol, the study showed that most horses return to training.
Incomplete/stress fractures

Horses with stress fractures in the humerus, tibia, or third metacarpal bone may be treated with ESWT (57, 58). Scheuch, et al found promising results 90 days after ESWT on metacarpal stress fractures in 10 horses (57). Six horses showed clinical and radiographic resolution of their stress fractures and 2 horses showed signs of healing in 120 days. The 2 other horses were retired. Analgesic effects offered by ESWT when applied to stress fractures may lead horses to returning to work before stress fractures are actually healed. Therefore, radiography and scintigraphy should be used to evaluate stress fracture response to ESWT before returning a treated horse to work (58).

Proximal splint bone fractures

A recent study used ESWT on a total of 7 horses; 4 non-infected and 3 infected proximal splint bones (Weinberger, T unpublished data, 2003). The horses with infected fractures were given local and systemic antibiotics, their fracture sites were curetted and lavaged, and the skin defect was allowed to heal before ESWT was performed. All 7 horses received 3 treatments at 10 to 14 day intervals. Depending on the size of the lesion, either the 5 mm and 20 mm or the 20 mm and 35 mm probes were used to deliver a total of 600 to 900 pulses to the fracture sites at an EFD of 0.15 mJ/mm². Horses with closed fractures returned to training 10 to 12 weeks after the fracture while the horses with open fractures took 1 to 6 weeks longer to become sound.

Navicular syndrome

ESWT has been evaluated as a treatment for navicular syndrome in horses (58). In a recent study, 16 horses with navicular syndrome were administered 1000 pulses (0.89 mJ/mm²) through the frog and 1000 pulses between the heel bulbs of the affected feet with while under general anesthesia. Blinded evaluators subjectively graded the lameness in each horse before and 6 months after ESWT. On a lameness scale of 0 to 5, the average lameness grade was 1.8 when trotted in a straight line on a hard surface before treatment. When the affected limb was inside while trotting in a circle, the average lameness grade pre-treatment was 2.6 (0 to 4 scale). After treatment, 9 of 16 (56%) horses improved and the mean
lameness grade decreased to 0.7 and 0.9 while trotting in a straight line and in a circle, respectively. Radiographs were performed before ESWT. It was proposed that horses with radiographically evident enthesopathy of the navicular suspensory ligament or radiolucent erosions of the navicular bone flexor cortex do not benefit from ESWT.

TENDONS AND LIGAMENTS - RESEARCH

Chronic Achilles tendinopathy

Studies involving ESWT effects on the tendons and ligaments of animals have increased in recent years. Orhan, *et al* used rat Achilles tendons to assess the effects of ESWT on tendon healing by observing histological and biomechanical parameters (59). The right Achilles tendon of 28 rats were cut and then sutured. Five hundred pulses (14 kV) were applied to the Achilles tendon of 14 rats. Fourteen other rats underwent a sham operation and served as the control group. The rats were sacrificed 3 or 9 days after ESWT and biochemical studies were performed to measure hydroxyproline levels. Hydroxyproline is a major component of collagen and provides stability to the triple-helical structure of the protein. Levels were found to be higher in the treated groups. The histopathology findings and the increased hydroxyproline levels revealed that ESWT might facilitate tendon healing after trauma.

A second study by Orhan induced lesions in the 48 rat Achilles tendons with an 18-gauge needle and the animals were divided into 3 groups (60). The first group received only radiation after the operation and the second group served as untreated controls. The third received 500 pulses (15 kV) of ESWT on the second post-operative day. All the rats were killed 21 days after surgery. Histopathology results showed an increase in the number of capillaries and less formation of adhesions in the ESWT group compared with the control group (*p* = 0.03). Additionally, a significantly greater force was required to rupture the tendon in the ESWT group (*p* = 0.028).

The effect of shock waves on canine Achilles tendon/bone interface has been studied. Wang, *et al* treated the Achilles tendon-bone junctions in 8 dogs with 1,000 pulses at 0.18 mJ/mm² (61). Biopsies were taken from the treated tendons at 4 weeks and 8 weeks after
shock wave application. Microscopic neovascularization and myofibroblasts were found in the ESWT-treated specimens 4 weeks and 8 weeks after shock wave application, but none were seen in the control specimens. The study concluded that ESWT increases neovascularization at bone/tendon interfaces.

The potential adverse effects of ESWT on tendons and ligaments have been evaluated in lab animals. In rabbit Achilles tendon models, dose dependent inflammation resulted with EFD greater than 0.28 mJ/mm² (62). However, EFDs greater than 0.28 mJ/mm² are used routinely in other mammals without complications. In another study using turkey mineralized gastrocnemius models, an EFD of 0.6 mJ/mm² had no effect on the material characteristics of the tendon. An EFD of 1.2 mJ/mm², however, resulted in decreased tensile strength (63).

**TENDONS AND LIGAMENTS - HUMAN CLINICAL APPLICATIONS**

*Calcifying tendonitis*

Shock wave therapy has gained increasing acceptance in treating tendonitis and desmitis in people. The Food and Drug Administration has approved its use for the treatment of plantar fasciitis (64). People with calcification of the rotator cuff are routinely treated with ESWT and have experienced dissolution of calcification and subsequent pain relief. Small areas of mineralization seen ultrasonographically respond better to ESWT than large areas seen radiographically (64, 65, 66).

*Plantar fasciitis (calcaneal, heel spurs)*

Plantar fasciitis is the most common musculoskeletal disorder investigated in recent ESWT data. The ability of ESWT to alleviate pain associated with plantar fasciitis is the primary focus of most of these studies. One prospective study administered 3 to 5 low energy ESWT treatments (0.09-0.18 ml/mm²) to the injured plantar fascia of 85 patients (25). A significant decrease in pain occurred after 5 months.

There has been discussion of how clinical results of ESWT for treatment of plantar fasciitis are affected if the patient receives local or general anesthesia (67). Sixty patients
with chronic plantar fasciitis were randomly assigned to receive either ESWT without local anesthesia (3 x 1500 pulses, EFD 0.09 mJ/mm² [Group A]), ESWT with local anesthesia (3 x 1500 pulses, EFD 0.18 mJ/mm² [Group B]) or ESWT with local anesthesia (3 x 1500 pulses, EFD 0.09 mJ/mm² [Group C]) (68). Group A without local anesthesia showed a significantly higher improvement in the VAS and subjective evaluation than groups B and C. A reduction of pain of at least 50% was achieved in 60% of group A, in 36% of group B and in 30% of group C. At 6 weeks, success rates after low-energy ESWT with local anesthesia (group A) were significantly lower than after identical low-energy ESWT without local anesthesia (group C). It has been concluded that ESWT should be performed without local anesthesia in patients suffering from chronic heel pain as local anesthesia applied prior treatment may reduce the efficiency of ESWT. To date, no studies have shown the mechanism responsible for the adverse influences that local anesthesia has on ESWT.

A 2004 study used ultrasound guided ESWT for chronic plantar fasciitis in 51 patients (69). Numerous subjective measures were used to evaluate pain. Fifty-six percent of the treatment group experienced a decrease in pain at 3 months and 94% experienced success at 12 months post treatment. The control group reported 47% success at 3 months post treatment. A 2005 study evaluated 30 patients with plantar fasciitis refractory to conservative treatment modalities after at least 6 months (70). Each patient received 3800 shock waves into the treated heel with ultrasound guidance. A statistically significant improvement was made in the mean VAS up to 124 days after ESWT. Twenty-five of 30 patients reported some degree of improvement, with 5 experiencing no change. A 2005 study by Hammer, et al also used ultrasound-guided ESWT on refractory plantar fasciitis (71). Twenty-two patients with unilateral plantar fasciitis were treated with 3 weekly treatments of 3000 shock waves at 0.2 mJ/mm². The contralateral plantar fascia was used as the control. The treated plantar fascia significantly decreased (p<0.05) in thickness as viewed by ultrasound up to 24 weeks later. Pain, based on the VAS, decreased by 79% and the comfortable walking time increased, both significantly (p<0.01). A second study by Hammer, et al evaluated the effect of ESWT in 44 patients with plantar fasciitis in which conservative treatment had failed (72). The patients received 3000 shock waves of 0.12
mJ/mm\(^2\) 3 times at weekly intervals. After a follow-up of 6 months, pain measured on a visual VAS decreased significantly and 70% of the painful heels improved.

A 2002 study out of Germany utilized 32 patients with plantar fasciitis randomly assigned into treatment and placebo ESWT groups (73). Treatment included 1000 impulses at 0.08 mJ/mm\(^2\) at repeated after 6 weeks or placebo (energy-absorbing foil). Eighty-eight percent of the treatment group were pain free or had good results up to 48 weeks later. The treatment group showed significantly improved morning and resting pain (VAS), pressure stamp-tolerance (pedograph), and walking ability. Although 33.3% of the control group had good results, none of the subjects were pain free.

Subcalcaneal spurs occurring secondary to plantar fasciitis have also been treated by ESWT in recent studies. A controlled study examined 60 patients with heel spurs (74). Thirty patients underwent an ESWT treatment and 30 received a sham treatment. The VAS was used to analyze the patients. Results found a significant decrease of VAS in the treated group, indicating decrease in pain. Radiographic evidence of reduction of enthesophytosis occurred in 9 (30%) group 1 patients. Ultrasonography did not show significant changes in the grade of enthesitis immediately after the end of treatment. However, a significant reduction was seen after 1 month in the ESWT group. In the control group no significant changes were observed on the VAS, radiographs, or ultrasound. ESWT was found to provide analgesia, structurally modify enthesophytosis, and reduce inflammatory edema associated with heel spurs.

In numerous studies, ESWT has alleviated pain associated with heel spurs in humans while few radiographic changes have been evident (75, 76, 77). A possible explanation is ESWT-induced increased osteoblastic activity and subsequent strengthening of subchondral bone and thickening of cortical bone (3, 78).

**Insertional desmopathy - tennis elbow**

The efficacy and safety of ESWT on human “tennis elbow” has been investigated extensively in recent years. Tennis elbow is also referred to as insertional tendonitis, chronic lateral epicondylitis, and epicondylitis humeri radialis. Furia *et al* treated 36 patients with chronic lateral epicondylitis with a single application of 3200 shock waves (79). Twelve
weeks after treatment, pain decreased and functionability increased in 28 of the 36 (77.8\%) subjects.

