Vertical force analysis in dogs with hip osteoarthritis undergoing treatment with chondroprotectors

Análise da força vertical em cães com osteoartrose coxofemoral sob tratamento com condroprotetores

doi:10.7213/academica.14.2016.02

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Abstract

This study was aimed at evaluating vertical forces generated during locomotion in dogs affected with hip osteoarthritis (OA) submitted to chondroprotective treatment with chondroitin sulphate and glucosamine (CS-GLU). Eighteen dysplastic dogs suffering from secondary bilateral hip OA and treated with CS-GLU (200mg and 300mg/10kg/SID respectively) for 60 days (treated group), and 18 lameness free dogs with normal hip joints (healthy group) were evaluated. A pressure sensitive walkway was used to measure peak vertical force (PVF), vertical impulse (VI) and stance phase (SP) duration. Data collection was performed prior to and within 30 and 60 days of treatment (treated group), or on a single occasion (healthy group). Longitudinal and intergroup comparisons were made using repeated measures ANOVA followed by the Tukey post-hoc test and the unpaired t-test respectively, with a significance level of 5% ($p<0.05$). Mean peak vertical force did not differ significantly within the treated group. However, mean PVF and VI were lower in the treated compared to the control group. A slight increase in mean VI was documented in one treated limb at time points 30 and 60. Results of this study suggest hip OA leads to decreased weight bearing and treatment with CS-GLU does not improve PVF in the short term.

Keywords: Osteoarthritis. Hip dysplasia. Vertical forces. Dogs. Chondroprotector.

Resumo

Este estudo teve por objetivo avaliar as forças verticais da locomoção em cães com osteoartrose (OA) coxofermoral sob tratamento com o uso de condroprotetores a base de sulfato de condroitina e a glucosamina (SC-GLU). Foram avaliados 18 cães com OA coxofemoral bilateral secundária a displasia que iniciaram o tratamento com SC-GLU (200mg-300mg/10 kg/SID) por 60 dias (grupo tratado) e 18 animais hígidos (grupo hígido). Uma plataforma sensitiva de pressão foi utilizada para mensurar o pico de força vertical (PFV),

impulso vertical (IV) e tempo de apoio (TA) nos tempos 0, 30 e 60 dias desde o início do tratamento do grupo tratado e uma avaliação única no grupo hígido. A comparação longitudinal foi realizada pelo teste ANOVA com mensuração repetida (pós-teste de Tukey) e a comparação entre os grupos pelo teste t não pareado (p < 0,05). Não houve diferença estatística na avaliação longitudinal do PFV no grupo tratado, contudo, foi detectada uma diminuição do PFV e do IV dos animais com OA em relação ao grupo de animais hígidos. O IV teve um ligeiro aumento em um dos membros afetados aos 30 e 60 dias. Os resultados sugerem que a OA coxofemoral leva a diminuição do apoio e que o tratamento com SC-GLU em curto prazo não melhora o PFV.

***Palavras-chave**: Osteoartrose. Displasia coxofemoral. Força vertical. Cães. Condroprotetor.*

Introduction

Osteoarthritis (OA) is a pathological condition characterized by changes in joint architecture due to articular cartilage degeneration (Arnbjerg, 1999). Osteoarthritis develops in response to mechanical and biological events that interfere with articular cartilage degradation and synthesis, and ultimately affect chondrocytes, extracellular matrix and subchondral bone. Osteoarthritis may be age-related, traumatic or secondary to other conditions (Budsberg and Bartges, 2006). Primary OA has a much lower prevalence compared to secondary OA resulting from mechanical stress such as hip dysplasia (Arnbjerg, 1999), one of the most common orthopedic conditions in dogs (Lafond et al., 2002), with high prevalence in several countries (Verhoeven et al., 2012).

Chondroprotectors are widely used for conservative treatment of canine OA. Although moderate pain relief can be achieved, scientific evidences of effects in dogs, cats and horses are weak (Aragon et al., 2007; Sanderson et al., 2009; Vandeweerd et al., 2012).

Chondroitin sulphate-glucosamine (CS-GLU) is a popular chondroprotective combination (Souza et al., 2010). These compounds are known to have synergistic effects (Lippiello et al., 2000) and chondroprotective anabolic properties, leading to reduced cartilage degeneration (McCarthy et al., 2007). Dogs with mild to moderate OA are thought to benefit more from CS-GLU supplementation than severely affected patients (Beale, 2004).

Clinical improvement with enhanced physical performance in osteoarthritic dogs treated with CS-GLU has been suggested (Dobenecker et al., 2002; McCarthy et al., 2007). However, quantitative weight bearing data are scarce (Gupta et al., 2012) compared to data concerning treatment with other drugs, such as non-steroidal anti-inflammatory drugs (NSAIDs) (Holtsinger et al., 1992; Vasseur et al., 1995; Budsberg et al., 1999; Moreau et al., 2003; Lipscomb et al., 2002).

