A Study of the Effect of HealthyMouth™ Canine Anti-Plaque Water Additive with Mobility Support on the Mobility Levels of Dogs with Impaired Mobility

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Abstract

This study investigated the effectiveness of a water additive in improving the mobility levels of a sample of dogs with moderately impaired mobility. The water additive contained Boswellia Serrata (Boswellic Acid) and Turmeric (source of Curcumin) as its primary bioactive ingredients. A sample of 40 mobility-impaired dogs were stratified by gender and randomly assigned to control and treatment groups. A double blind protocol was used whereby neither the owner dispensing the drinking water nor the clinicians rating the dogs were aware of whether a dog was in the control or treatment group. The control group received a placebo which looked and tasted the same as the treatment water. All dogs were rated on nine aspects of mobility on an 11-zone visual analog scale on day 0 and on day 56. The control and treatment groups were compared on their difference scores for the nine items and their overall mean using ANCOVA, controlling for day 0 levels. The results indicated that the positive change in mobility for the treatment group was significantly greater than that for the control group ($p < .0001$) on all nine items and on overall mobility. This degree of significance was essentially unchanged when corrections were made for violations of normality and variance homogeneity assumptions. The average percentage improvement on the nine mobility items for the treatment group was 43.56% compared to -.23% for the control group. On the overall mobility score, the mean percentage change for the treatment group was 34.76% compared to -.91% for the control group.

Arthritis or some form of lameness or gait problems affects one in every five adult dogs in the U.S. These problems as a group constitute one of the most common sources of chronic pain in dogs that veterinarians treat. The search for effective pharmaceutical treatments of these conditions has produced some success. The most commonly used drugs, nonsteroidal anti-inflammatory drugs (NSAIDS) are effective in producing palliative effects , but can have side effects ranging from vomiting, loss of appetite, depression, lethargy, and diarrhea to gastrointestinal bleeding, ulcers, perforations, kidney damage, and liver problems. These potential side effects have motivated a continuing interest in the possibility of identifying non-pharmaceutical, natural substances that may have positive therapeutic effects.

One such natural substance that has been reported to have positive therapeutic effects in humans is *Boswellia serrata*. Also called Indian frankincense, this substance has been part of traditional Indian medicine for thousands of years. It is derived from the resin of the Boswellia tree, a native Indian plant. It has several biologically active components, including Boswellic acid. Boswellic acid inhibits the activity of an enzyme called 5-lipoxygenase, which produces inflammatory molecules in the body's tissues. It also suppresses the activity of immune cells that have a role in initiating inflammation. In a recent clinical trial of *Boswellia serrata* extract published in the journal "Arthritis Research and Therapy" (Sengupta, Alluri, Satish, Mishra, Golakoti, Sarma, Dey, and Raychaudhuri, 2008), human subjects who consumed an enriched form of the extract (viz., 5-Loxin) experienced a significant improvement in their arthritis symptoms compared to those who took a placebo. In another study, Sengupta, Alluri, Satish, Mishra, Golakoti, Sarma, Dey, and Raychaudhuri (2008) reported significant reduction in pain and improvement in physical function among osteoarthritis patients at both low (100 mg/day) and moderate (250 mg/day) dosage levels of *Boswellia serrata* extract, with no detectable side

effects. Finally, a study on patients with osteoarthritis of the knee showed that Boswellia extract decreased pain and swelling and increased range of motion and endurance (Kimmatkar, Thawani, Hingorani, and Khiyani, 2003).

Several animal studies of the anti-arthritic properties of *Boswellia serrata* extract have also been reported. The extract exhibited significant anti-arthritic efficacy in Sprague-Dawley rats. For example, nonsteroidal anti-inflammatory drugs (NSAIDs) can cause a disruption of glycosaminoglycan synthesis, accelerating articular damage in arthritic conditions. An in vivo animal study examined Boswellia extract and ketoprofen for effects on glycosaminoglycan metabolism. Boswellia significantly reduced the degradation of glycosaminoglycans compared to controls, whereas, ketoprofen caused a decrease in total tissue glycosaminoglycan content (Reddy, Chandrakasan, and Dhar, 1989).