A 2002 study by Decker et al treated 85 patients with a chronic lateral epicondylitis with ESWT, which was resistant to previous therapies for at least 6 months (80). Three weekly sessions of ESWT were performed under local anesthesia (EFD 0.05-0.18 mJ/mm\(^2\)). Seventy-eight of the 85 patients could be evaluated subjectively after a mean follow-up of 30.7 months. Of these patients, 30.8\% had an excellent and 42.3\% a good result, while 11.5\% had a fair and 15.4\% a distinctly poor outcome. Pain perception assessed by the VAS decreased significantly after ESWT \((p < 0.0001)\). Sixty-two of the 85 patients were satisfied with their ESWT and would agree to further treatment sessions.

Hammer, et al evaluated the effect of ESWT on 19 patients with refractory tennis elbow (72). Three-thousand shock waves of 0.12 mJ/mm\(^2\) were delivered to the injured elbows 3 times at weekly intervals. After a follow-up of 5 months, pain measured on a VAS decreased significantly and 63\% of the elbows improved.

**Insertional Achilles tendinopathy**

A 2005 study aimed to determine the efficacy of ESWT for the treatment of 68 adults with chronic insertional Achilles tendinopathy (81). A total of 35 patients were treated with a single dose of ESWT (3000 pulses of 0.20 mJ/mm\(^2\)) while 33 patients were treated with a sham procedure. Subjectively, 51\% of the ESWT patients and 39\% of the control patients were assigned an excellent or good result. This study determined that ESWT is a safe and effective treatment for chronic insertional Achilles tendinopathy in humans.

**Supraspinatus tendonitis**

The efficacy of low-energy ESWT on supraspinatus tendonitis without calcification has been evaluated in human research. Schmitt, et al performed a controlled, randomized study dividing 40 patients into 2 groups of 20 subjects (82). The treated group received local anesthesia and 6000 impulses (EFD 0.11 mJ/mm\(^2\)) divided into 3 sessions. The control group had 6000 pulses of sham treatment after local anesthesia. At 6 and 12 weeks, no
A statistically significant difference was found between the groups with an increase in function and a reduction of pain in both groups (p < or = 0.001).

A similar study by Haake, et al analyzed the effect of ESWT focused on either the calcified region or the insertion of the supraspinatus tendon (83). One group consisted of 50 patients who received 2 sessions of 4000 impulses (EFD 0.78 ml/mm²) to the insertion of the supraspinatus under local anesthesia. The other patients received ESWT focused on the calcified region. At 12 weeks after treatment, functional improvement and pain reduction were found in both groups. ESWT focused on the calcified region showed significantly more alleviation of pain and improved mobility. The study concluded that fluoroscopic-guided ESWT focused on the calcification rather than on the insertion of the supraspinatus tendon is significantly more effective.

**Rotator cuff calcifying tendonitis**

Calcific tendonitis of the shoulder is often associated with chronic pain and impairment of function. ESWT is considered to be a viable treatment option. A 2005 study by Moretti et al treated 54 patients with rotator cuff calcifying tendonitis with 4 sessions of medium-energy ESWT (0.11 mJ/mm²) (84). Pain was evaluated at the end of each session while shoulder function was assessed at 1 and 6 months after the end of procedure. Thirty-eight patients (70%) reported satisfactory functional results. Radiographs and sonographs showed a disappearance of calcium deposit in 29 patients (54%) and a greater than half reduction in 19 patients (35%). A correlation was found between residual calcium deposit and the clinical outcome up to 6 months follow-up. Some patients, however, showed a reduced pain without modification of calcium deposit. This study concludes that medium-energy ESWT may provide desirable pain modulation in rotator cuff calcific tendonitis.

A 2004 study compared 2 different ESWT regimens in 43 patients (57 shoulders) with symptomatic calcific tendonitis of the shoulder of more than 6 months duration (85). Thirty-one shoulders comprising the treatment group received 2 treatments of 2000 impulses of 0.28 mJ/mm² at a 2 week interval. The control group consisting of 26 shoulders was given pretreatment analgesia and administered 2000 impulses of 0.07 mJ/mm². Improvement in shoulder function was significantly higher in the treatment group at all follow-up visits (p <
0.05) from 1 week to 7 months following ESWT. Radiographs taken 7 months post-treatment showed that calcifications resolved completely in 19% of the treatment group and 8% of the control group, and greater than a 50% reduction was observed in 19% and 8% respectively. At 1 week, a significant reduction in pain (VAS) was noted in the treatment group compared with the control group (p < 0.05). However, at the 3-month and 7-month visits, no significant difference in pain between the groups could be detected. The study concluded that ESWT with an EFD of 0.28 mJ/mm² leads to a significantly greater improvement in shoulder function and a slightly greater dissolution of calcified deposits compared with the control group. This application, however, did not result in reduction of pain.

A similar study by Peters, et al investigated clinical and radiological efficacy of different energy levels of ESWT in calcific tendonitis of the shoulder (86). All 90 subjects had radiographically verified calcific tendonitis of 1 shoulder, restriction of shoulder mobility, and pain for at least 6 months. The subjects were divided into 3 groups. Group 1 received ESWT at an energy level of 0.15 mJ/mm², group 2 received ESWT at 0.44 mJ/mm², and the control group received sham treatment. Treatment was given at 6 weekly intervals until symptoms resolved, 5 treatments had been given, or the subject dropped out of the program. All subjects in groups 1 and 2 completed the program. Those subjects in group 1 (0.15 mJ/mm²) had significantly less pain during treatment but more treatments required than those in group 2 (0.44 mJ/mm²). At 6 months, 87% of group 1 had residual calcification and recurrence of pain. Subjects in group 2 had no residual calcification or recurrence of pain. Sham treatment had no effect. The study concluded that ESWT at an energy level of 0.44 mJ/mm² is an effective treatment in calcific tendonitis of the shoulder with few significant side effects.

A 2003 single blind study evaluated ESWT on 70 patients showing chronic, symptomatic, calcifying tendonitis of the shoulder (87). Thirty-five patients underwent regular EWSST treatment (group 1) and 35 received simulated treatment (group 2). The results found that ESWT-treated individuals experienced a significant decrease of pain and a significant increase in shoulder function. Radiographic examination showed partial resorption of the calcium deposits in 40% of cases and complete resorption in 31% of cases.
in the ESWT group. The control group showed no significant improvement in pain, function, or radiographic resolution of calcium deposits. The researchers considered ESWT as an acceptable adjunctive treatment for chronic calcific tendonitis of the shoulder due to its clinical radiological response, safety, and tolerability.

Jakobeit, et al used ultrasound-guided ESWT in 80 patients with chronic rotator cuff calcifying tendinopathy (88). The patients were treated 1 to 5 times at an interval of 4-6 weeks with 1800 shock waves (EFD of 0.08-0.42 mJ/mm²). At the end of treatment, 85% of the patients had decreased or absent symptoms. Shoulder calcification completely resorbed in 57 (71.2%) patients and partially resorbed in 16 patients (20%). The researchers concluded that ESWT is a very effective and non-invasive surgery alternative for symptomatic calcareous tendinopathy of the shoulder.

A prospective study with short-term follow-up performed by Pigozzi, et al involved 72 patients affected by chronic shoulder pain lasting more than 6 months (89). All patients received weekly ESWT for 8 weeks with 2,000 impulses (EFD 0.21 mJ/mm²). Based on radiographs and the VAS, 53% of the patients scored excellent results, 14% good, 13% fair and 20% poor. Thirty-seven percent of the patients with calcifying tendonitis experienced a reduction in calcification and 63% had no change. The researchers conclude that even with a limited number of cases, ESWT showed to be risk-free and efficacious treatment of chronic painful shoulder when resistant to other conservative methods.

**TENDONS AND LIGAMENTS – VETERINARY CLINICAL APPLICATIONS**

*Suspensory ligament desmitis*

Proximal suspensory ligament desmitis in horses was one the first equine musculoskeletal injuries treated by ESWT and many researchers have found beneficial results. In 2004, McClure, et al performed a controlled study to evaluate the healing effects of ESWT on collagenase-induced suspensory desmitis (90). Four thousand international units (IUs) of collagenase were injected into normal suspensory ligaments in both forelimbs of 4 horses and ESWT was administered to 1 forelimb in each horse 3 weeks later while the horse’s other forelimb served as a control. Three treatments of 0.13 mJ/mm² at 3 week
intervals were administered. A 35 mm probe delivered 500 pulses to the palmar aspect and a 5 mm probe delivered 500 pulses to both the palmar-lateral and palmar-medial aspect of the ligament. Ultrasound revealed a significantly faster decrease in cross-sectional area of the ligament lesions in the ESWT-treated limbs up to 12 weeks after ESWT. The subjects were then euthanized and the suspensory ligaments were fixed and evaluated histologically. The total percent lesion ($p = 0.01$), total fiber alignment score ($p = 0.0167$) and total echogenicity ($p = 0.0023$) were all improved in the ESWT-treated ligaments. Additionally, the ESWT-treated ligaments had a more concentrated area of metachromasia associated with healing while the untreated ligaments had a more diffuse area of metachromasia throughout the ligament. This study showed that ESWT improves the rate of healing of SULs as assessed by ultrasound.

A Brazilian veterinary research team performed a similar ESWT study on equine desmitis in 2005 (91). Two collagenase injections were administered 2 weeks apart into the hind suspensory ligaments of 10 horses. The right hind limb of each horse was treated with ESWT (3 treatments at 3-week intervals) while the left hind limb served as the control. Periodically during the study, the ligaments were evaluated ultrasonographically to assess for lesions. Four weeks after the last ESWT treatment, biopsy specimens were collected from all ligaments for histology evaluation and immunocytochemical analysis of osteogenic TGF-β. Compared with control ligaments, ESWT-treated ligaments had smaller, more newly formed collagen fibrils and significantly greater expression of TGF-β ($p<0.05$) 4 weeks after the last ESWT treatment was administered. This study also suggests that ESWT may assist in healing in horses with naturally occurring suspensory ligament desmitis.

The application of RPWT on chronic or recurrent proximal suspensory desmitis was evaluated in 65 horses (92). The horses were treated 3 times at 2-week intervals (2000 pulses at 10 Hz) and followed a controlled exercise program. Each subject was reassessed clinically and ultrasonographically 10 to 12 weeks after treatment. Forty-one percent of horses with hindlimb lameness and 53% with forelimb lameness improved clinically and returned to full work in 6 months. The researchers concluded that although more research is warranted, RPWT is a useful treatment modality for chronic or recurrent proximal suspensory desmitis when combined with controlled exercise.
Superficial digital flexor tendonitis

Superficial digital flexor tendon (SDFT) lesions are common injuries in performance horses and numerous modalities have been attempted to assist their healing. The efficacy of ESWT in treating SDFT tendonitis in racehorses has recently been investigated (93). An electrohydraulic generator delivered 150 shock waves per centimeter of length of the core lesions (0.13 to 0.15 mJ/mm²) in the SDFT of 8 horses for 3 sessions at 3-week intervals. All lesions showed improvement ultrasonographically. ESWT appeared to speed the rate of healing of the significant type 3 core lesion and decreased the cross sectional area of the lesion faster than conservative methods. Four of the 8 ESWT treated horses went on to race successfully. One horse took a year of rest before returning to training. Two subjects re-injured their SDFT and 1 horse retired before returning to training. Horses with acute diffuse type 1 tendonitis (slightly more hypoechoic than normal) have also responded very well to ESWT (94). Within days of treatment, ultrasonographic evaluation of these tendons revealed a prominent decrease of fluid in the tendon. Detectable pain parameters such as heat and pain on deep palpation also decreased.