Peak vertical force is an accurate parameter for lameness diagnosis and can be measured using kinetic analysis (Fanchon and Grandjean, 2007). Dogs affected with hip OA can present with complex gait changes that make subjective lameness diagnosis extremely challenging; however, decreased weight bearing secondary to hip OA has been described based on vertical force parameters (Souza et al., 2015). This study was aimed at weight bearing quantification in dogs affected with hip OA treated with CS-GLU over a 60-day period. The hypothesis was that apparent clinical improvement would reflect increased weight bearing amenable to detection using sensitive pressure walkway.

Material and methods

The sample in this study comprised 18 dogs affected with hip OA secondary to hip dysplasia (treated group) and 18 lameness-free dogs with normal hip joints (healthy group). Inclusion criteria were as it follows: Hip OA confirmed or ruled-out based on radiographic assessment; absence of clinical signs of concurrent orthopedic or systemic conditions; large dogs aged over 2 years and weighing over 20 kg, regardless of breed and gender; no drug treatment over the last 30 days; no previous orthopedic surgery; mild to moderate lameness and pain on hip joint extension (treated group).

Dogs in treated group were supplemented with chondroitin sulphate-glucosamine (200mg/10

kg/SID and 300mg/10 kg/SID respectively) for 60 days. Dogs were part of the HOVET-USP case load. This study was approved by the FMVZ-USP Bioethics Committee; informed owner consent was obtained in all cases.

Dogs were submitted to pressure sensitive walkway (7100 QL Virtual Sensor 3 Mat System, Tekscan Inc. South Boston, MA, USA) prior to treatment (day 0), then within 30 and 60 days of treatment start (days 30 and 60 respectively). A sensitive pressure platform consisting of 3 plates capable of generating frames at 50Hz was used; plates were arranged in sequence (total construct size 1.5m x 0.5m x 0.005m) and contained 68644 pressure sensitive cells each. Frames were analyzed using software (I-scan 5.231, Tekscan Inc.,South Boston, MA, USA) for extraction of PVF, VI, SP and velocity data; PVF and VI were given in Newton, then standardized as percentage of body weight (% BW). Five valid passages out of a maximum of 20 passages were considered in the analysis; the first 3 passages were always discarded. Passages were recorded by the same examiner, in a straight line at 0.9-1.2 m/s velocity ± 0.1 m/s2 acceleration. Dogs were handled by their respective owners; owners were instructed not to allow dogs to turn the head, alternate the centre of mass or step outside the plate.

Statistical analysis

Normal data distribution was determined using the Kolmogorov-Smirnov test. Treated group pelvic limbs means were compared using repeated measures ANOVA and the Tukey post-hoc test. Treated group pelvic limbs means obtained on days 0, 30 and 60 were compared to healthy group means using the unpaired t-test. The unpaired t-test was also employed to compare age, body weight and velocity data between groups. The level of significance was set at 5% ($p<0.05$).

Results

Mean dog age and body weight were 4.1 (2-6.4 ± 2.4) years and 30.1 (21-38 ± 4.3) kg. Dog age and body weight did not differ significantly between groups ($p>0.05$).

Mean passage velocity and stance phase duration corresponded to 1.0 m/s and 0.47 seconds respectively, with no significant differences among groups. Peak vertical force and VI data are given in Table 1.

Discussion

Supplementation with CS-GLU is aimed at joint metabolism improvement and pain control. These compounds are thought to influence the expression or activity of different OA mediators, with several effects demonstrated in vitro (Neil et al., 2005; Lippiello et al., 2000).

Beneficial effects on gait have been suggested in subjective clinical studies (Canapp et al., 1999; Dobenecker et al., 2002) with patients treated with CS-GLU. Nonetheless, objective data are limited and contradict the hypothesis that such compounds would promote improved weight bearing (Moreau et al., 2003). The lack of scientific evidence supporting beneficial effects of CS-GLU supplementation has been repeatedly emphasized (Aragon et al., 2007; Sanderson et al., 2009; Vandeweerd et al., 2012). This study set out to obtain quantitative weight bearing data from osteoarthritic dogs undergoing treatment with CS-GLU, given the unreliable nature of visual analogue scales and other subjective methods employed in lameness evaluation of dogs with OA (Hielm-Björkman et al., 2011).

Kinetic analysis is the current gold standard for lameness diagnosis and gait evaluation in dogs. Force plates have been employed in pioneer kinetic analysis studies (Budsberg et al., 1987); however, sensitive pressure plates provide accurate vertical force measurements and can therefore be used in lameness diagnosis (Fanchon and Grandjean, 2007). Pressure plates are thought to be as reliable as force plates, with reduced equipment costs and good portability; also, a complete gait cycle can be evaluated in a single passage, with shorter examination time due to the lower number of passages required (Besancon et al., 2003).