The broad spectrum safety of *Boswellia serrata* extract was tested using a battery of human safety studies conducted according to OECD guidelines and it was found to be safe (Krishnaraju, Sundararaju, Vamsikrishna, Suryachandra, Machiraju, Sengupta, and Trimurtulu, 2010). The safety of the extract in animals was supported by a study of acute and dose dependent subchronic safety in rats by Lalithakumari, Krishnaraju, Sengupta, Subbaraju, and Chatterjee (2006), which demonstrated that *Boswellia serrata* extract is safe even at dose levels 2,000 to 3,000 times higher than the human equivalence dose. In addition, *Boswellia serrata* extract was found to be non-genotoxic per the standard AMES bacterial reverse mutation assay, the chromosomal aberration test in Chinese hamster cells, and the mouse peripheral blood micronucleus assay (Chang, J.T., 2007a, 2007b; Indrani, 2006; Trimurtulu, Sen, Krishnaraju, and Sengupta, 2010).

Another natural substance which has attracted considerable research attention is turmeric. The bioactive component of turmeric is curcumin, which has been used as a remedy for

osteoarthritis and rheumatoid arthritis in Indian and Chinese systems of medicine. Curcumin shows excellent safety and has been demonstrated to be safe in six human trials (Chainani-wu, 2003). Today, scientific research is increasingly recognizing the remarkable properties of this ancient spice for treating modern joint related disease and possessing powerful health benefits for humans and animals. Recent research attributes its mechanism to being a compound that inhibits both COX-2 and lipoxygenase enzyme activity, along with decreasing levels of IL-1 beta (IL-1b) (Banerjee, Tripathi, Srivastava, Puri and, Shukla, 2003), and to its role in mediating the upregulation of peroxisome proliferator-activated receptors (Jacob, Wu, Zhou, and Wang, 2008; see also Aggarwal and Harikumar, 2008).

Early studies of the therapeutic effects of curcumin revealed that it did not produce appreciable benefits. It was subsequently determined that in order for curcumin to be effectively assimilated into the bloodstream, it must be combined with very small amounts of piperine (a component of black pepper). Piperine has been shown to enhance the absorption of curcumin in humans and animals without any adverse effects. Subsequent studies of the effects of curcumin have conventionally focused on the piperline and curcumin combination. In one study of patients with rheumatoid arthritis, curcumin was compared to phenylbutazone and produced comparable improvements in shortened duration of morning stiffness, lengthened walking time, and reduced joint swelling.

Recent studies have shown that its anti-arthritic effect to be comparable to that of popular pharmaceutical drugs without the potential side effects and toxicity. For example, Funk, Fye, Oyarzo, Kuscuoglu, Wilson, McCaffrey, Stafford, Chen, Lantz, Jolad, Sólyom, Kiela, & Timmermann (2006) reported that curcuminoids "...profoundly inhibited joint inflammation and periarticular joint destruction in a dose-dependent manner" in experimentally-induced arthritis.

The present study will investigate the effectiveness of a product containing a combination of Boswellia extract and turmeric, along with a number of other natural botanically derived substances in improving the mobility levels of dogs afflicted by moderate degrees of mobility impairment. This product, which has the commercial name of *HealthyMouth Canine Anti-Plaque Water Additive with Mobility Support,* has been subjected to numerous clinical trials which have consistently found it to be effective in reducing plaque and gingivitis in canine, feline, and equine samples. A summary of the results of these trials appears in Table 1.

