CAN SYNOVIAL FLUID VISCOSITY BE USED AS A PHYSICAL MARKER FOR OSTEOARTHRITIS SEVERITY?

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INTRODUCTION

Healthy synovial fluid (SF) is highly viscous allowing it to act as a natural lubricant in the joint. In persons with osteoarthritis (OA), the synovial fluid has been shown to have a decreased viscosity and thus has less effective lubrication. There has been little exploration in using viscosity change as an outcome measure for OA clinical studies. We propose that based on the etiology of the disease, synovial fluid viscosity is a clinically relevant and valid outcome measure for clinical trials of OA treatments. Specifically our hypotheses are 1. SF viscosity is a reliable indicator of disease. 2. SF viscosity can be correlated to established clinical parameters of pain and function.

The objective of this project is to test these hypotheses using data from two separate studies, one in dogs and one in humans. The canine study was initiated to evaluate whether intravenous injections of hyaluronic acid in dogs with acute and chronic cranial cruciate ligament rupture are beneficial. It is well known that dogs that rupture the cranial cruciate ligament are predisposed to developing OA (pond-nuki model) [1]. The human study was initiated to determine whether glucosamine and chondroitin sulfate was effective in improving rheological and clinical symptoms in subjects with severe OA.

BACKGROUND

It has been shown that pathologic changes in joints will result in alterations in the synovial fluid viscosity. However, in very few studies has viscosity been used as an outcome measure for OA treatment. If the loss of viscoelasticity is directly related to the severity of OA then viscosity should be a good correlation to the level of disease. One limitation of viscosity measurements is the availability of synovial fluid. Pathological joints generally produce larger amounts of fluid (2-5 mL) than normal joints (0.3 - 1 mL) but the amount available for aspiration is highly variable.

Traditionally laboratory analysis of synovial fluid has consisted of determining the type and number of cells present in the fluid, the volume of fluid aspirated and qualitative analysis of rheologic behavior of the fluid. While it has been shown that there is an association between viscosity and joint pathology, clinical use of viscosity in diagnosis and treatment of musculoskeletal disease remains minimal. This situation is due to the lack of simple viscometers capable of testing small fluid volumes.

MATERIALS AND METHODS

Microrheometer

Often in medical applications it is difficult, if not impossible, to collect large volumes of samples for testing. In response to this challenge, Tran-Son-Tay (1988) developed an acoustically tracked falling ball rheometer, capable of testing fluid samples as small as 20μL [3]. The theory for this rheometer is based on Stokes solution for a ball falling through a finite tube. By tracking the displacement of the ball with an ultrasound transducer, the falling velocity can be calculated. Since the diameters of the ball and tube, and the densities of the ball and fluid are known, the viscosity of the fluid can be calculated

Canine Study

The population for this study consisted of clinical canine patients with evidence (clinical and radiographic) of cranial cruciate ligament injury (partial or complete, acute or chronic). Synovial fluid was aspirated at baseline for all dogs in the study. SF viscosity was measured using the microrheometer. To date five dogs have been evaluated, 3 were determined to have chronic rupture and 2 acute rupture. SF was also drawn from the contralateral non-injured stifle (knee) to be used as a normal control.

Human Study

Eleven subjects with severe OA were followed over a 20 week clinical trial of glucosamine and chondroitin sulfate. Synovial fluid was aspirated from the subjects' knee at weeks 0, 4, 12 and 20. Subject pain, function and SF viscosity were examined at baseline and 4, 8, and 20 weeks after randomization. Pain was measured by using patient assessed visual analog scales, function was measured using SF-36 and SF viscosity was measured using Brookfield cone-plate viscometer (required 0.5mL fluid). In this analysis, both placebo and

treatment groups were included. Since patients in this study had severe OA, obtaining sufficient fluid volume for testing in the cone-plate viscometer was rarely a problem.

Subjects with normal joints exhibited significantly higher synovial fluid viscosity as compared to either chronic of acutely injured dogs (Fig. 1). Those subjects with chronic joint symptoms displayed a slightly higher viscosity compared to those with acute symptoms. This observation in acute joints is most likely due to local inflammation and swelling which increases fluid content in the joint and therefore would dilute the synovial fluid. In the chronic condition it is possible that the joint has moved beyond the initial inflammation seen in the acute condition and therefore the decreased viscosity is due to mechanical and biochemical destruction of hyaluronic acid, secondary to osteoarthritis. There is approximately one order of magnitude difference in magnitude between normal and diseased SF. This observation is in agreement to what others have reported using different techniques [3].

