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EFFECT OF THERAPEUTIC PULSED ULTRASOUND IN DOGS WITH EXPERIMENTAL STIFLE JOINT OSTEOARTHRITIS

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Summary

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The purpose of this study was to investigate the effect of therapeutic ultrasound upon some functional parameters in dogs with stifle joint osteoarthritis. Experimental osteoarthritis was induced in 6 mixed-breed dogs by injections of sodium monoiodoacetate in the left knee joint. The right joint served as control. The clinical and goniometric status of dogs was monitored at post injections days 1, 30, 60, 105 and 130. Therapeutic ultrasound was applied between days 105 and 130 using a 1 cm^2 transducer, 3 MHz frequency, power density 1.20 W/cm² and a pulsed wave duty cycle of 1/2 (impulse time/interval). Nine procedures were performed. Synovial fluid viscosity was also improved without alterations of its volume. Therapeutic ultrasound improved the clinical status, increased the muscle mass of the affected limb, the motility but not the circumference of the osteoarthritic knee joint in dogs. This physical factor had a beneficial effect on physicochemical properties of synovial fluid. At the same time, ultrasound therapy did not influence the chronic fibrous alterations in soft tissues.

Key words: dog, knee joint, osteoarthritis, therapeutic ultrasound

INTRODUCTION

Osteoarthritis (OA, degenerative joint disease) is a chronic polyetiological arthropathy of weight-bearing joints. The disease is characterized with progressive degeneration of joint cartilage, subchondral osteosclerosis, marginal osteophytes and low-degree synovitis, resulting in permanent disability (May, 1994; Harari, 1997). Osteoarthritis is a chronic illness that could be successfully controlled but not permanently healed (Ehrlich, 2003).

It is acknowledged that contemporary therapeutic protocols for control of canine osteoarthritis are purely symptomatic (Jones & Doherty, 1992; Lipowitz, 1993; Henrotin *et al.*, 2005). They include a variety of medications, nutritive and physical factors aimed to improve the quality of life (MacPhail, 2000; Scott, 2007), although not all of them are proved to be efficient (Mazzuka & Brandt, 2003; Abadie *et al.*, 2004; Dougados, 2006; Hochberg & Clegg, 2008; Sanderson *et al.*, 2009). The conventional therapy reduces the discomfort, slows down the destructive events and achieves a joint motility without pain (Lipowitz, 1993). Martinez (2000) and Davatchi (2000) have formulated the principles of osteoarthritis therapeutic schedule: flexible pharmacotherapy, body weight control, rest and modified locomotor activity.

After the discovery of ultrasound in the 1950-ties, it became widely used in different pathological states (Maxwell,

1992). Ultrasound is employed for decades in musculoskeletal injuries (Kozanoglu *et al.*, 2003). Despite its extensive clinical application, the mechanisms of its action are not completely understood. It is supposed that US stimulates reparative processes in tissues via the following effects: non-thermal (micromassage, increased membrane permeability, increased calcium transport, metabolic and phagocyte activities, cavitation), thermal (increase in local temperature to 40–45 °C that influences pain, effusion and blood supply) and physicochemical (fine dispersion and emulgation of various compounds) (Dyson & Suckling, 1978; Patrick, 1978; Millis & Lavine, 1997; Bryant & Milne, 1998).

A number of authors (Gam & Johannsen, 1995; Welch *et al.*, 2001; Denis & Marcellin-Little, 2004) do not share the optimism about ultrasound application as the results from functional studies were not convincing, due to the rather various etiopathogenesis of knee osteoarthritis in patients. According to Srbely (2008), ultrasound demonstrates a wide range of therapeutic effects that justify its reliable and efficient application for treatment of osteoarthritis in men. At the same time, similar studies in dogs with degenerative joint diseases are rather few.

The purpose of the present trial was to investigate the effect of therapeutic pulsed ultrasound upon some clinical and functional parameters in dogs with experimental knee joint osteoarthritis.

MATERIALS AND METHODS

Six clinically healthy dogs aged 2 to 2.5 years from both genders, weighing 15±2 kg were used. Animals were housed in individual boxes of 3 m^2 and had permanent access to fresh water and dry canine food (Canil®, Brazil). Ten days prior to the experiment, dogs were treated against endoparasites (1 tablet per 10 kg, p.o., Biheldon®, Golashpharma, Bulgaria containing 0.05 g praziquantel and 0.05 g pyrantel pamoate per tablet).

The clinical and blood laboratory status of each animal was determined.