Table 1

Summary of Results of Prior Clinical Trials of the HealthyMouth Anti-Plaque/Mobility Support Product

Product	Trial	Subjects	Date Completed	Result (% Plaque Reduction)
Water Additive	1	Dogs	March 2008	76%
Water Additive	2	Dogs	December 2008	72%
Topical Gel	3	Dogs	April 2010	62% (& 82% for gingivitis)
Topical Spray	4	Dogs	August 2011	78%
Water Additive	5	Cats	August 2010	85%
Water Additive	6	Cats	September 2010	88%
Topical Gel	7	Cats	March 2010	82%
Topical Spray	8	Cats	May 2011	79%
Water Additive	9	Dogs	September 2011	78%
Water Additive	10 - 12	Horses	August 2010	80%

In every one of the clinical trials in Table 1, the difference between the treatment and control groups was highly significant ($p < .0001$) in the desired direction.

Method

Participants

The participants in the study consisted of 40 dogs of a variety of breeds owned by patrons of a veterinary clinic. The dogs ranged in age from 3 to 15 years, and in weight from 6 and 85 pounds. The 40 dogs, stratified by gender, were randomly assigned in equal numbers to treatment and control groups, resulting in exactly equal gender representation in each study group. The 40-dog sample had been selected from a larger group of 100 patron-owned dogs on the basis of their not being overweight and having a mobility status in the moderately impaired range. The latter requirement meant that the dogs had exhibited a clinically observable reduction in their mobility but not to point where they were being medicated or unable to walk on their own. In addition, in order for a dog to be selected into the final sample, its good health had to be ascertained through blood tests and clinical examination.

Design

The dependent variable in this study consisted of mobility level as measured by a 9-item visual analog scale (see below). The independent variable consisted of the condition of either receiving the HealthyMouth treatment or receiving the placebo. The mobility levels of the two study groups were assessed on day 0 of the study (immediately prior to any treatment), on day 28, and on day 56. Of primary interest was the comparison of the treatment vs. control group change in mobility levels between day 0 and day 56. The study's design can be characterized as a 2-level between design with pretest (i.e., day 0) levels statistically controlled.

Instruments

The instrument used to measure this study's dependent variable (i.e., mobility) was a 9-item rating on a 4-inch (10.16 cm) visual analogue scale. The range of the scale extended from 0

to 10, but these points were used only as guides for zones along the rating continuum rather than to demarcate discrete intervals. These 11 mobility "zones" were defined as follows:

0 = Severe: dog has an inability to do anything for itself; worst possible pain for that condition.

1 = Just less than severe as not complete inability to do anything for itself.

2 = Unable to manage stairs; inhibited activity needing owner assistance.

3 = Considerable pain; impacting daily activity.

4 = More than moderate pain; starting to impact daily activity (0 - 4 rating = limited mobility).

5 = Moderate pain; able to go up & down stairs (5 - 10 = able to have an increasingly active live).

6 = Less than moderate.

7 = More than mild.

8 = Mild pain.

9 = Able to participate in and enjoy an active lifestyle without owner assistance.

10 = None; dog has complete normality; no pain.

The nine items to which the above rating scale was applied were:

1. Willing to walk
2. Willing to run
3. Willing to play
4. Willing to jump
5. Usually stiff and sore
6. Ease in lying down

7. Ease in rising

8. Difficulty in moving

9. Difficulty in sleeping

Scores were computed by dividing the distance (in cm) of the center of the x marked for each item by 10.16 and multiplying the result times 10. The result was rounded to the nearest integer.

Treatment

The product to be tested contained the following ingredients:

- Purified Water
- Organic Glycerin
- Organic Pomegranate
- Organic Yucca Extract
- Zinc
- Gluconate
- Organic Blueberry
- Natural Xanthan Gum
- Organic Papain (Papaya Extract)
- Riboflavin (Vitamin B2)
- Ascorbic Acid (Vitamin C)
- Organic Clove Extract
- Organic Cinnamon Extract
- Boswellia Serrata (source of Boswellic Acid)
- Turmeric (source of Curcumin)
- Chlorophyll
- Sorbic Acid (natural preservative)
- Black Pepper Oil (source of Piperine)

The placebo treatment consisted of drinking water with human grade food coloring that made the water a green color, like that of the test product. The liquids were supplied to the dog owners in the both groups, without being identified, in 12-gallon containers, to be administered to their dogs at the rate of between 200 and 2000 ml per day, with a minimum recommended daily dose of about 200 ml. As the composition is not toxic, the dogs were allowed to consume whatever amount they required to meet their hydration needs.