A blinded controlled study investigated the efficacy of ESWT on collagenous-induced lesions in the SDFT of 6 horses (95). One thousand IU of collagenase were injected into the center of both front SDFT. The maximum injury zone was located and the first ESWT was begun 31 days after induction of the lesion. The second and third ESWT sessions occurred on days 49 and 70. Each treatment consisted of 1500 pulses at 0.14 mJ/mm² focused on the lesion on a randomly assigned forelimb while the other SDFT served as a control. The ESWT-treated lesions showed a significant increase in neovascularization histologically. Further evaluations of mechanical and histological effects of ESWT on SDFT injuries are indicated.

While the previously described studies involve ESWT and acute tendonitis, some equine clinicians promote ESWT for chronic tendonitis or tendon calcification. Studies recommend that ligamentous lesions and chronic tendon lesions 4 weeks old or greater be treated with EFDs of 0.15 mJ/mm² while acute lesions should be treated with EFDs of 0.01 mJ/mm² (54).
Calcification in the equine ligamentum nuchae

Training and competing dressage horses are asked to maintain their head flexed at the poll. Injuries such as chronic insertional desmopathy and enthesophyte formation at the attachment of the ligamentum nuchae on the occipital bone are common in European Warmbloods used for dressage (54, 96). Avulsion fractures of the occipital bone and subsequent calcification within the supraspinous bursa are often evident radiographically or scintigraphically. ESWT has been investigated as a therapy for these disorders of the ligamentum nuchae. Brems and Weiss treated 12 equine patients with clinical signs of neck pain and radiographic evidence of calcification of the occipital bone or the ligamentum nuchae (96). All subjects were treated 3 times at 4 to 8 day intervals with 2000 pulses applied to the insertion of the nuchal ligament with the focused shock wave generator. Clinical signs completely resolved in 10 of the 12 horses after 20 weeks and they returned to normal riding. One horse showed 50% improvement and 1 seemed unimproved. The study concluded that insertion-desmopathy of the nuchal ligament can be treated successfully by ESWT. Since many horses show radiographic changes of the neck, the success of ESWT should be measured by clinical and functional improvement rather than by radiographs alone.

A separate trial found that horses with ligamentum nuchae abnormalities respond well to 2 or 3 treatments in 14-day intervals (54). Four weeks post ESWT; the 22 subjects were ridden without forced neck flexion and were given non-steroidal anti-inflammatory medication for 8 days following each treatment. Four weeks following the final shock wave treatment, signs of neck pain resolved in 12 of the 22 horses, improved in 6 horses, and showed no change in 4 subjects. Those horses that responded well to therapy returned for a fourth treatment 6 to 12 months later and, again, responded favorably to ESWT.

JOINTS - RESEARCH

Osteoarthritis

The osteoprogenic qualities of ESWT have been evaluated via in vivo research on degenerative bone and joint diseases (3). Recent studies have investigated the efficacy of ESWT on equine osteoarthritis (4, 92). A study by McIlwraith compared ESWT to polysulfated glycosaminoglycan in treating equine osteoarthritis (97). The positive controls
were given 500 mg IM polysulfated glycosaminoglycans (Adequan) every 4 days for 28 days. The shock wave group was administered 2000 shocks at E4 (0.13 mJ/mm$^2$) and 1500 shocks at E6 on days 14 and 28, respectively. The negative control group received no treatment. Osteochondral fragments were experimentally induced on the distal radial carpal bone in each subject. Clinical lameness assessment 14 days post treatment showed significant improvement in the ESWT group versus positive or negative controls. Both the positive control and the ESWT group continued to improve in lameness evaluations up to 42 days after the last treatment. By 70 days from the start of the study, the ESWT horses had significantly lower synovial fluid protein than the negative and positive control horses. These results indicate reduced synovitis and capsulitis with ESWT. This study suggests that ESWT has more of an effect on periarticular soft tissues rather than articular cartilage and is effective for reducing clinical lameness and synovitis but not histologic arthritis progression. It is, therefore, suggested that ESWT be used in conjunction with a chondroprotective agent for osteoarthritis (97).

**JOINTS – HUMAN CLINICAL APPLICATIONS**

*Heterotrophic ossification*

ESWT has been utilized in numerous periarticular and intra-articular diseases and for the alleviation of pain associated with these diseases (50, 98, 99). Heterotrophic ossification (HO) is the formation of bone within extraskeletal soft tissues. The exact mechanism for these changes is unknown. Localized HO occurring secondary to damage to the nervous system, such as spinal cord injury, is called neurogenic. Non-neurogenic HO occurs from direct injury to the muscles. Fibrous, cartilaginous, and osseous tissues near bone are affected (100). A 2005 study by Brissot, *et al* evaluated ESWT on 26 patients with HO of the hip joint (101). The subjects received once weekly sessions of ESWT (4000 pulses, EFD 0.54 - 1.06 mJ/mm$^2$) for 4 consecutive weeks. Heterotrophic ossification was neurogenic in 5 patients and non-neurogenic in 21. Pain (on the VAS), joint flexion, and walking distance significantly improved in the subjects. Radiographs did not show significant changes
between treatments. This study showed that ESWT could complement medical treatment, physiotherapy, and pre-surgery therapy for hypertrophic ossification.

Osteoarthritis

Objective in vivo studies examining the effects of ESWT on clinical osteoarthritis in humans are lacking in published literature.

JOINTS – VETERINARY CLINICAL APPLICATIONS

Osteoarthritis of tarsometatarsal joint (bone spavin)

Early use of ESWT on horses involved treatment of hock lameness. McCarroll and McClure placed 74 horses with lameness grades of 1 to 3 (0 to 5 scale) under general anesthesia and administered 2000 pulses at 0.89 mJ/mm² in each of the 4 joints in their hocks (17). The probe was directed toward the radiographically evident hock lesions. At 90 days post ESWT, 80% (59 of the 74) horses improved 1 lameness grade or more. Horses with osteophytes on the dorsal to dorsomedial aspect of the tarsometatarsal joint improved the most. Of the 15 non-responsive horses, 8 horses received an additional shock wave treatment and 4 of these horses improved. This study proved that ESWT alone (80% lameness resolution subjective evaluation) is equally as effective in resolving lameness as surgically facilitated ankylosis (79% lameness resolution) and chemically facilitated ankylosis (80% lameness resolution). The advantage of ESWT is the non-invasive nature of the treatment (102, 103). Some researchers hypothesize that ESWT may result in remodeling and assisted ankylosis. ESWT-enhanced osteoblastic activity results in thickening of cortical bone (3). Additionally, the subchondral bone remodels and strengthens in response to loading, absorbs shock, maintains joint shape, and protects cartilage from damage (56). These researchers conclude that these bony changes may be responsible for resolving lameness. Despite improved joint function, radiographic changes are not always evident. This decrease in lameness in the absence of radiographically evident changes has also been noticed with ESWT-treated heel spurs in humans (75).
Simultaneous intra-articular therapy and ESWT has been performed with an additive effect, whether injected before or after ESWT (54). With the horse standing, the affected hock was palpated and 800 to 1000 pulses at 0.15 mJ/mm\(^2\) were administered to the entire tarsometatarsal region. Intra-articular medication may be injected before or after ESWT during the same visit. Researchers suggest that ESWT may be used on equine hock arthritis unresponsive to medical therapy alone.

*Canine osteoarthritis*

ESWT has also been used to treat dogs with osteoarthritis of the hip or elbow joint (104). Nine dogs with hip and elbow arthritis were either treated 3 times with ESWT at 2 week intervals or served as controls. The treated dogs showed a 20% improvement over baseline force platform measurements while the control dogs showed decreasing force platform values indicating increasing lameness.

The canine stifle is frequently affected with osteoarthritis. A group of dogs with consistent osteoarthritis offers a more controlled study population to investigate the effects of ESWT on osteoarthritis. However, additional studies are required to define this role. The objective of the publication presented in Chapter 3 of this thesis is to evaluate ESWT on osteoarthritis of the canine stifle in a blinded controlled study. An objective examination of the results is performed by force platform analysis.

**OTHER ESWT APPLICATIONS**

*Skin*

Low EFD shock waves have resulted in re-epithelialization of partial thickness wounds (105). Meirer et al investigated the effect of ESWT on compromised epigastric skin flaps of 20 rats (106). The rats were divided into 2 groups (ESWT group and control group). The ESWT group received 2500 impulses (EFD 0.15 mJ/mm\(^2\)) immediately after surgical elevation of the epigastric skin flap. The control group received no treatment after surgery. Seven days after ESWT, the treated skin flaps had significantly reduced surface areas of necrosis compared to the control groups (p < 0.01). This study suggests that ESWT is a
feasible modality to improve blood supply in ischemic tissue. A case study performed by the same research group evaluated the efficacy of treating partial thickness burns with ESWT. One thousand-five hundred pulses (EFD 0.11 mJ/mm²) were applied to the right forearm of a 31-year-old man who had suffered partial thickness burns while using hot cooking oil. The burn area was treated at days 3 and 7 after the injury. The majority of the surface area of the burn had re-epithelialized by day 15 after the injury. At 6 months, the burn area had healed without scarring (107).

Haupt et al also displayed the re-epithelialization capabilities of low energy shock waves on animal skin models (105). Split thickness wounds were made with an electrokeratome in 3 Yorkshire piglets and a fourth piglet was used as a model for delayed healing by irradiating the skin before the wounds were created. Ten to 1000 shock waves were delivered at 14- or 18-kV to each wound on each piglet. The animals were euthanized and the skin wounds were evaluated histologically. The wounds treated with low-dose ESWT (10 pulses at 14kV) showed significant enhancement in both the normal and irradiated specimens. High dose applications (100 pulses at 18kV) inhibited healing of both groups. Histologically, the low dose ESWT resulted in increased vascularization of the dermis and increased thickness of the epidermis over the wounds.

