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Abstract

Shock wave therapy can induce a period of cutaneous analgesia after treatment. Shock wave therapy does not induce microfractures nor does it have an effect on the modulus of elasticity of bone.

1. Introduction

Extracorporeal shock wave therapy (ESWT) and radial shock wave therapy (RSWT) have become popular treatment modalities for equine musculoskeletal problems. Extracorporeal shock waves are pressure waves generated outside the body that can be focused at a specific site within the body. Shock waves are characterized by high positive pressures of up to 100 bar and negative pressures of 5 - 10 bar [1]. They have a rapid rise time of 30 - 120 ns and a short (5 µs) pulse duration [1]. More recently, the use of RSWT has gained popularity [2,3]. RSWT uses a projectile mechanism to stimulate a pressure wave. Pressure waves generated by this mechanism are transmitted radially, decreasing in energy proportional to the square of the distance from the surface. The two modalities have different wave forms [4].

Analgic effects after both ESWT and RSWT have been reported. In humans, the analgesic effects have been noted, but no studies that identify the mechanism or duration have been completed. Various hypotheses such as destruction of nerves and/or nerve receptors and central control of sensory input have been proposed, but none have been truly supported. Some in vitro data are available concerning the direct effect of shock waves on sciatic nerves from frogs in which shock waves were used to repetitively generate action potentials from the nerves [5]. The conclusion was that shock waves do not directly affect nerves, but the nerves are affected through the interaction with small gas bubbles. This in vitro mechanism may not be applicable in vivo, particularly in the distal equine limb. Furthermore, particularly with RSWT, the nerve would essentially be trapped between the generator and the bony structures, which would seem to make it more susceptible to direct damage by the therapy. To date, there have been no investigations of this possibility.

Another plausible mechanism of anesthesia is the depletion of neuropeptides. Neuropeptides such as substance P (sP) and calcitonin gene-related peptide (CGRP) are contained in small diameter afferent fibers. These fibers conduct impulses that lead to the sensation of pain and can contribute to the inflammatory response [6]. sP and CGRP can be released from peripheral nerve endings of nociceptive primary afferents and exert pro-inflammatory effects in peripheral tissues. sP and CGRP have been identified in the periosteum and joint capsule of multiple species. Additionally, sP and CGRP have been identified in the marrow, periosteum, and cortex of long bones [7]. In horses, sP innervation was identified in areas of disease suggestive that sP is important in signaling and maintenance of pain associated with osteoarthritis [8].

Another potential concern is the effect of ESWT and RSWT on bone. Early studies of ESWT in laboratory rodents demonstrated microfractures in bone [9]. Subsequent studies have not supported these finding in larger species [9,10]. However, if ESWT and RSWT alter the modulus of elasticity and microstructure of equine bone, the bone would be weakened, predisposing it to catastrophic failure.

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. Furthermore, any effect on the modulus of elasticity could put the
horse at risk of fracture. The objectives of these studies are to evaluate the effect of shock waves on (1) cutaneous sensation, (2) nerves, and (3) the modulus of elasticity of bone.

2. Materials and Methods

Effect of Shock Waves on Cutaneous Sensation

Cutaneous sensation in the horse after ESWT and RSWT was evaluated two ways. First, sensation of the skin directly in the treatment area of the mid cannon bone was measured. In addition, another treatment site that was directly over the palmar digital nerve was selected. Skin sensation in an area that was innervated by this nerve distal to the treatment site was also measured. This allowed measurement of the effect on skin sensation directly and indirectly by treating the nerve that innervated the skin distal to the treatment site.

Analgesia was assessed by the current stimulus threshold. Two electrodes were placed in the treatment area 2 cm apart. The level of current (mA) at which the horse first moved or indicated that the stimulus was recognized was recorded as the threshold. This was repeated in a random pattern between all four legs.

All of the horses were measured for 3 days before treatment to establish a baseline. The horses were then treated with ESWT or RSWT and measured daily for another 7 days. The treatment consisted of 1000 pulses at 0.15 mJ/mm² for ESWT or 1000 pulses at 0.16 mJ/mm² for RSWT, distributed evenly around the 3 cm diameter treatment site. This experiment used six horses. Their legs were the unit of randomization. Each horse had one control leg, one ESWT treated leg, one RSWT treated leg, and one randomly treated leg, with ESWT, RSWT, or control. This resulted in eight ESWT, eight RSWT, and eight control sites. The treatments were block randomized to legs. Stimulation threshold measurements were obtained for baseline (3 consecutive days before treatment), immediately after treatment, and then every 24 h for 7 days. The result is 11 serial measurements per leg.

The object of inference is the earliest time point for which there is no anesthetic effect (i.e., the stimulation threshold at the treatment sites is not statistically different from the control). This was assessed using cross-sectional paired t-tests.