Procedure

Owners of the dogs in the sample were required to sign a consent form and a compliance form, affirming their agreement to give the drinking product with which they would be supplied to their dog on every day of the study. On the first day of the study the owners were instructed on the proper method of dispensing the drinking product and the amount to dispense. The placebo consisted of water that had been treated to look and taste exactly like the treatment product. The study was conducted according to a double-blind protocol: neither the dog owner nor the clinician doing the mobility ratings knew whether a dog was in the treatment or control group. The conduct of the study consisted of the owners dispensing the drinking product with which they had been supplied on each of the 56 days of the study. Dogs were rated by the veterinary clinician on the mobility scale on Day 0, Day 28, and Day 56 of the study.

All of the dogs in both the control and treatment groups were fed the same diet during the entire duration of the trial. This diet consisted of Science Diet Dry Formula For Adults mixed with Innova Evo Adult Dry Dog Food.

Data Analysis

The data analysis consisted of first computing the descriptive statistics for each of the 9 mobility scale items for each of the study groups. Next, Cronbach's alpha was computed to evaluate the reliability of the total mobility score. This was followed by analysis to assess whether the mobility item and total scores for each group met the primary assumptions of parametric analysis of variance (i.e., normality of distributions and homogeneity of variance between the study groups). Analysis of covariance was then used to test the hypothesis that the treatment group would exhibit a significantly greater positive change in mobility over the study interval. Although analysis of covariance is robust to moderate departures from its assumptions,

when these departures are more extreme it is necessary to conduct follow-up tests to ascertain whether the assumption departures could have affected conclusions about the significance of the results. The data collected in this study required these supplemental analyses.

Results

Descriptive statistics for the nine mobility items and the overall mobility score are presented for the two study groups in Table 2.

Table 2

Descriptive Statistics for the Nine Mobility Items and the Overall Mobility Score for the Two Study Groups

	Control Group			**Treatment Group**		
Mobility Score	**Day O** mean (sd)	**Day 56** mean (sd)	**Change** mean (sd)	**Day O** mean (sd)	**Day 56** mean (sd)	**Change** mean (sd)
Willing to Walk	8.1 (1.21)	8.1 (1.21)	0 (0)	8.05 (1.05)	9.7 (.47)	1.65 (.745)
Willing to Run	7.7 (1.42)	7.6 (1.353)	-0.1 (.308)	7.8 (1.105)	9.65 (.489)	1.85 (.875)
Willing to Play	8.05 (1.32)	7.75 (1.209)	-0.3 (.571)	7.75 (1.585)	9.7 (.47)	1.95 (1.432)
Willing to Jump	6.1 (2.05)	5.95 (2.164)	-0.15 (1.268)	5.15 (2.11)	8.7 (.801)	3.55 (1.791)
Usually Stiff and Sore	7.65 (1.424)	7.65 (.933)	0 (1.170)	6.25 (1.618)	9 (.725)	2.75 (1.482)
Ease in Lying Down	7.5 (1.15)	7.35 (1.226)	-0.15 (.587)	6.55 (1.669)	8.95 (.605)	2.4 (1.353)
Ease in Rising	7.6 (1.314)	7.55 (1.276)	-0.05 (.605)	6 (1.622)	8.3 (2.055)	2.3 (2.08)
Difficulty in Moving	7.45 (1.05)	7.45 (1.099)	0 (.973)	6.7 (1.593)	9.1 (.553)	2.4 (1.353)
Difficulty in Sleeping	8.65 (.875)	8.7 (.979)	0.05 (.51)	8.4 (0.883)	9.65 (.489)	1.25 (.851)
Overall Mobility	7.64 (1.02)	7.57 (1.032)	-0.078 (.437)	6.96 (1.13)	9.19 (.512)	2.23 (.82)

