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Serum Hyaluronic Acid- An Effective Biomarker for Early Detection of Osteoarthritis in Young Dogs with Canine Hip Dysplasia

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ABSTRACT

Background: Most of the biomarkers used in joint disease are articular cartilage components such as chondroitin sulphate (CS), keratan sulphate (KS), hyaluronic acid (HA), or type II collagen. Some of these biomarkers, alone or together, could have the potential to provide clinically useful indices of the effects of isolated joint injury, the progression of joint changes and/or the response to therapy. Serum concentration of HA were elevated in human patients with osteoarthritis which increase is considered a reliable biomarker reflective of cartilage damage and synovitis in these patients.

Methods: Blood samples were collected from all the dogs and serum concentration of hyaluronic acid was determined by Canine Hyaluronic Acid Elisa kit (catalogue No.ITE070452), SIZE -96T, Reactivity: Canine, Range: 2 ng/ml -700ng/ml and sensitivity: 1.04 ng/ml, supplied by G Biosciences.

Result: Serum concentration of HA were lower in dogs aged between 0 to 12 months with CHD when compared to dogs of similar age with healthy hip joints and that this significant decrease in serum HA in dogs can be considered a reliable biomarker reflective of CHD and serum HA levels can be used as an effective biomarker for osteoarthritis in dogs with CHD.

Key words: Biomarker, Canine hip dysplasia, Osteoarthritis, Serum hyaluronic acid.

INTRODUCTION

Canine Hip Dysplasia (CHD) is a complex developmental disorder characterized by joint laxity and osseo Arthritis (OA) in one or both coxofemoral joints. The etiology of CHD is polygenic, multifactorial and occurs at a relatively high rate in large-bodied and brachycephalic dogs as well as those with high body length to height ratios (Schachner and Lopez, 2015). It is one of the most commonly diagnosed orthopaedic diseases in dogs. Standardized diagnostic protocol consists of the clinical sign, a physical examination and evaluation of the radiographic results may not detect OA in its early stages (Vilar *et al.,* 2016). Making the radiographic diagnosis is sometime possible when the disease has markedly progressed. Hence, a simple yet potential screening method for early prediction of hip dysplasia will be of help in preventive management and control of CHD and the current paper reports one such. The current study attempts to evaluate whether the use of serum HA, the most important cartilage bio-molecule as a biomarker could be effective as an indicator of clinical development of CHD in dogs at early stages.

MATERIALS AND METHODS

The present study was conducted on four large breeds of dogs *i.e*., GSD, Labrador Retriever, Doberman Pinscher and Rottweiler presented to the Department of Veterinary Surgery and Radiology and Department of Veterinary Clinical Complex, College of Veterinary Science, SVVU, Tirupati over a period of one year. 32 dogs from each breed confirmed radiologically as CHD were included in the study and divided in to two groups.

Group I (Dogs aged below six months)	Dogs with healthy hip joints (n=4)	Dogs with dysplastic hip joints (n=12)
Group II (Dogs aged between six to twelve months)	Dogs with healthy hip joints (n=4)	Dogs with dysplastic hip joints (n=12)

All the dogs were subjected to radiographic evaluation and different morphometric parameters belonging to

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proximal femur (Hip Axis Length (HAL), Femoral Neck Axis length (FNALa and FNALb), Acetabular Width (AW), Femoral Shaft Cortex width (FSC), Femoral Head Diameter (HD), Femoral Neck Diameter (ND), Trochanteric Width (TW), Femoral Shaft Diameter (FSD), Femoral Inclination Angle (FIA) and Head- Neck Index of Heyman and Herndon) acetabular measurements (Acetabular Angle (AA), External Acetabular Angle (EAA) and Acetabulam Head Index (AHI) and other measurements (Percentage coverage (PC), Norberg Angle (NA), Distraction Index (DI) and Subluxation Index (SI)) were measured (degree) and analyzed using The CARESTREAM vita flex CR (Computed Radiography) system with customized animal image processing, vet specific order entry and exam views and full suite of veterinary measurement tools, with added IMAGE SUITE software version 4.0 to distinguish between non-dysplastic and dysplastic hip joints in dogs.