**Back pain**

Focused ESWT has been used to treat origins of back pain in horses. The probe may be focused on visible areas of bone sclerosis or insertional desmitis identified by radiographs, ultrasonography, and scintigraphy. It may also be used to locate painful muscular lesions that are not identifiable by these diagnostic tools (108). Clinical response to treatment depends on the severity of the lesions and conformation of the horse and the number of pulses and the probe size should be appropriate for the size and site of the back lesion. In the noted study, 50 pulses were directed to both sides of a 1 cm long area of bone sclerosis on a dorsal spinous process (54). Up to 5 treatments at 2 to 4 week intervals for up to 3 months have been used. It is suggested that well muscled horses with mild pain as detected by the rider benefit from 1 to 2 treatments at 0.15 mJ/mm². Severely affected horses require
additional treatments, should receive modified training programs, and have a 65% chance of returning to normal work.

Soft tissue back pain may also be addressed by ESWT in performance horses. Probes between 20 mm to 80 mm with EFDs up to 0.15 mJ/mm² and 2000 pulses have been administered (54). The probe is moved over the affected area until the horse responds with muscle fasciculations. The probe is held in that location for 80 pulses before moving. With this method of probe placement, horses with muscle fasciculations showed nearly 100% improvements for up to 10 months as reported by the rider.

**ESWT EFFECTS ON ANALGESIA**

The analgesic effects of ESWT were discovered inadvertently during its application for orthopedic disease (109). The pain-relieving properties of ESWT are believed to be the dominant therapeutic quality of ESWT in the treatment of humeral epicondylitis, plantar fasciitis, and heel spurs in people (109). During its extensive use, the presence of antinociceptive effects after ESWT has been described. However, the exact mechanisms and duration of analgesia have yet to be defined. Clinically evident analgesia after ESWT varies among subjects as well as among treatment locations. The short-term analgesia following ESWT may occur for reasons unrelated to the mechanisms that result in healing.

**Analyse - potential mechanisms**

*Neural/Perineural inflammation*

Perineural inflammation or nerve disruption could result in analgesia. Schelling et al applied shock waves directly to sciatic nerves of frogs *in vitro* (110). The study concluded that action potentials generated from the nerves were due to gas bubbles elicited by the shock waves and not from the action of the shock waves themselves.

Bolt et al suggested that axonal swelling might cause the analgesia and alter peripheral pain perception in horses after ESWT (111). The group treated the forelimb palmar digital nerves of 6 horses with RPWT. Three and 7 days after ESWT, the conduction velocity along the palmar digital nerves was significantly slower. Transmission electron
microscopy of treated nerves revealed significantly more axonal swelling up to 35 days after treatment.

In a sheep study model, McClure et al also found significant perineural inflammation and axonal swelling up to 4 days after treating the mid-cannon bone area of 30 sheep with ESWT and RPWT. This group found that RPWT produced significantly more nerve inflammation than ESWT or controls (112).

Cutaneous/Local effects

Conflicting results have occurred with studies investigating the local effects of ESWT or RPWT-induced analgesia. The results of these studies suggest that the analgesic effects of pressure waves may depend upon the characteristics of pressure wave used.

Bolt treated the third metacarpal bone of 12 horses with 2000 pulses of RPWT and tested limb withdrawal reflex latency using thermal stimulation (113). The other metacarpus served as a control. No significant difference existed between treated and untreated limbs. Brown et al also used RPWT when treating 9 horses with unilateral navicular syndrome (114). One thousand five hundred pulses at 10 Hz were applied through both the frog and heel bulbs and force platform analysis was used to objectively analyze changes in lameness for 7 days. The study found that 1 treatment of RPWT had no influence on short term analgesic in horses with navicular syndrome.

Conversely, McClure detected local analgesic effects after ESWT (112). The study administered ESWT (1000 pulses at 0.15 mj/mm²), RPWT (0.16 mj/mm²), or sham treatment to the metacarpi of 6 horses and studied electrical stimulus response. While the RPWT and sham group had no effect on local analgesia, ESWT resulted in trends towards local cutaneous anesthesia between days 0 and 3 after a single treatment. Waldern also utilized both ESWT and RPWT and evaluated skin sensitivity to electrical stimulation distal to the treatment site (115). No analgesia following ESWT or RPWT of the palmar digital nerve was detected. The variability of results among these studies suggests that local cutaneous analgesic effects may depend upon the different techniques used to generate the pressure waves.
Depletion of neuropeptides

Inconsistent findings have been made when evaluating the role of neuropeptides in pressure wave-induced analgesia. Substance P (SP) and calcitonin gene-related peptide (CGRP) neurotransmitters are found in small diameter afferent nerve fibers. These afferent fibers contribute to pain sensation by conducting impulses through the nerve (116). SP and CGRP have been isolated in the periosteum, marrow and cortex of long bones (117). Substance P innervation has been located in areas of osteoarthritis in horses suggesting its role in signaling and maintaining pain (118).

In 2001, Ohtori *et al* investigated the ability of ESWT to produce analgesia due to morphologic changes it produces in cutaneous nerve fibers (119). Nerve fibers immunoreactive for protein gene product (PGP) 9.5 as well as CGRP innervate normal rat skin. After ESWT, there was a loss of PGP 9.5 and CGRP in the skin indicating nearly complete degeneration of intracutaneous nerve fibers. This study suggests that analgesia associated with ESWT may involve depletion of neuropeptides.

Neuropeptide studies performed in sheep models have also had contrasting results. One thousand pulses of ESWT at 0.15 mJ/mm² or 1000 pulses of RPWT at 0.16 mJ/mm² were delivered to the mid metacarpal/metatarsal regions in 30 sheep (112). The skin, periosteum, and nerves were harvested from 2 sheep immediately after treatment and at daily intervals for 14 days in the remaining 28 sheep. The concentration of substance P was measured. There was no difference in substance P and CGRP concentration between treated and non-treated limbs questioning the role of neurotransmitters and nerve fiber depletion in post-ESWT or RPWT analgesia.

Gate control theory

A “Gate Control Theory” has also been postulated and suggests that analgesia results when pain stimuli from small afferent nerve fibers are modulated or disrupted by large afferent nerve fibers and descending spinal pathways as they enter the substantia gelatinosa (121). Consequently, transmission of the pain stimuli to ascending spinal pathways in the dorsal horn is blocked or gated (66, 120).
Haake et al. investigated the possible influence of low-energy ESWT on inhibition of the expression of the sP and CGRP in presynaptic neurons in the lumbar spinal cord of the rat (121). The animals were treated either once with 1000 pulses (0.043 mJ/mm²) or 3 times with 1000 pulses (0.11 mJ/mm²). The animals were then sacrificed at either 4 or 72 hours after treatment. Immunohistochemical analysis of the expression of the sP and CGRP and revealed no regulatory effects of ESWT on either neuropeptide in the dorsal horns of the treated rats. The study concluded that due to the absence of significant changes in the sensory system, it is unlikely that the application of ESWT triggers the endogenous pain control system of the rat through hyperstimulation analgesia.

Another analgesia study by Haake et al. investigated whether the long-lasting analgesic effects of ESWT involved the gate control mechanism. Transcription factor c-Fos, which interferes with the molecular expression pattern of neurons, was utilized as a marker for neuronal activity in the study. ESWT at and EFD of 0.33 mJ/m² was focused on the paws of rats and c-Fos expression was analyzed in the dorsal horn of the spinal cord. Regardless of EFD, c-Fos protein expression did not vary in the dorsal horn from 4 to 72 hours after ESWT. Furthermore, the mRNA of the c-Fos protein did not change expression in the treatment area of the paw. The study concluded that ESWT with an EFD up to 0.33 mJ/mm² does not modify neuronal activity and ESWT is unlikely to induce stimulation-produced analgesia via the gate control mechanism (122).

Endogenous spinal opioid system

The aim of the 2001 study by Haake was to investigate if the analgesic effect of ESWT is caused by modulation of the endogenous spinal opioid system (123). Rats were treated with 2 different EFDs (0.04 and 0.11 mJ/mm²) and immunohistochemical analysis of met-enkephalin (MRGL) and dynorphin (Dyn) was performed at 4 or 72 h after ESWT. ESWT did not alter MRGL or Dyn immunoreactivity in the spinal cord at either EFD regardless number of pulses or treatment sessions. Furthermore, a delayed effect of ESWT at 72 hours after treatment was not detectable. The study suggested that the analgesic effects of ESWT do not involve the modulation of endogenous opioids.
Analgesia – presence and duration

Numerous hypotheses have been proposed as to the mode of analgesic action induced by ESWT. None, however, have been truly proven. The presence of anesthesia after ESWT in horses has not yet been defined. The importance of this data applies to both horse and rider as risks may be involved if pain comprehension by the horse is absent during performance. Regulations based on empirical data have been implemented in multiple horse racing jurisdictions due to these dangers. Therefore, further objective evaluations of the analgesic period following ESWT in horses are needed in the literature. The main objective of the manuscript in Chapter 4 is to measure the duration of acute analgesia following a single session of ESWT in horses with naturally occurring unilateral forelimb lameness.

Cutaneous analgesia

Effects of cutaneous analgesia appear to depend upon the technique used to generate the pressure waves. A 2004 study by Bolt *et al* aimed to determine the onset, magnitude, and duration of cutaneous analgesia after RPWT (113). A single RPWT treatment was applied over dorsal aspect of 1 metacarpus in 12 horses. The limb withdrawal reflex latency (LWRL) assessed cutaneous sensation in the treated and untreated metacarpi by using a focused light source. No significant difference in decrease of LWRL over time was found between treated and control areas compared with baseline values. The study suggests that cutaneous analgesia does not occur after RPWT application to the equine metacarpus.

McClure *et al* also studied equine skin sensation in the treatment region over the middle aspect of the third metacarpal bone (112). However, McClure used focused ESWT as well as RPWT and electrical stimulation. A constant current was delivered to the skin surface at the treatment site between the heel bulbs. The milliampres were increased until the horse acknowledged the current. Acquired analgesia was detected if a greater current was required to elicit a response in the horse. A baseline measurement was achieved in each horse by averaging the measurements taken for 3 days before the beginning of ESWT or RPWT. Then the horses were treated with ESWT or RPWT and measured daily for the next 7 days. A difference from baseline for both ESWT and RWPT was detected for the first 4
days following treatment. The study indicates that cutaneous analgesia may be achieved up to 4 days following ESWT and RPWT.

**Duration of analgesia**

The characteristics and duration of analgesia after ESWT varies among individuals and among musculoskeletal treatment locations. Buch *et al* found that direct post treatment analgesic effects of shock wave therapy on heel spurs may last for up to 3 or 4 days (75). Ogden, however, explained a bimodal analgesic response after treating human patients for heel spurs (124). Patients reported a decrease in pain for 3 to 4 days after treatment, and then a gradual return of pain followed by a decrease in pain as healing occurred.