The data were subjected to evaluation for conformity to the assumptions of the analysis of covariance method which was to be used in the analysis. There are two primary assumptions

on which this method relies: normality of the subgroup distributions and homogeneity of variance. The score to be used in the analysis was the change score expressing the difference between the score on day 56 and the score on day 0. It was these change scores that were subjected to the tests for conformity to the assumptions. The first assumption tested was that of normality of the distributions of each of the nine items and of the overall score in each of the study groups. This test was conducted by means of the Shapiro-Wilk test, the results of which are reported in Table 3.

Table 3

Results of Shapiro-Wilk Tests for Normality of the Day 56 - Day 0 Change Scores for the Two Study Groups

Day 56 - Day 0 Change Score	Study Group	Shapiro-Wilk		
		Statistic	df	Sig.
Willing to Walk	Control	*	20	.000
	Treatment	.855	20	.006
Willing to Run	Control	.351	20	.000
	Treatment	.870	20	.012
Willing to Play	Control	.583	20	.000
	Treatment	.721	20	.000
Willing to Jump	Control	.578	20	.000
	Treatment	.874	20	.014
Usually Stiff and Sore	Control	.735	20	.000
	Treatment	.873	20	.013
Ease in Lying Down	Control	.609	20	.000
	Treatment	.899	20	.039
Ease in Rising	Control	.613	20	.000
	Treatment	.761	20	.000
Difficulty in Moving	Control	.757	20	.000
	Treatment	.848	20	.005
Difficulty in Sleeping	Control	.688	20	.000
	Treatment	.874	20	.014
VAS Mean Day	Control	.609	20	.000

Day 56 - Day 0 Change Score		Shapiro-Wilk		
	Study Group	Statistic	df	Sig.
	Treatment	.925	20	.122

* no variation in scores

The results in Table 2 indicate that the distributions of the change scores on the nine mobility items departed significantly from normality for both the treatment and control groups in all cases. For the overall mobility change score, the distribution of the control group's scores departed significantly from normality, but that of the treatment group's scores did not.

The results of the Levene test for homogeneity of variance are presented in Table 4.

Table 4

Results of Levene's Test of Homogeneity of Variance of the Day 56 - Day 0 Change Scores for the Two Study Groups

Day 56 - Day 0 Change Score	Levene Statistic (F)	df1	df2	Sig.
Willing to Walk	.[a]			
Willing to Run	8.506	1	38	.006
Willing to Play	1.331	1	38	.256
Willing to Jump	10.922	1	38	.002
Usually Stiff and Sore	5.480	1	38	.025
Ease in Lying Down	14.417	1	38	.001
Ease in Rising	7.890	1	38	.008
Difficulty in Moving	8.807	1	38	.005
Difficulty in Sleeping	8.995	1	38	.005
Overall Mobility	13.520	1	38	.001

[a] The absence of variance in the control group prevented computation of the Levene statistic

The results in Table 4 indicate that in every case except for the Willing to Play item, the assumption of homogeneity of variance was violated. This assumption can also be expected to be violated for Willing to Walk since the control group had zero variance and the treatment group had about the average level of variance displayed on the other items.

As a consequence of these considerable violations of the assumptions underlying the ANCOVA model, the results obtained in the ANCOVA will be checked in two ways. First, a one-way ANOVA of the residualized change scores (i.e., the residual of the regression of the change score on the day 0 score) will be conducted using the Brown-Forsythe correction for heterogeneity of variance. Second, the nonparametric Mann-Whitney test will be conducted on the residualized change scores. The use of residualized change scores using the combined groups regression estimate has been shown by Maxwell, Delaney, and Manheimer (1985) to result in extremely conservative estimates of p-values, which is appropriate in the present case.