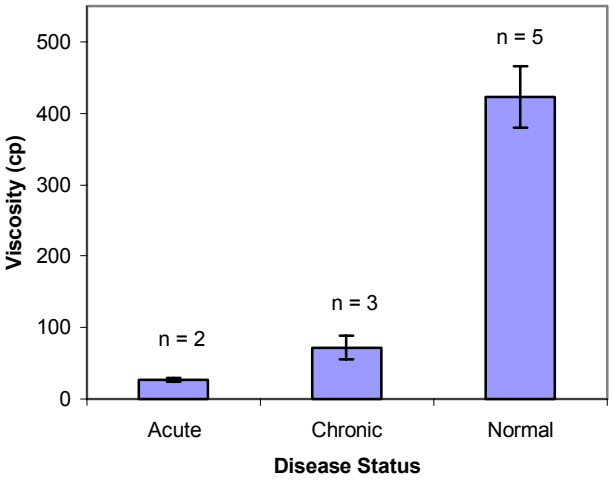

Figure 1. Synovial fluid viscosity measured in dogs with different levels of disease.

Human Study

There were two statistically significant correlations ($p<0.05$) between SF viscosity changes and clinical changes as measured by SF-36 and VAS pain scales (Figures 2 and 3). These effects were a positive association with SF-36 Role Physical score and an inverse association with pain at night.

The Role Physical score of the SF-36 is indicative of the level of function an individual is able to obtain in work and other daily activities. A high score means disease does not cause a problem with work or daily activities. Pain at night is measured with VAS in which a high score indicates worst pain imaginable.

CONCLUSION

This study gives credence to the practice of using viscosity as additional tool in the researcher's armamentarium as an outcome measure for future OA clinical studies. Viscosity is found to be an extremely good marker since there is about one order of magnitude difference between healthy and diseased synovial fluid. In addition, viscosity offers insight into the mechanical condition of the joint, and plays an important role in the lubrication and protection of cartilage. No other currently used outcome measures can give this information. This finding could have a great impact on the evaluation of treatments for OA and in the assessment of its severity.

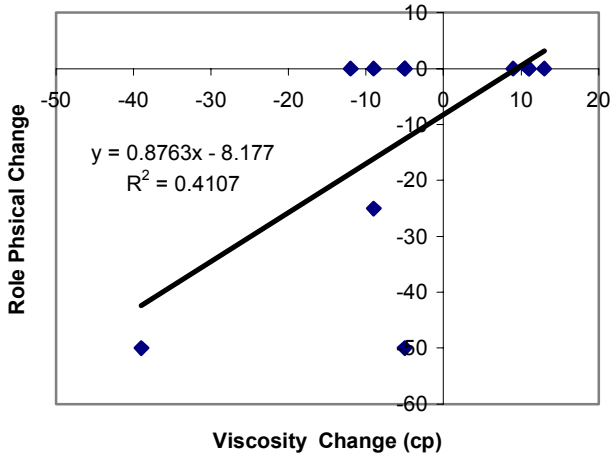

Figure 2. An increase in Physical health as related to work and daily activities is correlated with a likewise change in synovial fluid viscosity (p=.05)

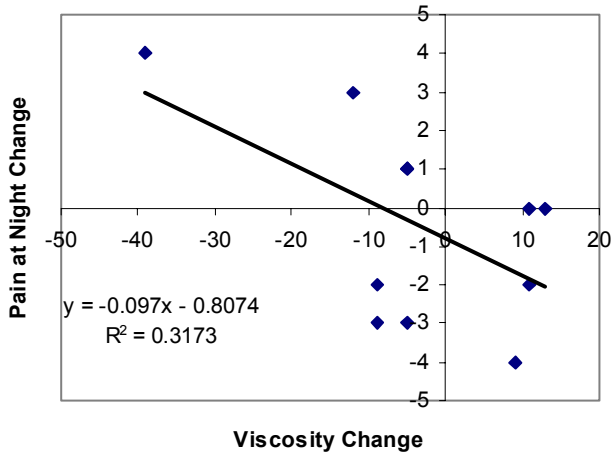

Figure 3. A decrease in pain is correlated with an increase in synovial fluid viscosity.

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