Brown *et al* used a force platform to determine the duration of analgesia after RPWT in horses with navicular syndrome. One thousand five hundred pulses of non-focused RPWT (10 Hz) were delivered to the frog and heel bulb. Ground reaction force measurements were recorded at 15 minutes and at 24-hour intervals for 7 days. The results showed no difference in lameness between treated and untreated limbs after a single RPWT treatment (114).

Lischer *et al* assessed limb load distribution in equine subjects using an instrumented treadmill after ESWT was applied to proximal suspensory desmitis (125). Force plate analysis revealed that analgesia lasted 3 days after ESWT. Twenty-four hours after ESWT, analgesia was comparable to local or perineural analgesia.

**POTENTIAL COMPLICATIONS OF ESWT**

Potential adverse effects of ESWT on tendons and ligaments of laboratory animals have been discussed previously. The effects were seen at EFD greater than 0.28 mJ/mm², which have not shown to be detrimental to larger mammals (62, 63). Tissue necrosis may occur at excessive energy levels (126). Haake *et al* systemically recorded the side effects of ESWT in the treatment of tennis elbow in a randomized, placebo-controlled study (127). More side effects were documented in the ESWT group than in the placebo group and included mild reddening of the skin (21.1%), pain (4.8%) and small hematomas (3.0%). The researchers also report the unlikely occurrence of migraine or syncope after ESWT. ESWT
commonly used for tennis elbow with an EFD from 0.04 to 0.22 mJ/mm² has very few side effects.

Shock waves should never be directed at gas/tissue interfaces such as lung and intestine (128). Lung bleeding is the most serious side effect when shock waves are used to fragment gallstones in dogs. Delius placed pressure probes into dogs between the lung and the diaphragm. Shock wave pressures over 2 MPa could be administered safely, whereas a pressure of 10 MPa caused bleedings in small to medium sized dogs. The acoustic impedance of soft tissue is markedly greater than that of air. Thus, maximum acoustic pressure is reflected at the air/soft tissue interface and serious tissue damage may result.

A 1993 study found that ESWT might damage arterial intimal membranes (129). When human umbilical cords were exposed to shock waves of varying EFDs, grossly visible hematomas and superficial holes appeared. Histologically, vessel wall necrosis and rupture, and complete detachment of endothelial cells were observed. An EFD of 0.3 mJ/mm² is the lower threshold for the occurrence of severe vascular damage. Additional complications of ESWT include premature closure of physes in laboratory animals (130). Therefore, active physes should be avoided (54). Finally, mild cutaneous petechiation is a common, yet benign, side effect encountered in shock wave studies and procedures performed on animals and humans (80, 127).

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CHAPTER 3. EXTRACORPOREAL SHOCK WAVE THERAPY IN NATURALLY OCCURRING OSTEOARTHRITIS OF THE STIFLE JOINT IN DOGS

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Published in Veterinary and Comparative Orthopaedics and Traumatology 2005; 18 (3): 147-152

Summary

Extracorporeal shock wave therapy (ESWT) has expanded from the original uses of human urinary calculi treatment to veterinary orthopedic applications. This paper investigates the feasibility and efficacy of treating dogs with osteoarthritis of the stifle joint with ESWT. In this study, dogs with persistent stifle lameness despite previous surgical or medical treatment were either treated with ESWT or served as untreated controls. The more lame rear limb of each dog was determined by force platform analysis. The range of motion of the stifle joints was assessed by goniometry. Force platform gait analysis and goniometry were performed on both groups for 4 visits at 3-week intervals and a final examination 4 weeks later. Shock wave therapy was performed 3 times on the treated dogs, once at each of the first 3 examinations. A placebo treatment consisting of clipping and wetting the hair was performed on the control dogs. The vertical forces were evaluated for objective analysis of treatment response. For peak vertical force (PVF), 4 of 7 treated dogs improved, while only 1 of 5 of control dogs improved. The PVF for the within group analysis did not show any significant change for the treated group; however, the control group has a significant
decrease (p=0.05) in PVF consistent with an increase in lameness. The range of motion (ROM) of the stifle joint improved in 5 of 7 treated dogs and 3 of 5 controls. Dogs in the treated group had a trend toward increased ROM (p=0.07) and a “positive slope” when compared to dogs in the control group which did not have a significant change (p=0.78) and had a negative slope indicating the dogs were developing a decrease in ROM. The subjective data provided by client questionnaire did not show significant difference between groups.

Introduction

Extracorporeal shock wave therapy (ESWT) was developed for fragmentation of urinary calculi in the 1970s (4). Subsequent investigations have evaluated ESWT for the treatment of various musculoskeletal disorders in both humans and animal species (6, 10, 13). In humans, ESWT has resulted in long-term decreased pain in patients with plantar fasciitis, lateral epicondylitis, calcifying tendonitis and clinical improvement in patients with femoral head necrosis where effects were still apparent at 1-year follow-up examination (11, 17, 18, 19, 20, 21). The exact mechanisms by which ESWT affects tissue are not completely understood. The bone-tendon interface in dogs has been shown to have an increased neovascularization following treatment (23). To date, the primary use in veterinary medicine has been in for equine musculoskeletal diseases, such as distal hock osteoarthritis, suspensory desmitis, and stress fractures (12, 13, 14). When applied to osteoarthritis of the tarsometatarsal joint and distal intertarsal joints in horses, ESWT has been shown to decrease lameness in 80% of the horses (12).

In research studies using dogs as models, it has been found that ESWT can affect bone formation (8). In a radius non-union model in beagles, 100% (5 of 5) of the ESWT treated dogs reached radiographically observable bony union 12 weeks post treatment compared to only 1 of 5 control dogs (8). Clinically, ESWT has proven beneficial in treating multiple bone disturbances when surgery is not viable or when implants are not feasible. Furthermore, previous studies performed on dogs have suggested ESWT is beneficial in the treatment of delayed or non-union fractures. These initial experiences have revealed than ESWT assists in hard callus formation of mid-diaphyseal and supracondylar defects less than
5mm in gap width. Additionally, a case report documented that a non-union can be stimulated to heal following ESWT (10). ESWT has also been used to treat dogs with pain from osteoarthritis from hip and elbow osteoarthritis, with treated dogs showing a decrease in lameness (3, 10).

Stifle joint lameness in dogs is most commonly the result of instability and osteoarthritis, associated with rupture of the cranial cruciate ligament. Multiple surgical techniques have been described that attempt to surgically re-establish joint stability following CCL trauma (9). The objective of surgery is to improve limb function and prevent the development of, or delay further progression of pre-existing osteoarthritis in the joint. Despite repair, osteoarthritis generally develops and progresses with some patients having persistent lameness. Commonly used management options for these dogs include weight reduction, exercise modification and management of pain and inflammation using non-steroidal anti-inflammatory drugs (NSAIDS), parenteral administration of glycosaminoglycan products, or oral supplementation with nutraceuticals (16). Prolonged use of NSAIDs can contribute to gastric ulceration or renal papillary necrosis and the response to parenteral administration of glycosaminoglycans is variable (2, 7, 16). If ESWT can decrease the lameness associated with chronic stifle disease, dogs affected would be less dependent on pharmaceutical therapies. The objective of this study was to evaluate ESWT as a therapy for stifle lameness in dogs with osteoarthritis of the stifle.

Materials and Methods

Subjects - In the study 14 client-owned dogs that had chronic lameness localized to the stifle joints secondary to osteoarthritis. To be included the dogs had to be greater than 18.18 kilograms (40 pounds) in body weight, in good health other than the diagnosed lameness attributable to the stifle joint, have a history of lameness for greater than 6 months, and have a visible gait abnormality in the affected limb. The dogs were included if there was stifle osteoarthritis present or if surgery had been performed bilaterally providing that they were predominantly lame in 1 limb. They were excluded if there had been an injection into the joint within 90 days, surgery on the joint in 180 days or if they had been treated with
topical or systemic medications such as oral corticosteroids, non-steroidal-anti-inflammatory drugs, glucosamines or antibiotics 14 days prior to starting the study. After confirmation of eligibility for entry into the study, the dogs were randomly assigned to the treatment or the control group. Physical examination and stifle radiographs were completed to ensure that osteoarthritis was present. The most severely affected limb of each subject was determined by force plate analysis. The Iowa State University Animal Care and Use Committee approved this study.

**Force platform gait examination-** Force platform gait analysis was performed using a biomechanical platform embedded in an 8-m walkway. Three sets of retroreflective photocell receptors, were attached 1 meter apart in series and positioned in the walkway, with the middle sensor positioned at the middle of the force plate, and were used to determine velocity and acceleration over the 2-m measurement region. The dogs were walked across the platform at a comfortable speed and ground reaction forces for the forelimb and hind limb stance phases were recorded for each pass. Passes were repeated until 5 valid measurements were obtained for each limb (trial velocity between 1.20 to 1.40 m/s; acceleration variation +/- 0.5 m/s²). A trial was considered valid if a forelimb and ipsilateral hind limb foot strike were isolated on the force plate consecutively. The first valid passes were used for analysis. The ground reaction forces in the vertical direction were normalized for the dogs' body weight and used for analysis of limb function. Then data evaluated were peak vertical force (PVF, N100*N/N units/s), vertical impulse (VI, N/s(s)) and average falling slope (AFS, N/m * sec).

**Range of motion-** Before sedation, goniometry was performed on the stifle of all dogs. Each subject was positioned in lateral recumbency with the study limb uppermost. The maximum degrees of joint extension and flexion were recorded. Range of motion extremes were identified by the first negative behavioral response (e.g. turning of head, pulling leg away) of the dog. The difference was determined as the range of motion and was measured at each visit.
Client questionnaire – The clients were required to complete a pre-treatment and 4 post-treatment questionnaires at the respective visits. They were also asked to score multiple daily activities with regard to pain in the joints, stiffness, activity level and comfort level. A score of ‘1’ designated as most severe and absolute hesitation while a score of ‘7’ correlated to no hesitation at all.