Although the reliability of the individual items can only be assessed using inter-rater data, which was not collected in this study, the reliability of the combination of items could be assessed from an internal consistency perspective. It is appropriate to produce such a reliability estimate in this case because the nine items were designed to assessed manifestations of a common underlying construct --mobility--and their measurement should consequently exhibit a substantial degree of internal consistency if the items are in fact measuring what they purport to measure. Cronbach's alpha was computed for the nine items using the Day 0 measurements, the Day 56 measurements, and the Day 56 - Day 0 change score, with the results reported in Table 5.

Table 5

Cronbach's Alpha Reliabilities for the 9-item Mobility Scale Measurements on Day 0, Day 56, and for the Difference Score

Measurements	Cronbach's Alpha
Day 0	.905
Day 56	.938
Change score	.935

The reliabilities of the measurements of overall mobility on Days O and 56, and of the change score, were very satisfactory, well above the threshold of adequacy for measures used even for important decision-making in real world settings. This indicates that a construct is being reliably measured, and in the absence of any indications to the contrary, that construct can be inferred to be mobility.

The test of the study's hypothesis -- that the group treated with the HealthyMouth product would exhibit a significantly greater positive mean gain than the group treated with the placebo -- was conducted using an analysis of covariance (ANCOVA) of the Day 56 - Day 0 gain scores on each of the 9 mobility items, and on the overall mobility score, controlling for differences in the pretest (i.e., Day 0) scores. The results of this analysis are presented in Table 6.

Table 6

Results of ANCOVA of Gain Scores on the Nine Mobility Items, and on the Overall Mobility Score

Dependent Variable	**Source**	**df**	**F**	***p***	**η^2**
Willing to Walk	Group	1	147.116	<.001	.788
	Error	37	(.182)		
Willing to Run	Group	1	140.154	<.001	.810
	Error	37	(.280)		
Willing to Play	Group	1	88.377	<.001	.366
	Error	37	(.482)		
Willing to Jump	Group	1	67.360	<.001	.522
	Error	37	(1.489)		
Usually Stiff and Sore	Group	1	44.368	<.001	.253
	Error	37	(.548)		
Ease in Lying Down	Group	1	73.250	<.001	.445
	Error	37	(.509)		
Ease in Rising	Group	1	11.258	.002	.178
	Error	37	(2.108)		
Difficulty in Moving	Group	1	57.401	<.001	.420
	Error	37	(.578)		
Difficulty in Sleeping	Group	1	32.625	<.001	.422

Dependent Variable	Source	df	F	*p*	η^2
	Error	37	(.358)		
Overall Mobility Score	Group	1	148.612	<.001	.598
	Error	37	(.253)		

Note. Values enclosed in parentheses represent mean square error.

The results of the ANCOVA were strongly significant for all nine mobility items and for the overall mobility score. In addition, reference to the mean change scores in Table 2 indicates that in comparison to the control group, the mean changes of the treatment group were all higher and in the positive direction. The higher positive change scores in the treatment group persisted without exception after the means were adjusted for the pretest (Day 0) scores. On the basis of these results, it may be tentatively concluded that the null hypothesis of no difference in mobility improvement between dogs receiving the HealthyMouth treatment and those in the placebo condition is rejected.

The above conclusion must remain tentative until the results of two other series of tests have been reported. These additional tests are required in order to account for the violations of the assumptions of homogeneity of variance and normality. In order to address each of these problems, change scores had to be derived that were adjusted for differences in the pretest. This was necessary because there is no accepted variance heterogeneity adjustment for use with ANCOVA, and there is no nonparametric analog of ANCOVA. Thus, the adjustment for the control variable that occurs in ANCOVA had to be accomplished prior to the analysis of the data by the methods used to check the effects the assumption violations. The procedure used to derive the adjusted scores was to regress the change scores on the pretest (i.e., Day 0) scores, and to save the residual as the adjusted dependent variable. This was done for the change scores for all nine mobility items and for overall mobility. The resulting scores will be referred to as residualized change scores.