Similar to human baropodometry, sensitive pressure plates can provide detailed quantitative

Table 1 – Mean (±SD) peak vertical force (PVF) and vertical impulse (VI) recorded in pelvic limbs of dogs in the treated and healthy groups

PVF*	Day	RPL	LPL	P value
Treated group	0	26.6^{a} ± 6.4	28.8^{a} ± 7.0	<0.001
	30	26.7^{a} ± 6.5	28.6^{a} ± 6.3	<0.01
	60	26.6^{a} ± 6.2	28.1^{a} ± 6.6	<0.05
Healthy group	0	30.5^{b} ± 5.0	30.6^{b} ± 5.0	0.6534
VI*	**Day**	**RPL**	**LPL**	**P value**
Treated group	0	13.1^{a} ± 2.5	13.4^{a} ± 2.6	0.6679
	30	12.6^{a} ± 2.6	14.0^{b} ± 2.8	<0.05
	60	13.2^{a} ± 2.5	14.7^{b} ± 2.5	<0.05
Healthy group	0	14.9^{b} ± 2.7	14.7^{b} ± 2.6	0.8142

Legend: PL - pelvic limb; R - right, L - left.

Note: *PVF and VI expressed as % of body weight. Different superscript letters in the same column differ significantly (p<0.05).

weight bearing data collected from different limb pads in lame (Souza et al., 2014) as well as non-lame dogs (Souza et al., 2013). Despite this highly level of detail, the slight increase in VI detected in the treated group on day 30 in this study must be interpreted with caution. Vertical impulse data are known to have 80% accuracy, thus a 20% margin for error must be taken into account. Peak vertical force is a high (92%) accuracy lameness detection parameter (Fanchon and Grandjean, 2007); similar PVF in dogs in this sample supports data given elsewhere (Moreau et al., 2003; Gupta et al., 2012) and suggest weight bearing was not significantly improved by CS-GLU supplementation. Chondroitin sulphate-GLU combination is thought to have beneficial long term effects (Bucsi and Poor, 1998); still, treatment recommendations should be based on reliable, objective parameters.

As documented in pretreatment assessment (day 0) in this trial, VI tends to be low in lame dogs. However, VI is highly variable in dogs presenting with hip OA (Souza et al., 2015), with some studies failing to detect differences in VI between dysplastic and healthy dogs (Bennet et al., 1996). Overall, results of this study effectively demonstrate decreased vertical impulse in dogs with OA secondary to hip dysplasia, supporting data given elsewhere (Poy et al., 2000; Grisneaux et al., 2003; Lister et al., 2009; Seibert et al., 2012).

Passages in this trial were limited to a maximum of 20 to minimize variation between analyses (Lascelles et al., 2006) without compromising the number of repetitions required for data collection (Weigel et al., 2005). This method also provided enough rest for patients and allowed the necessary velocity control for reliable longitudinal and intergroup comparisons (Evans et al., 2003), given mean vertical force values tend not to vary significantly across trials in healthy dogs (Nordquist et al., 2011).

Dogs in this sample had similar age and body weight. Still, differences in conformation may impact weight bearing data. Although errors can be minimized by data expression as percentage of body weight (Bertram et al., 2000; Lee et al., 2004; Mölsä et al., 2010; Voss et al., 2010), lack of breed

standardization may have masked subtle differences in this study. True randomization and blind evaluation requires a placebo group, which was not included; on the other hand, the lack of significant differences and the potential bias introduced by the placebo effect could lead to inclusion of unreliable, subjective data in the analysis (Lascelles et al., 2008; Burton et al., 2009; Malek et al., 2012).

Comparisons within the treated group were the major control for the results presented and a group comprised of healthy dogs was only included for the sake of quantification of weight bearing deficiencies in dogs in the treated group. Detection of weight bearing improvements would necessarily require evidences of decreased mean PVF values, given not all dysplastic dogs show decreased PVF and the degree of dysplasia tends to be negatively correlated with PVF (Souza et al., 2015).

Osteoarthritis secondary to hip dysplasia is amenable to surgical treatment; articular capsule denervation (Lister et al., 2009), colocephalectomy (Grisneaux et al. 2003) and coxofemoral prosthesis (Seibert et al., 2012) should be considered in cases associated with severe pain that fail to respond to conservative therapy (i.e., more severe cases). Although surgical techniques differ, postoperative kinetic studies (Grisneaux et al., 2003; Lister et al., 2009; Seibert et al., 2012) suggest promotion of improved weight bearing overall.

In order to isolate the effects of CS-GLU and avoid potential confounding factors in the analysis, other ancillary treatments for OA were excluded from this study. However, caloric restriction, physical activities (Mlacnick et al., 2006) and concurrent NSAID therapy (Neil et al., 2005), among other modalities, may act synergistically, with beneficial effects in osteoarthritic dogs (Beale, 2004). Therefore, extrapolation of the results presented to comprehensive medical treatments plans should be done with caution.

Conclusion

Based on results of this study, 60-day treatment with chondroprotective medication consisting of chondroitin sulphate and glucosamine does not promote significant weight bearing improvement in dogs with hip OA secondary to hip dysplasia when PVF is adopted as the parameter of reference. Long term benefits cannot be ruled out; although, the initial hypothesis of improved weight bearing in the short term was not confirmed.

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Recebido em: 22/10/2015
Received in: 10/22/2015

Aprovado em: 19/03/2016
Approved in: 03/19/2016