Treatment – The dogs were heavily sedated with a combination of xylazine\(^\text{iv}\) at 0.55 mg/kg, butorphanol tartrate\(^\text{v}\) at 0.44 mg/kg, and glycopyrrolate\(^\text{vi}\) at .01 mg/kg or medetomidine\(^\text{vii}\) at .01 mg/kg administered intravenously. Sedation was performed on control subjects as necessary for radiography at the initial visit. The dogs in both groups were clipped over the stifle joint. Coupling gel was applied and 200 shock waves were applied at 4 sites caudolaterally, dorsolaterally, dorsomedially and caudomedially using a probe with a focal pressure depth of 20 mm. This was followed by another 700 shockwaves divided into the same locations, at a focal depth of 5 mm with a frequency of 4 pulses per second, with an energy flux density of 0.14 mJ/mm\(^2\), for a total of 1500 pulses. Three treatments were repeated at 3-week intervals from visit 1 to visit 3. After treatment, the dogs were either allowed to recover spontaneously or when appropriate, had their drug effects reversed with yohimbine\(^\text{viii}\) at 0.55 mg/kg or atipamazole\(^\text{ix}\) at .011 mg/kg administered intramuscularly.

Follow-up examination - After an initial pretreatment visit, each dog returned 4 times at days 21, 42, 63, and 98 for evaluation for force plate evaluation, goniometry, and further ESWT if assigned to the treatment group. The dogs in the treatment group were treated a total of 3 times. The owners were not informed as to the group their dog had been assigned until the study was complete.

Data analysis - The age and weight of the treatment and control groups were compared using \(t\)-tests. The pre-treatment data were compared to the data from the final visit. In order to compare differences between groups, the treatment and control groups were compared using a matched pair \(t\)-test that adjusted for differences in baseline between groups. Additionally, a matched pair \(t\)-test was used to compare within group changes. To
evaluate the trend of the data between the treated and control groups, the slopes of the change in the data over time were calculated for each parameter for each dog. The subjective data provided from the client questionnaires was evaluated by a one-way analysis of variance. Data were considered significant at $p \leq 0.05$; a trend was defined as a p-value from 0.05 to 0.1.

**Results**

Fourteen dogs were enrolled in the study and 12 dogs successfully completed the study. One dog was removed for health reasons not associated with the study and another dog was refractory to repeated examinations. The treated group consisted of 4 spayed females and 3 castrated males with a mean age of 7.6 yrs (range 5.5-9 yrs) and a mean weight of 40.6 kg (27-65.9 kg). The dogs represented 6 breeds (Rottweiler, Labrador and Chesapeake Bay Retrievers, Newfoundland, Dalmatian, Boxer) and 1 mixed breed dog. The control group had 4 spayed females and 1 castrated male. They were a mean 9.6 yrs of age (7-13) and 44.7 kg (25.6-63 kg). There were 2 Rottweilers, and 1 Golden retriever, 1 German Shorthair Pointer, and 1 mixed breed dog. There was no significant difference in age ($p = 0.13$) or weight ($p = 0.55$) between the treatment and control groups. Five of the 7 treated dogs and 4 of the 5 control dogs had bilateral osteoarthritis.

While the majority of treatments were carried out without complications, mild discomfort was evident in 2 of the treated dogs immediately following treatment. One dog showed subtle reluctance to use the treated limb the night after his second ESWT. However, after the third treatment, the dog was unaffected. A second dog had some petechiation on the medial stifle. These signs resolved within 24 hours.

PVF increased in 4 of 7 treated dogs, while an increase was measured in only 1 of 5 of control dogs (Figure 1). For PVF, a significant difference was not found between the groups; however, the dogs in the control group had a significant decrease ($p=0.05$) in PVF consistent with an increase in lameness in the control dogs (Table 1). VI significantly increased in both treated and control groups and no difference was found between groups. A significant change in AFS was not found within, or between, groups. The ROM of the stifle
joint improved in 5 of 7 treated dogs and 3 of 5 controls (Figure 2) with the dogs in the treated group having a trend toward increased ROM (p=0.07) and a positive slope (3.34), compared to the control dogs which did not have a significant change (p=0.78) and had a negative slope (-1.26). This difference was not significantly different between groups (Table 1). The subjective data provided by client questionnaire did not show significant difference between groups (Table 3).

Discussion

Although the dogs in the “treatment group” demonstrated some improvement the level of improvement did not reach statistical significance. In contrast, the dogs in the sham treatment group did not improve and their limb function worsened significantly over the 98 day study. This is likely attributable to continued inflammation in the affected stifle secondary to progressive osteoarthritis. With this in mind, one could argue that ESWT treatment did not lead to improvement but it did seem to attenuate the progression of the disease. Certainly the limited sample size and variation in lameness severity in both groups contributed to our difficulty in achieving statistical significance for many measured variables. The graph of the data for PVF (Figure 1) indicates that improvement was evident at 21 days and continues to be more evident at each subsequent treatment. Continuation of treatments, more pulses or higher energy at each treatment, or a longer follow-up period may have resulted in statistically significant differences in the PVF.

The results of this study were similar to a previously described canine ESWT study (3). A group of 9 dogs with hip and elbow osteoarthritis were used in a 28 day study in which dogs were given ESWT 3 times at 2 week intervals. The dogs treated with shock wave therapy showed improvement from 2 to 20 % over baseline force plate measurements compared to control dogs that were typically less (more lame) than baseline measurements. Significant differences were achieved from that report between treated and control subjects because PVF and ROM improved from day 0 to day 28. (3) One obvious difference between the studies was the joints studied. It is possible that the mechanism of inflammation and OA
is different between the joints and that ESWT will be more effective for OA in the elbow or hip as compared to OA in the stifle.

The reason for improvement is not known. Shock wave therapy does not seem to slow progression of osteoarthritis but it does decrease the pain. This has been shown in a dog with coxofemoral osteoarthritis that had less lameness following treatments, but the disease progressed radiographically (10). However, the dogs in the study presented here in this study were not radiographed at the completion of the study and it is unlikely that there would be a detectable change over the short period of this study. In addition, it has been reported that the severity of osteophytosis as noted on radiographic evaluation of the stifle does not have any correlation to limb function (5).

It is common for dogs with cruciate ligament disease to develop bilateral ruptures of the cranial cruciate ligament. Based on the history provided by the owner, and the physical examination performed during the initial visit, the limb to be treated was selected. It would have been ideal to evaluate only dogs with unilateral lameness, because dogs with bilateral disease could have shifting leg lameness, making it more difficult to identify improvement seen with the therapy. However, we found recruitment of dogs with unilateral lameness from osteoarthritis in the stifle to be very difficult.

Multiple mechanisms have been suggested for the efficacy of ESWT, but there is little scientific evidence available. In a carpal osteochondral fragment model in horses, joints that had been subjected to shock wave treatment had significantly decreased lameness and decreased synovial fluid total protein than had the untreated carpi (15). Assuming similar mechanisms are occurring in dogs, the shock wave therapy would appear to help decrease inflammation in the joint. Furthermore, because there is only the potential for mild adverse reactions, ESWT could be used repetitively in these cases. There are only reports of transient discomfort and mild petechial hemorrhage as side effects of ESWT (22).

Evaluation of ESWT therapy on osteoarthritis of the canine hip and elbow joint has recently been performed on 9 dogs with OA of the elbow and hips (3). This study was identical to ours in that force platform gait analysis and range of motion were used to analyze joints insertion points treated with ESWT at 0.14 mJ/mm².
Communication with owners at each visit resulted in very diverse accounts of subjective improvements among the groups. Five of the 7 owners of the treated dogs were very enthusiastic about the treatment and asked if their dog could receive monthly ESWT. The owners appreciated the improvement that resulted from the treatment and noticed increased activity of their animals. Four of the 5 ‘control dog’ owners had not noticed any change before a gradual decrease in activity of their pet. However, when evaluating the owner questionnaire, these reported changes did not result in a significant difference between groups.

As a result of these findings, further evaluation of stifle osteoarthritis should take into consideration that progression of the disease would cause ground reaction forces to change over time. Variability in vertical gait is likely to be related to repeat cycling of joint instability, consequent cartilage and meniscal injuries, and eventual fibrosis of the retinaculum (1). The dogs in our study were, no doubt, in varying stages of osteoarthritis. Regardless of severity of OA, it should be noted that dogs display inter-day variation in the production of force plate data. The mechanisms for this variation have been interpreted as deriving from external and internal environmental factors. Minor traumas unnoticed by owners and researchers, time of day, weather, may also cause inter-day variation in data gathered from individual subjects (20).

The limited number of cases this study indicate that there were clearly potentially positive outcomes associated with the treatment. One must consider these data as a pilot study to validate the need for additional larger studies. Future studies that evaluate the uses of ESWT in canine osteoarthritis cases need to evaluate a larger number of patients that include dogs that are not as advanced as the chronic cases included here, include an attempt to correlate outcome with radiographic and clinical findings, and to evaluate ways to improve treatment such as changes in the treatment protocol.
Footnotes

1 OR6-6-1000, Advanced Medical Technology, Inc, Watertown, MA, USA
2 Mek 92-Tpad Retroreflective Photocell, Sircon Controls, Missisauga, Ontario, Canada
3 Sharon software, Inc, Dewitt, MI, USA
4 Sedazine; Fort Dodge Animal Health, Overland Park, KS, USA
5 Torbugesic-S; Fort Dodge Animal Health, Overland Park, KS, USA
6 Robinul – V; Fort Dodge Animal Health, Overland Park, KS, USA
7 Dormitor; Pfizer Animal Health, New York, NY, USA
8 Yobine; Lloyd Laboratories, Shenendoah, IA, USA
9 Antisedan; Pfizer Animal Health New York, NY, USA

References


Legend of Figures

Figure 1. The mean (± SEM) peak vertical forces of treated and control groups for each of the 5 visits. ESWT was performed on the treatment group on visits 1, 2, and 3.

Figure 2. The mean (± SEM) stifle joint range of motion of treated and control groups. Goniometer analysis of ROM was performed at each of 5 visits.

Legend of Tables

Table 1. The pre and post treatment vertical force parameters and range of motion with the slope and the within group match pair $p$ value for both the treated and control groups are shown. The between group matched pair $p$ values are on the right side of the table.

Table 2. Subjective analysis gathered from treated and control client questionnaire completed at each of five visits. A score of '1' means that the symptoms are very severe and the dog won't attempt or is unsuccessful with the task. A score of '7' means no symptoms exist and that ability is as good as when the dog was younger. The mean scores and $p$ values from the one way analysis of variance are shown.
Figure 1.