Blood samples were collected from all the dogs and serum concentration of hyaluronic acid (HA) was determined by Canine Hyaluronic Acid Elisa kit (catalogue No.ITE070452), SIZE -96T, Reactivity: Canine, Range: 2 ng/ml -700 ng/ml.

RESULTS AND DISCUSSION

The Hyaluronic acid (HA) is a ubiquitous component of the ECM of most animal tissues. HA is a linear macromolecule that is composed of a repeating disaccharide units β-1,4-glucuronic acid-β-1,3-N-acetylD-glucosamine mainly produced by fibroblasts and other specialized connective tissue cells. HA is widely distributed throughout the body (umbilical cord, nasal cartilage, vitreum, cutis or lymph of the thorax) and the highest concentration is found in synovial fluid and connective tissue such as the synovial membrane. Serum concentration levels of HA has been linked to a variety of diseases (Leipold *et al*., 1989 and Nganvongpanit *et al*., 2008) and used as a very early markers to detect toxic liver injury in human patients and liver fibrosis in canines (George and Stern, 2004; Kanemoto *et al*., 2009; Glinska-Suchocka *et al*., 2015 and Ceplacha *et al*., 2018).

The mean±S.E values (ng/ml) of serum HA in dogs below 6 months of age with a healthy hip joint or with a dysplastic hip joint were tabulated in Table 1. The mean serum concentration of HA in dogs with healthy hip joint was 56.13±5.57 ng/ml and in dogs with dysplastic hip joint the mean serum concentration of HA was 35.12±3.41 ng/ml.

The mean±S.E values (ng/ml) of serum HA in dogs between 6 to 12 months of age with a healthy hip joint or with a dysplastic hip joint were tabulated in Table 2. The mean serum concentration of HA in dogs between 6 to 12 months of age with healthy hip joint was 90.45±3.74 ng/ml and in dogs of similar age but with a dysplastic hip joint was 37.19±7.81 ng/ml. Statistically significant difference (pd".05) was found in the serum HA concentration between dogs with healthy hip joint and dogs with dysplastic hip joint in Group-I. Serum HA concentration was low in dogs with CHD where as statistically highly significant difference (p<.001) in serum HA concentration was observed in Group-II between dogs with healthy hip joint or dysplastic hip joint. Dogs with CHD had lower serum HA concentration.

Table 1: Serum hyaluronic acid concentrations (ng/ml) in dogs below 6 months of Age (Group-I).

Dogs below 6 months of age (Group I)	Serum HA concentration (ng/ml)
With healthy hip joint	56.13+5.57[a]
With dysplastic hip joint	35.12+3.41[b]

Values with different superscripts are significantly different p<.05.

Table 2: Serum hyaluronic acid concentrations (ng/ml) in dogs between 6 to 12 month of age (Group-II).

Dogs between 6 to 12 months of age (Group-II)	Serum HA concentration (ng/ml)
With healthy hip joint	90.45+3.74[a]
With dysplastic hip joint	37.19+7.81[b]

Values with different superscripts are significantly different p<.001.

In the present study serum HA concentrations in the dogs with CHD were always lower than the dogs without CHD. Similar finding were also recorded by Nganvongpanit *et al.* (2008 and 2014) in inflammatory joint disease and HD in dogs. The changes in the HA levels in the serum were dependant on the severity of joint disease and directly related to the cartilage metabolism. (Arican *et al*., 1994; Seki *et al*., 2010 and Lidburn *et al*., 2016). The diagnosis of CHD was generally based on clinical and radiographic changes and making the radiographic diagnosis is sometime possible when the disease has markedly progressed. Serum HA concentration, the most important cartilage bio-molecule can be used as a biomarker effectively as an indicator of clinical development of CHD in dogs at early stages to facilitate disease monitoring, predicting disease progression and studying the effects of therapeutic interventions in joint diseases (Vilar *et al*.,2016).

CONCLUSION

HA is widely distributed throughout the body, the highest concentration is found in synovial fluid and also connective tissue such as the synovial membrane. In the present study, serum HA concentrations in the dysplastic dogs was lower than that of the non-dysplastic dogs. The diagnosis of CHD was generally based on clinical and radiographic changes that occur in later stage of the disease. The biomarkers like serum HA concentration could aid in monitoring disease status, and the changes in the HA levels in the serum were dependant on the severity of joint and was directly related to the cartilage metabolism.

Conflict of interest: None.

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