Osteoarthritis was induced by injection of sterile 0.9% NaCl aqueous solution of sodium monoiodoacetate (MIA) (MERCK Schuchardt, # S05800 228) into the stifle joint of the left leg. Ten weekly joint injections of MIA (0.12; 0.12; 0.16; 0.16; 0.96; 1.28; 1.28; 3.00; 5.00 and 10.0 mg/kg) were done aseptically. The right contralateral joints served for control purposes.

The evaluation of the clinical status was performed according to the kinetic gait analysis system developed by Cross *et al.* (1997) (Table 1). The following goniometric parameters were individually monitored: femoral muscle circumference, stifle joint circumference, range of motion between maximum flexion and extension of the joint (Robins, 1990; Millis & Levine, 1997).

Synovial fluid (SF) samples were obtained from all joints for determination of volume (mL) and its viscosity (length of the viscous synovial fluid string, cm) (Harari, 1997).

After hair shaving and contact gel application (BRYMORE®, San Marino), nine procedures were performed with 1 cm^2 transducer, power density of 1.20 W/cm^2 and a pulsed wave duty cycle of 1/2 (impulse time/interval) as recommended by the manufacturer. The procedures were performed between the 105th and the 130th day of the experiment, every other day with increasing duration of 5, 5½, 6, 6½, 7, 7½, 8, 8½ and 9 min. A ultrasound wave generator BTL-07

Table 1. Kinetic gait analysis system for clinical evaluation of lameness, pain and joint effusion of knee osteoarthritis in dogs (Cross et al., 1997)

Parameter	Score	Clinical sign
Standing lameness	1	Normal weight-bearing
	2	Partial weight-bearing
	3	Intermittent toe touching
	4	No weight-bearing
Trotting lameness	1	Normal weight-bearing
	2	Marked lameness with partial weight-bearing
	3	Marked lameness with intermittent toe touching
	4	No weight-bearing
Pain response	1	Absence of pain and response
	2	Slight pain, allowing manipulations of the limb within the normal range of motility, manifested by turning the head and pulling the limb away
	3	Moderate pain, not allowing manipulations of the limb within the normal range of motility, manifested as described for score 2
	4	Significant pain, not allowing manipulations of the limb
Joint effusion	1	Normal – palpatory compression upon the patellar ligament
	2	Weak – slight increase, the patellar ligament is palpated
	3	Moderate – marked increase, slightly perceptible ligament
	4	Significant – the patellar ligament is not palpated

(Beautyline® BTL Czech Republic) was used for the therapy.

Results were presented as mean ± SEM and processed by the non-parametric tests of Friedman and Mann-Whitney by a statistical software (Statmost for Windows, Datamost Corp, USA). Differences were considered as statistically significant at the $P<0.05$ level.

RESULTS

The data from the kinetic gait and goniometric analysis are presented in Table 2. Using the kinetic gait analysis score system of Cross *et al.* (1999), the locomotor status of dogs was assessed to 4±0 points by day 1, 11±1 points by day 30; 10±1 points by days 60 and 105 and 6±0 points by day 130 ($P<0.01$ vs day 1). The differences prior to and after the ultrasound therapy were also statistically significant ($P<0.01$). With advancement of the disease, the atrophy of femoral muscles of the left hindlimb became more prominent. The circumference of the femur decreased to 25±1 cm by the 60th day ($p<0.05$ vs 29±1 cm by day 1) and 24±1 cm by days 105 and 130 ($p<0.01$ vs baseline). There was a statistically significant difference between both limbs by day 130 (24±1 vs 26±1 cm, $P<0.05$). The circumference of the joint did not change noticeably. The range of motion of osteoarthritic joints decreased during OA development from 113±2° by day 1 to 93±5° on day 30; 89±4° on day 60 and 79±5° on day 105 ($P<0.01$ vs baseline and vs the contralateral joint), and showed a statistically significant improvement after the pulsed US therapy up to 98±3° ($P<0.01$ vs day 1).

The analysis of synovial fluid (SF) showed that the volume of aspired fluid did not change significantly throughout

the experiment (Table 3). There were neither variations between left and right joints with regard to SF volume. The SF viscosity of osteoarthritic joints decreased considerably compared to control joints and vs the beginning of the study from 7.0±0.42 cm by day 1 to 1.0±0.44 cm by day 105 (P<0.01 vs baseline) and increased to 4.0±0.64 cm after the physical therapy (P<0.01 vs baseline). SF viscosity showed statistically significant differences between both joints at all studied time intervals (P<0.01 by days 30 and 60; P<0.05 by days 105 and 130).