Effect of Shock Waves on Nerves and Neurotransmitters

To study nerves and neurotransmitter substances after shock wave therapy, a sheep model was used. The four legs of 30 sheep were treated over the mid metacarpus and metatarsus. Legs were randomly assigned one of the two treatments (ESWT or RSWT), and the control group was the same as was described for the previous study. This treatment site allowed for the collection of nerve, skin, and periosteum. Specimens were collected from two sheep immediately post-treatment and at daily intervals for 14 days. The skin and periosteum were evaluated for concentrations of sP and CGRP. The nerves directly underlying the treatment sites were fixed and evaluated histologically for any changes associated with the treatment. A two-way analysis of variance, which looked for both the treatment and the time effects for sP and CGRP for the skin and periosteum, was completed.

Effect of Shock Waves on the Modulus of Elasticity and Microstructure of Bone

Specimens (3 x 1 x 1 cm) were harvested from the proximo-dorsal cortex of the third metacarpal bone of 16 healthy horses. Density was measured according to the Archimedes principle. The baseline E was determined by the measured density (ρ) and unidirectional transmission ultrasound speed (v) of each specimen according to the equation $E = \rho v^2$. Measurements of v were made in a saline bath between two 2.5 Mhz ultrasonic transducer-receivers. Eight randomly assigned specimens were then treated with 500 pulses of 0.15 mJ/mm² of ESWT, and eight specimens were treated with 500 pulses of 0.15 mJ/mm² of RSWT. After treatment, v was determined again. This sequence was executed three more times, resulting in 2000 pulses being delivered to each specimen. At the completion of this treatment, ρ of each sample was measured again. Histological evaluation of the specimens was performed using toluidine blue and basic fuchsin stains. Four incremental post-treatment Es were calculated per group. The data was analyzed with multivariate analysis of covariance (MANCOVA), which accommodates the correlation induced by repeated measurements on the same subjects as well as adjusts for baseline to determine if there was a difference between treatments.

3. Results

Effect of Shock Waves on Cutaneous Sensation

In the horses that were treated on the cannon bone region, there was a decreased sensitivity from baseline for both ESWT and RSWT sites for the first 3 days after treatment, indicating there was some local cutaneous anesthesia (Fig. 1 and Fig. 2). There are substantial differences in the P values between days 0 - 3 and days 4 - 6, reflecting a greater chance that a group (control versus focused or radial) difference exits for days 0 - 3. When the palmar digital nerve that innervates the heel was treated, there was not a notable analgesic effect in the skin distal to the treatment site.
Effect of Shock Waves on Nerves and Neurotransmitters
There were no significant differences in concentrations of sP and CGRP in the skin, SC tissue, and periosteum between the treatment groups and control group. The histologic evaluation of the nerves provided more information. For each nerve, multiple histologic factors were evaluated. The categories that had significant findings were perineural inflammation and presence or absence of axonal swelling and fat saponification. The effect of time post-treatment was significant for perineural inflammation (p < 0.001) and axonal swelling (P = 0.04). These data indicate that the nerves within the treatment field for both ESWT and RSWT had a significant amount of inflammation and swelling for at least 3 days post-treatment.

Effect of Shock Waves on the Modulus of Elasticity and Microstructure of Bone
The number of pulses by group interaction for E was not significant (P = 0.48), and the treatment group (ESWT or RSWT) effect was also not significant (P = 0.79). The number of pulses by group interaction for ν was not significant (P = 0.43), and the treatment group effect was also not significant (P = 0.77). There was no effect on the modulus of elasticity with either treatment, which means that there was no effect on the mechanical properties of the bone (Fig. 3). No histological changes could be attributed with certainty to either treatment modality. Using this treatment regimen, ESWT and RSWT do not influence the equine cortical bone breaking strength.

4. Discussion
These studies indicate that there is a potential risk associated with post-treatment analgesia in the horse. These data indicate that a horse should not be subjected to strenuous activities where local analgesia might pre-dispose the horse to injury for at least 4 days after ESWT or RSWT treatment. This supports the racing jurisdictions that have instituted withdrawal periods post-treatment. In most situations where these treatment modalities are being used correctly, the horses should be under limited exercise programs for the underlying musculoskeletal problem.

Nerve inflammation that was seen in the second study could contribute to the analgesic effect noted in the first study. The effects of treatment were significant for perineural inflammation and fat saponification. This is somewhat contradictory to the data generated from the first study where we directly treated the nerve in the distal limb of the horse and did not see any cutaneous analgesia as a result. Interestingly, the control nerve had more perineural inflammation than the ESWT treated nerve. Further studies on the effect of shock waves on nerves in the horse are indicated.

The mechanism to evaluate the bone in this study for microfractures is extremely sensitive. The development of any microfractures or other effects such as disruption of collagen fibers would be measured by this mechanism. The energy settings for this study were near the maximum that could be generated by these devices. It is possible that the results could be different with a higher energy or a greater number of pulses, but the study evaluated treatment levels similar to what is used clinically. A previous study that used extremely high energy (1.8 mJ/mm²) did not elicit any microfractures when evaluated histologically [10].

This study evaluated one ESWT and one RSWT generator. There are differences in generators, energy levels, and number of pulses that could affect outcome. These studies used two common machines and a relatively high number of pulses in a small area. Using a higher energy or number of pulses could lead to a different outcome.

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