Figure 2
<table>
<thead>
<tr>
<th></th>
<th>Treated Group</th>
<th>Control Group</th>
<th>Matched Pairs p Value</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Pre-Treated Mean (SE)</td>
<td>Post-Treated Mean (SE)</td>
<td>Slope (SE)</td>
</tr>
<tr>
<td>Peak Vertical Force (N/s)</td>
<td>37.33 (1.0)</td>
<td>37.86 (1.18)</td>
<td>0.15 (0.31)</td>
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<td>Vertical Impulse (N/s(s))</td>
<td>13.62 (0.64)</td>
<td>15.3 (0.72)</td>
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<td>Average Falling Slope (N/m*sec)</td>
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<td>-0.34 (0.04)</td>
<td>0.01 (0.01)</td>
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<td>Range of Motion (degrees)</td>
<td>96.43 (5.74)</td>
<td>113.29 (3.89)</td>
<td>3.34 (2.35)</td>
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Table 1
<table>
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<tr>
<th>Parameter</th>
<th>Pre-Treated Mean (SE)</th>
<th>Post-Treated Mean (SE)</th>
<th>Pre-Control Mean (SE)</th>
<th>Post-Control Mean (SE)</th>
<th>$p$ value</th>
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</thead>
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<tr>
<td>Reluctance to rise from resting</td>
<td>4.86 (0.40)</td>
<td>5.83 (0.31)</td>
<td>3.6 (0.81)</td>
<td>4.75 (0.63)</td>
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<td>Reluctance to jump off sofa/bed</td>
<td>4.8 (0.37)</td>
<td>6.0 (0.41)</td>
<td>3.4 (0.98)</td>
<td>4.5 (0.96)</td>
<td>0.8</td>
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<td>Reluctance to jump in car</td>
<td>4.5 (0.99)</td>
<td>6.0 (0.63)</td>
<td>2.2 (0.73)</td>
<td>5.25 (0.63)</td>
<td>0.4</td>
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<td>Stiffness in morning</td>
<td>4.0 (0.58)</td>
<td>5.33 (0.42)</td>
<td>4.0 (0.84)</td>
<td>4.5 (0.87)</td>
<td>0.68</td>
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<td>Stiffness all day</td>
<td>4.86 (0.34)</td>
<td>5.5 (0.34)</td>
<td>4.2 (0.8)</td>
<td>4.75 (0.63)</td>
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<td>Stiffness post exercise</td>
<td>3.07 (0.66)</td>
<td>5.17 (0.54)</td>
<td>2.4 (0.24)</td>
<td>3.5 (0.87)</td>
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<td>Time spent playing</td>
<td>5.0 (0.49)</td>
<td>5.5 (0.56)</td>
<td>3.0 (0.71)</td>
<td>3.5 (0.65)</td>
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<tr>
<td>Follow family</td>
<td>6.0 (0.31)</td>
<td>6.17 (0.31)</td>
<td>5.0 (1.05)</td>
<td>5.5 (1.19)</td>
<td>0.4</td>
</tr>
<tr>
<td>Daily Walk</td>
<td>3.75 (1.03)</td>
<td>4.0 (1.0)</td>
<td>3.4 (0.68)</td>
<td>4.5 (1.32)</td>
<td>0.74</td>
</tr>
<tr>
<td>Comfort Level</td>
<td>4.25 (0.44)</td>
<td>5.0 (0.45)</td>
<td>3.2 (0.66)</td>
<td>4.5 (0.5)</td>
<td>0.92</td>
</tr>
<tr>
<td>Reluctance to climb stairs</td>
<td>5.29 (0.47)</td>
<td>6.0 (0.26)</td>
<td>4.0 (0.84)</td>
<td>4.25 (0.48)</td>
<td>0.56</td>
</tr>
</tbody>
</table>

**Table 2**
CHAPTER 4. FORCE PLATFORM EVALUATION OF ANALGESIA FROM FOCUSED EXTRACORPOREAL SHOCK WAVE THERAPY IN UNILATERAL FORELIMB LAMENESS

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Accepted for publication in the Journal of the American Veterinary Medical Association

Summary

Nine horses with chronic unilateral forelimb lameness were included in the study. Force plate measurements of peak vertical force (PVF) and vertical impulse (VI) were obtained for 3 days to determine baseline data. Local anesthesia was administered to eliminate the lameness and PVF on VI measured. Focused extracorporeal shock wave therapy was administered to treat the lameness and force platform data was obtained 8 hours later (day 0) and daily for 7 days.

There was a significant increase in PVF and VI on days 0 and 2 post treatment. The PVF was similar between day 2 and the post anesthesia measurements. Results show that there is a 2 day period of analgesia following ESWT in naturally occurring lameness in horses.
Introduction

The application of focused extracorporeal shock wave therapy for equine musculoskeletal diseases has been an area of clinical interest and research in recent years. A number of studies have evaluated the effects of ESWT on multiple musculoskeletal diseases of the horse (1-6). Two different types of pressure wave generators have been used in the horse (7). True focused extracorporeal shock waves (ESWT) meet the definition of a shock wave with a rise and fall of pressure in within 1 microsecond and the maximum pressure is at a focal point within the tissues (7). These generators are capable of pressures up to 100 MPa. Radial pressure wave therapy (RPWT) has the maximum pressure deposited on the surface and it dissipates from that point. The pressure waves from the radial generators have much lower peak pressures, approximately 7 MPa, similar positive and negative components, and longer pulse durations of greater than 4 microseconds (7).

While the devices create different wave forms, there have been analgesic effects reported for both ESWT and RPWT. There have been multiple hypotheses as to the mechanism of analgesia including destruction of nerves or nerve receptors, disruption of neurotransmitters, and central control of sensory input, but none are truly supported (8-10). Some data is available as to the direct effect of ESWT on nerves. Sciatic nerves from frogs were repetitively stimulated with ESWT (11). The conclusion was that shock waves do not directly affect nerves, but the nerves are affected though the interaction with small gas bubbles. This mechanism as shown in vitro may not be applicable in vivo. In a sheep model, ESWT did not result in inflammation or disruption of the nerves. However, RPWT created significantly more inflammation in the nerves than ESWT or untreated control nerves (12). Two separate studies in horses that utilized both ESWT and RPWT and evaluated skin sensitivity to electrical stimulation distal to the treatment site that included the palmar nerve (12, 13). Following ESWT or RPWT, no analgesia of the nerve was found in either study. In another study in horses RPWT slowed sensory nerve conduction velocity of palmar nerves up to 35 days after treatment and caused disruption of the myelin sheath (14).

Neurotransmitters have been investigated as a potential mechanism of analgesia following ESWT or RPWT. Depletion of the neurotransmitters CGRP and PGP of nerves in rat paws was seen following treatment with 1000 pulses of ESWT at 0.08 mJ/mm² (15).
However, analgesia in a thermal testing mechanism was not present. The reinnervation was complete within 2 weeks. In a sheep model, local neurotransmitters, sP and CGRP were not found to decrease in concentration following ESWT or RPWT (12).

Analgesia after shock wave treatment has been reported in humans (6, 8, 16). After application of focused ESWT for the treatment of heel spurs in people, there is a bimodal analgesic effect. Pain decreases for 3 to 4 days after treatment, which is followed by a gradual return of pain that then again decreases as healing progresses. Painful diseases of bone and ligament or tendon junctions in humans will result in a rapid decrease in pain without radiographic changes (17). In many of these cases, the analgesic effect appears to be independent of the healing process (17).

In the horse, there is some information as to the presence of analgesia following therapy. A local cutaneous analgesia was identified for 72 hours following ESWT using an electrical stimulus (12). Following RPWT in a thermal stimulation model, no local cutaneous analgesia was found (18). In horses with navicular syndrome, no immediate analgesia was seen following RPWT (19).

The importance of the anesthetic effects of ESWT and RSWT are quite evident. The risk to both horse and rider when working without full comprehension of pain is significant. This concern has resulted in regulations being involved in multiple racing jurisdictions and the Federation Equine International. The objective of this study was to evaluate the duration of analgesia associated with ESWT in the horse. Our hypothesis is that a single treatment of ESWT will result in a decrease in lameness. The objective of the study reported here was to determine the short term effect of ESWT on lameness by force platform evaluations.

Materials and Methods

Horses – Nine horses with chronic unilateral lameness localized to a forelimb were included. To be included the horses had to be in good health other than the diagnosed lameness, have a history of lameness for greater than 6 months, and have a lameness grade of 2 or 3 out of 5 on the AAEP lameness scale (20). They were excluded if there had been an injection into the joint within 90 days, surgery on the joint in 180 days or if they had been
treated with topical or systemic medications such as non-steroidal-anti-inflammatory drugs, glucosamines or other oral products for lameness 14 days prior to starting the study. All horses had lameness localized by perineural and or intra-articular anesthesia and confirmation of the specific lameness by radiographic evidence. The Iowa State University Animal Care and Use Committee approved this study.

**Force platform gait examination** – Force platform gait analysis was performed using a biomechanical platform embedded in a 30-m walkway. Three sets of retroflective photocell receptors, were attached 1 meter apart in series and positioned in the walkway, with the middle sensor positioned at the middle of the force plate, and were used to determine velocity and acceleration over the 2-m measurement region. The horses were trotted across the platform at a comfortable speed and ground reaction forces for the forelimb and hind limb stance phases were recorded for each pass. Passes were repeated until 5 valid measurements were obtained for each limb (trial velocity between 1.80 to 2.60 m/s; acceleration ± 0.5 m/s²). A trial was considered valid if a forelimb and ipsilateral hind limb foot strike were isolated on the force plate consecutively. The first 5 valid passes were used for analysis. The ground reaction forces in the vertical direction were normalized for the horses' body weight and used for analysis of limb function. The data evaluated were peak vertical force (PVF, N/s), vertical impulse (VI, N/s(s)).

**Procedure** – Two clinicians not associated with the project independently assigned a lameness score prior to enrollment of the horse into the study and on day 7 of the study. Force plate data were obtained daily for each horse for 3 days (day-3 to -1) prior to ESWT. In addition, following the force platform analysis on the first day (day -3), local anesthesia was used to alleviate the lameness and a force platform analysis was completed. On day 0, ESWT was done in the morning and the first post treatment force plate analysis was completed 7 to 8 hours later. Force plate analysis was repeated daily though day 7.

**ESWT** – The horses were lightly sedated with detomidine at 0.01 mg/kg, administered intravenously and were clipped over the area to be treated. Horses diagnosed
with navicular syndrome had the frog pared and the foot soaked for 8 hours prior to treatment. There were 1000 pulses administered through the frog with a 35 mm focal depth at 0.15 mJ/mm² with a focused shock wave generator. Another 1000 pulses were administered from between the heel bulbs at the same energy. For horses with osteoarthritis coupling gel was applied and 800 shock waves were divided 4 sites caudolateral, dorsolaterally, dorsomedially and caudomedial using a probe with a focal depth of 20 mm. This was followed by another 800 shockwaves divided into the same locations, at a focal depth of 5 mm at an EFD of 0.14 mJ/mm², for a total of 1600 pulses. The objective was to completely treat the circumference of the joint.