DISCUSSION

On the base of clinical and goniometric data it was shown that the chemical experimental model of OA used in this study, resulted in fast worsening of locomotory function of the stifle joint in all treated animals. By the 30th day, there was a marked joint effusion, pain and restricted motility and by the 60th–105th day – muscle atrophy of affected limbs. Similar findings for impaired locomotor function are reported by Guinamp *et al.* (1997), Bovine *et al.* (2003), and Bey-

Table 2. Clinical evaluation and goniometric analysis of dogs with experimental osteoarthritis of the left knee joint (mean + SEM; n=6)

Parameter	joint	Days after experimental osteoarthritis induction				
		1	30	60	105	130
Kinetic gait analysis score, points		4±0	11±1**	11±1**	10±0** ##	6±0**
Femur circumference, cm	L	29±1	26±2	25±1*	24±1**	24±1**
	R	29±1	29±1	28±1	27±1	26±1*
Knee joint circumference, cm	L	23±1	25±1	24±1	24±1	21±1
	R	23±1	22±1	21±1	21±1	19±1
Range of motion, degrees	L	113±2	93±5**	89±4**	79±5**	98±3**
	R	113±2	112 ±2^	111±2^	111 ±2^	112±2

*P<0.05; **P<0.01 vs day 1; #P<0.05; ##P<0.01 between days 105 and 130; ^P<0.01 between the left OA joint (L) and the right control joint (R).

Table 3. Synovial fluid volume and viscosity in dogs with experimental osteoarthritis of the left knee joint (mean + SEM; n=6)

Parameter	joint	Days after experimental osteoarthritis induction				
		1	30	60	105	130
Volume, mL	L	0.3±0.04	0.4 ±0.03	0.4±0.09	0.3±0.04	0.3±0.03
	R	0.3±0.05	0.3±0.05^	0.3±0.05	0.3±0.03	0.3±0.03
Viscosity, cm	L	7.0±0.42	2.0±0.47**	2.0±0.49**	1.0±0.44**	4.0±0.64*
	R	7.0±0.42	7.0±0.43^^	7.0±0.26^^	7.0±0.08^	7.0±0.08^

*P<0.05; **P<0.01 vs day 1; ^P<0.05, ^^P<0.01 between the left OA joint (L) and the right control joint (R).

reuther *et al.*, (2007) in rats treated intraarticularly with MIA, depending on the dose of the agent and with cumulative effects according to treatment duration.

Synovial fluid volume did not exceed the normal amount for healthy canine stifle joints (about 0.5 mL). Thus, other joint conditions – rheumatoid, infectious etc. were excluded (Houlton, 1994; Clements, 2006). Decreased SF viscosity however is always related to arthropathies (Lumsden *et al.*, 1996). Given that the reference range is between 2.5–7.0 cm, Fernandez *et al.* (1983), Harari (1997), and Clements (2006) have obtained SF string length of 1–2 cm from dogs with osteoarthritis, confirmed by our data as well. With advancing of the degeneration process, viscosity further decreased (Houlton, 1994). With osteoarthritis, the electrostatic and hydrodynamic interactions of synovial fluid are altered and its viscosity is reduced (Mansat & Piron, 2007).

The applied therapeutic protocol has improved the clinical status of experimental animals. Ultrasound exerted a positive effect on the circumference of the femoral muscles, probably due to increased blood circulation and trophic effect, as well as to inhibition of pain that allowed a more extensive loading of the limb. According to Speed (2001) the thermal effect is the factor that improves muscle extensibility and frees from pain. The differences between ranges of motion of both joints after the US therapy were no more statistically significant. These results are similar to those of Reed & Ashikaga (1997) obtained in human osteoarthritic knee joints, where a better motility and extensibility of knee joint ligaments were reported.

Another beneficial effect of the therapy was the improved synovial fluid viscosity. Speed (2001) explains this event by the so-called acoustic microstreaming – one-way transport of fluids through the cell membranes, resulting in alterations in their structure, permeability and functions. Johns (2002) considers that the absorption of non-thermal mechanic ultrasound energy from proteins modifies their three-dimensional structure and thus, their functional activity; ultrasound dissociates high-molecular complexes and this way interferes in their function. Applying this mechanism to high-molecular collagenolytic enzymes, the achieved improvement after the ultrasound therapy could be plausibly explained.

In conclusion, therapeutic pulsed ultrasound improved the clinical status, increased the muscle mass, the range of motion and the loading of stifle joint in dogs with osteoarthritis. This physical factor improved the physical properties of synovial fluid of affected joints, resulting in higher viscosity. At the same time, US therapy did not influence the circumference of affected joint, due to chronic fibrous changes in soft tissues.

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