The supplemental analyses addressing the variance heterogeneity problem consisted of conducting one-way ANOVAs of the residualized change scores, incorporating the Brown-Forsythe correction to the error degrees of freedom. The results of these analyses are reported in Table 7.

Table 7

Results of ANOVAs of Residualized Change Scores for the Nine Mobility Items and Overall Mobility, Using the Brown-Forsythe Correction

Residualized change score	F	df1	df2*	Sig.
Willing to Walk	150.707	1	35.353	<.001
Willing to Run	142.828	1	33.705	<.001
Willing to Play	87.460	1	32.374	<.001
Willing to Jump	59.903	1	26.308	<.001
Usually Stiff and Sore	30.620	1	35.846	<.001
Ease in Lying Down	55.933	1	26.722	<.001
Ease in Rising	8.240	1	26.543	.008
Difficulty in Moving	48.820	1	26.506	<.001
Difficulty in Sleeping	32.216	1	36.228	<.001
Overall Mobility	99.639	1	26.416	<.001

*Reflecting the Brown-Forsythe correction

The results of the Brown-Forsythe corrected ANOVAs reported in Table 6 indicate that the p-values resulting from the correction for variance heterogeneity did not appreciably increase for any of the dependent variables. The results remained strongly significant and supportive of the conclusion to reject the null hypothesis.

The supplemental analyses addressing the non-normality problem consisted of applying the nonparametric Mann-Whitney test to the comparison of the treatment and control groups on the residualized change scores. The results of these analyses are reported in Table 8.

Table 8

Results of Mann-Whitney Test of Difference between Treatment and Control Groups on the Residualized Change Scores for the Ten Dependent Variables

Residualized Change Score	Mann-Whitney U	Z approximation	Exact Sig. [2*(1-tailed Sig.)][a]
Willing to Walk	1	-5.431	<.001
Willing to Run	0.5	-5.432	<.001
Willing to Play	4	-5.343	<.001
Willing to Jump	5	-5.281	<.001
Usually Stiff and Sore	21	-4.866	<.001
Ease in Lying Down	13	-5.089	<.001
Ease in Rising	22.5	-4.828	<.001
Difficulty in Moving	19	-4.93	<.001
Difficulty in Sleeping	48.5	-4.153	<.001
Overall Mobility	2	-5.356	<.001

[a] not corrected for ties.

The results reported in Table 8 indicate that the p-values resulting from a test based on nonparametric assumptions did not appreciably increase for any of the dependent variables relative to the results of the parametric tests. The results remained strongly significant and supportive of the conclusion to reject the null hypothesis.

It is recognized that applying multiple statistical tests to the same sample results in a predictable inflation of the family-wise error rate. In the present case, the tests were applied 10 times to the sample. Using the Bonferroni estimate of the resulting inflation of family-wise error, it would be appropriate to reduce the critical value for Type 1 error to .005. By this standard, only one of the dependent variables in one of supplemental tests -- Ease in Rising in the variance heterogeneity corrected analysis -- failed to meet the reduced critical value, and only by .003. This item also happened to have the second lowest item-total correlation in the overall mobility

scale analysis, which suggests that it may be influenced by factors extraneous to mobility or may present more difficulties in rating.

Discussion

This study found statistically significant differences between the treatment and control groups in the amount of positive change in mobility over a period of 56 days. These differences occurred on 8 of the 9 items on which mobility was rated, and on the overall mobility score consisting of the mean of the 9 items. The difference in positive change was not found to be significant on one item -- Ease of Rising -- but the alpha level by which its significance was judged had been set at a very conservative level and the change score computation used was known to underestimate group differences. Despite these restrictive conditions, it only missed significance by .003.