**Statistical analysis** – Five valid trials for each forelimb were combined for the mean at each time point. The 3 baseline measurements were combined for a single average baseline value. A matched pairs t-test was performed to compare between baseline, the post anesthetic block measurement and post treatment measurements 0 through 7. A within group t-test was used to look for a difference between the navicular syndrome and arthritis cases. For all analyses, values of \( P < 0.05 \) were considered to be significant.

**Results**

The horses included in the study were a median age of 9 years (range 6 to 28 years) and had a mean weight of 524.23 kg (441.78 to 639.83 kg). There were 5 geldings and 4 females. Two American Paint Horses, 3 Thoroughbreds, and 4 Quarter Horses were included. Six horses were diagnosed with unilateral navicular syndrome. Lameness was localized by palmar digital nerve anesthesia and they all had radiographic changes consistent with navicular syndrome. Three horses had degenerative joint disease localized to the distal interphalangeal, metacarpophalangeal, and middle carpal joint with intra-articular anesthesia and all 3 had radiographic findings consistent with chronic degenerative joint disease. There were no complications associated with the ESWT in any cases.

There was not a significant difference between the navicular syndrome and arthritis cases for any of the parameters measured at any time point so all cases were evaluated
together. There was no change in lameness score \((P = 0.59)\) from pretreatment (mean = 2.67, range 2 to 3) to day 7 (mean = 2.61, range 2 to 3).

The baseline was significantly different from post anesthesia for PVF \((P = 0.0062)\) and VI \((P = 0.0087)\). There was a significant difference between baseline PVF and PVF on day 0 \((P = 0.003)\) and day 2 \((P = 0.0156)\). The PVF after local anesthesia was not significantly different \((P = 0.14)\) than PVF 2 days after ESWT (Figure 1). The VI was significantly increased over baseline on day 0 \((P = 0.0244)\) and day 2 \((P = 0.0232)\). The VI was significantly different from the post anesthesia VI at all time points.

**Discussion**

The objective of the study reported here was to evaluate the short term analgesia following ESWT in horses with naturally occurring lameness. In this study the data indicate a period of analgesia that peaked on day 2 after treatment. For this study we selected horses that were grade 2 to 3 lame. This provided a group of horses with an adequate degree of lameness where improvement would be evident. It is possible that more subtle grade 1 lameness could be eliminated or not affected by ESWT. All of the horses in this study had a chronic lameness. The selection criteria were designed to decrease the likelihood of spontaneous improvement. This could potentially select cases that may not be as likely to respond with short term analgesia. In these cases of navicular syndrome and osteoarthritis, adhesions of the deep digital flexor tendon to the navicular bone, osteophytes, cartilage erosions or other anatomic changes may make more profound analgesia less likely to occur. It is unknown if the response would be similar in an acute lameness. In the osteochondral fragment model where ESWT was started on day 14 after the fragment was created, there was less lameness and lower protein in the synovial fluid in ESWT treated joints by day 28 (21).

There is a documented dose response of ESWT (22–24). There appears to be no effect at low energy or low pulse number, the desired effect at mid-range levels, and a destructive effect at excessively high energy and high pulse numbers. This has been documented in multiple studies, both *in vitro* and *in vivo*. *In vitro* the proliferation of human
chondrocytes and ovine bone marrow stromal cells were evaluated at EFDs of 0, 0.02 and 0.06 mJ/mm² and 0, 500, and 1000 pulses (24). The cells showed a dose and pulse dependent proliferative response. When shock waves were evaluated in partial-thickness wounds in pigs, lower energy treatment enhanced healing and the tissue had a larger number of microvessels (22). Healing was impeded at markedly higher energy and pulse numbers. The horses in this study were treated with a generator clinically available to the equine practitioner at energy levels and number of pulses typical for the application (1, 21). We did not investigate how the dose response will affect the post treatment analgesia period.

The objective of this study was to evaluate the presence and duration of analgesia after ESWT rather than the mode of analgesic action. However, it is apparent from this data that the maximum analgesia is not immediate. This is shown by the rise in analgesia to the peak at day 2 then decreasing. It would be unlikely that destruction of nerves or nerve receptors would respond in this fashion. The results of this study were similar to a controlled study with ESWT (12). By measuring the subject's response to electrical stimulation, the noted study detected a 3 day period of analgesia over the ESWT treatment site of the mid cannon bone (12).

The graphs of the PVF and VI show an increase from baseline to day 2. The day 0 and day 2 data were significantly different from baseline; however, the day 1 data was not statistically different (P=0.07) based on the level of significance set for this study. The data shown in the graphs are group means to illustrate the effect seen. The matched pairs t test utilized to evaluate the data, had a data point separate from the group resulting in the P value being greater than 0.05. However, the data clearly indicate the increase in analgesia from day 0 to the peak at day 2.

In a study with RPWT in horses with navicular syndrome, the force platform measurement results were different than reported here (19). The RPWT deposits the energy at the surface and it decreases proportional to the square of the distance. This would limit the energy that is transmitted to the navicular region in contrast to ESWT where the maximum energy is deposited at the focal point of the navicular region.

The kinematic parameters of PVF and VI presented here have been identified as the best mechanisms to reflect lameness severity and subclinical gait abnormalities (25). The
post anesthesia PVF and VI were similar to those reported for sound horses (25). The baseline PVF (8.19 N/s) and VI (1.8 N/s(s)) were associated with a mean lameness grade of 2.67 in this study. When comparing our data to the previously published lameness grade of 2.5, where the PVF and VI were 6.3 N/s and 1.1 N/s(s) respectively, there is some discrepancy. This is likely due to the differences in the velocity parameters used. We selected a range of 1.8 to 2.6 compared to a velocity of 2.5 to 3.5 used for the study comparing the vertical forces to the lameness grades. Because these horses were evaluated consistently throughout the serial exams, the change over time is the important outcome. It is important to note that relying solely on vertical force components at one time point can result in misleading data (26). For our study we did not do daily subjective lameness grades. The sensitivity of the force plate analysis and previously published data indicating the correlation of the data to lameness grades did not warrant daily subjective evaluation.

It can be difficult to interpret the clinical significance of a change of 1 N/s in PVF and a change of impulse of 0.14 N/s(s) from baseline to day 2 where analgesia peaked. The fact that the day 2 PVF was not significantly different from post anesthesia would indicate that this would be of clinical importance. In the study reported here, there was an acute analgesia lasting 2 days in these horses with naturally occurring unilateral lameness. This data should be considered when exercising horses following ESWT.

Footnotes


b. BP600900, Advanced Medical Technology, Inc, Watertown, Massachusetts.

c. Mek 92-Tpad Retroreflective Photocell, Sircon Controls, Missisauga, Ontario, Canada


e. Dormosedan, Pfizer Animal Health, Exton, Pennsylvania

f. Equitron, Sinuwave, Marietta, Georgia.
References


Legend of Figures

**Figure 1.** The mean (±SE) peak vertical force (PVF, Fig 1A) and vertical impulse (VI, Fig 1B) are shown for each time point of the study. The highest PVF and VI were obtained following local anesthesia to eliminate the lameness. The baseline was the mean of measurements obtained over 3 days prior to ESWT. The day 0 data was obtained 8 hours following ESWT and then every 24 hours after that for 7 days. The day 0 and 2 PVF and VI were significantly increased over baseline (*). The post anesthesia and day 2 PVF were not significantly different (†).
Figure 1A

Figure 1B
Orthopedic physicians and veterinarians encounter patients with many pathological bone and joint conditions for which routine conservative (rest, corticosteroids, medications, physical therapy) or surgical treatment may fail. Chronic musculoskeletal disorders include a wide variety of degenerative and inflammatory conditions in both the human and domestic animal musculoskeletal system. ESWT provides a non-surgical, non-invasive alternative for these patients and can theoretically be applied to a number of musculoskeletal disorders.

The principal effects of ESWT on tissue have been investigated for over a decade. Human medicine has adopted ESWT as an acceptable modality to treat numerous musculoskeletal diseases. Veterinary medicine began to utilize ESWT after it had become an accepted treatment approach in human medicine. Studies have shown analogous results among both humans and animals, but further studies in veterinary medicine are required to gain the same support seen in human literature to validate it scientifically.

The primary outcomes evaluated in the treatment of musculoskeletal disorders with ESWT are decreased pain and improvement in function. The first paper presented in Chapter 3 of this manuscript suggests that ESWT is a feasible treatment in dogs with osteoarthritis to avoid clinical signs of increasing lameness and decreasing range of motion of the affected joint. We were able to show an improvement in lameness after dogs with stifle osteoarthritis were treated with ESWT. Although, the improvement in lameness was not statistically significant, the control group experienced a significant increase in lameness. Indeed, a larger sample size and more uniform stages of arthritis among our subjects would assist in achieving statistical significance for many measured variables. This study evaluated the outcome, not mechanism of ESWT. Further studies are necessary to investigate the mode of actions of ESWT on musculoskeletal disorders.

The presence of analgesia after ESWT has been documented and numerous mechanisms have been proposed. The second paper described in Chapter 4 defines a period of analgesia after horses are treated with ESWT. Pain recognition of the horse after ESWT is of great importance to both horse and rider. Withdrawal times after ESWT have been
enforced at equine competitions but are only based upon subjective opinion and empirical data. We were able to objectively analyze the duration of analgesia with force platform analysis and found a 2-day period of analgesia after a single treatment of ESWT.

Our initial experiences evaluating the effects ESWT on osteoarthritis and analgesia showed effects in both categories. To date, there are few reliable studies investigating these mechanisms and randomized trials are still rare and required. The publications included in this thesis contribute to the emerging knowledge about ESWT in veterinary and human medicine and set the groundwork for future studies.
ACKNOWLEDGEMENTS

I am sincerely grateful for my major professor and mentor, Dr. Scott McClure, and all of his patience the last 3 years. It has been an honor and privilege to work with such a prominent and talented clinician, surgeon, researcher, and professor. He has opened doors of opportunity for me that I wouldn’t have known existed and has helped me define my career plans and aspirations. I will forever remember him as having a key role in shaping my future. I would also like to thank Dr. Michael Conzemius and Dr. Rich Evans for serving on my committee and allowing me to pursue this Master’s degree. These individuals have numerous obligations and commitments but always made time to assist me with my research, education, and career plans.

My research could not have been completed without the help of Dr. Duane Robinson and members of the Iowa State University Orthopaedic Research Lab. Additionally, although not included in their job descriptions, the Iowa State Veterinary Teaching Hospital equine technicians very graciously assisted me with my data collections on numerous occasions. This Master’s degree was a combined effort involving numerous people with a common interest in veterinary orthopedics and a common courtesy to assist me in the completion of my degree.