The power of this study to detect even a large effect size as significant at alpha = .05 was only .693. Thus, the finding of significance across essentially all the dependent variables invites confidence that the effects were not the result of chance.

The effect sizes were calculated using eta squared and are reported in Table 5. For the individual mobility items, the eta squared values ranged from .178 (Ease of Rising) to .810 (Willing to Run), with a mean of .467. For the overall mobility score, the eta squared was .598. These values reflect the proportions of the variance in the change scores accounted for by group membership (i.e., treatment vs. control). Any value of eta squared over .40 represents a very large effect size.

Eta squared values are useful in communicating the size of a treatment effect to the statistically literate, but tend to do little to enlighten the practitioner and consumer about the effectiveness of a treatment. More useful for the latter purpose are comparisons of the percentage

of change achieved in the treatment and control groups. For this purpose, the information in Table 9 is offered.

Table 9

Comparison of Percentages of Change in Mobility Measures from Day 0 to Day 56 in the Treatment and Control Groups

	Control Group			Treatment Group		
Mobility measure	**Day O Mean**	**Day 56 Mean**	**Mean Percent Change**	**Day O Mean**	**Day 56 Mean**	**Mean Percent Change**
Willing to Walk	8.15	8.1	0.00	8.05	9.7	21.99
Willing to Run	7.7	7.6	-1.13	7.81	9.65	25.85
Willing to Play	8.05	7.75	-3.38	7.75	9.7	38.32
Willing to Jump	6.1	5.95	-1.34	5.15	8.7	101.14
Usually Stiff and Sore	7.65	7.65	4.38	6.25	9	53.58
Ease in Lying Down	7.5	7.35	-1.94	6.55	8.95	44.11
Ease in Rising	7.6	7.55	-0.28	6.0	8.3	46.59
Difficulty in Moving	8.65	7.45	0.89	8.4	9.1	43.55
Difficulty in Sleeping	8.65	8.7	0.61	8.4	9.65	16.01
Overall Mobility	7.65	7.57	-0.91	6.96	9.19	34.76

The information in Table 9 is useful in conveying the practical meaning of the study's findings. For the control group, mean percent change in mobility was negative on 5 of the 9 mobility items and on overall mobility. On the remaining 4 mobility items the mean percent change was 1.47%, with a maximum of 4.38% on the Usually Stiff and Sore Scale. The averaged mean percent change on the 9 items was -.24%. The percent change for overall mobility was -.91%. By contrast, in the treatment group the mean percent change was positive for all 9 items and for overall mobility. The averaged mean percent change for the 9 mobility items was 43.56%. The mean percent change for overall mobility was 34.76%. The lowest mean percent change in the treatment group (16.01% for Difficulty in Sleeping) was nearly 4 times higher than the highest mean percent change (4.38% for Usually Stiff and Sore) in the control group. Another way of

viewing the findings is in terms of expected outcomes. Moderately mobility-impaired dogs not receiving treatment for their mobility, as represented by the control group, can be expected to exhibit a .91% decline in their overall mobility level over a 56-day period. Moderately mobility-impaired dogs receiving the HealthyMouth treatment can be expected to exhibit a 34.76% improvement in their mobility over a 56-day period.

The limitations of this study relate principally to the study's boundary conditions, having been conducted in one clinic on a limited representation of canine breeds and impairment etiologies. The generalizability of the findings to dogs living in different climates, across the full range of breeds, across the full range of canine life spans, across the full range of impaired mobility, across the full range of mobility impairment etiologies, and ultimately across different species should be the foci of future research efforts.

Despite these limitations, the study's highly significant findings empirically demonstrate that the therapeutic effectiveness of the HealthyMouth treatment, already proven to control plaque and gingivitis in canine, feline and equine studies (reports available upon request from the first author), extends to impairments of the canine musculoskeletal system.

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