



Original Contribution

HORMONAL AND RADIOGRAPHIC STUDIES IN GERMAN SHEPHERD DOGS WITH HIP DYSPLASIA

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ABSTRACT

PURPOSE: The role of thyroxine (T4), triiodothyronine (T3), insulin (INS) and growth hormone (GH) in the pathogenesis of canine hip dysplasia was studied. The changes in radiographic indices and their correlation with the hormone blood levels were determined.

METHODS: Two groups of German Shepherd male dogs (control and experimental) were used. All animals were aged between 8-12 months and were bred in a stock-breeding farm with similar diet and exercise. The control group included 8 clinically and radiologically healthy animals. The experimental group included 8 dogs with hip dysplasia.

RESULTS: Canine hip dysplasia was accompanied by increased serum-free thyroxine levels, compared with control animals. The other hormones did not show any changes. The parameters indicating early presence of hip laxity were the Norberg angle (NA) and the distraction index (DI), which were different in both groups of animals. The alterations in radiographic indices did not correlate with the studied hormone blood levels.

CONCLUSION: Elevation in plasma thyroxine levels in dysplastic animals suggested that this hormone might play a role in the pathogenesis of canine hip dysplasia. However, this is not the only factor implicated in the disease because of the lack of correlation between radiographic and hormonal changes.

Key Words: hip dysplasia, dog, hormones, thyroxine, distraction index, Norberg angle

INTRODUCTION

Hip dysplasia is a hereditary disease characterized by joint laxity and by secondary osteoarthritis (1). On the other hand many researchers indicated examples about similar alterations in the shoulder, elbow and lumbovertebral joints (2, 3) which suggest that hip dysplasia is probably a local manifestation of a common generalized disturbance of the locomotory system. The manifestation of the disease predominantly in the hip joints was explained by their unique anatomical structure - a conjunction between several bones and non-horizontal position of joint surfaces (4, 5).

The stability of the hip joint is

determined by the strength of the joint capsule, the depth of the acetabulum, the solidity of the round ligament and gluteal muscles. Therefore, the reason for joint instability could be damage to those elements.

Canine hip dysplasia was described for the first time by Schnelle (6). Later, Riser and Shiler (7) found that the disease developed during the period of growth. Since then many investigations about factors conditioning the development of the disease have been performed. Leighton et al. (8) and Hedhammer et al. (9, 10) found a heritability of 0.25 to 0.85 in different breeds, thus confirming the thesis of hereditary aetiology of the disease. The large variability of this factor indicates that the phenotype appearance depends on factors, which act on the skeleton during the growth period. The most powerful influence is that of hormonal disturbances leading to changes in endochondral ossification, abnormalities in growth plate, joint capsule and muscle tissue (1).

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The aim of the present study was to investigate the changes in blood growth hormone (GH), triiodothyronine (T3), thyroxine (T4) and insulin (INS) in dysplastic animals as indices of bone-cartilage metabolism during the development of hip dysplasia as well as the following radiographic indices - early indicators of the disease -: inclination angle (IA), Norberg angle (NA), distraction index (DI) and percentage of femoral head coverage (PC) (11, 12). The correlation between hormones and radiographic indices was also determined.

MATERIALS AND METHODS

The study was performed on 16 male German Shepherd dogs, aged between 8 and 12 months, bred in a stock-breeding farm with similar diet and exercise. Two groups of animals were formed. Eight clinically and radiographically healthy dogs were included in the control group. The experimental group comprised 8 animals with radiographic evidence of hip dysplasia without clinical appearance.

Prior to the radiological examination all animals were sedated with 0.02 mg/kg atropine sulphate (*Atropini sulfas* - *Sopharma*®, Bulgaria) and 1 mg/kg xylazine hydrochloride (Xylazine 2% - *Alfasan*®, Holland). Radiographs were taken in a standard ventrodorsal view according to the requirements of the Orthopaedic Foundation for Animals (OFA) (13). The characteristics of hip joints were determined using the indices of coxometry (IA, NA, DI and PC), as was described by Philipov (16).

Blood samples were collected from all animals after sedation recovery. Sera were separated and stored in -25°C in order to serve later for hormonal measurement. The following hormones were investigated by radioimmunoassay (RIA) using commercial kits (*Amersham Bioscience*):

- Free thyroxine (fT4), pmol/l;
- Free triiodothyronine (fT3), pmol/l;
- Insulin (INS), µU/ml;
- Growth hormone (GH), ng/ml.

The results were processed by the Students t-test at a level of significance of 0.05 and by correlation analysis to determine correlation coefficients between coxometric parameters and hormone levels (Statmost for Windows, DataMost Corp., 1994-1995).

RESULTS

All dogs included in the group of dysplastic animals showed radiographic signs of low to moderate degree of dysplasia (**Figure 1**). Significant differences between groups were observed for Norberg angles and distraction indices (**Table 1**). The first parameter had lower values ($100.3 \pm 7.2^\circ$, $P < 0.05$) in the experimental group than in the control group ($117.5 \pm 11.3^\circ$). The distraction index was elevated in the group of experimental animals (0.41 ± 0.15 , $P < 0.05$) compared to healthy animals (0.23 ± 0.05).



Figure 1. Radiographic evidences of hip bilateral dysplasia and lines of measurements made. Note broadened articular spaces and lateral displacement of the two femoral heads. The Norberg angle is almost 90 degree

The analysis of hormone blood levels showed significant differences only with regard to thyroxine (**Table 2**). It was increased in the experimental group (17.4 ± 1.08 pmol/l) compared to the control (14.3 ± 0.56 pmol/l), $p < 0.05$.

No significant correlation between parameters of coxometry and investigated hormone blood levels was detected after correlation analysis (**Table 3**).

DISCUSSION

Hip dysplasia is commonly seen in large and giant canine breeds. According to OFA surveys about breed distribution of the disease, the most affected animals were Saint Bernards (14). The disease often occurs in Rottweilers, German Shepherd dogs, Labrador Retrievers - 10-43% of all cases (15). In Bulgaria, it is a problem mostly in the German Shepherd dogs - about 30 % of all cases (16).

Table 1. Changes in radiographic indices in German Shepherd dogs with and without hip dysplasia. The data are presented as mean \pm standard deviation. (N = number of animals)

Parameter group	N	Norberg angle ($^{\circ}$) NA	Distraction index DI	Inclination angle ($^{\circ}$) IA	Percentage of femoral head coverage (%) PC
Healthy	8	117.5 \pm 11.3	0.23 \pm 0.05	141.5 \pm 7.9	69.6 \pm 6.9
Dysplastic	8	100.3 \pm 7.2*	0.41 \pm 0.15*	137.5 \pm 2.5	64.1 \pm 11.5

* $p < 0.05$ **Table 2.** Alterations in blood values of free thyroxine (fT4), free triiodothyronine (fT3), insulin (Ins) and growth hormone (GH) in German Shepherd dogs with and without hip dysplasia. The data are presented as mean \pm standard deviation. (N=number of animals)

Parameter group	N	fT4, pmol/l	fT3, pmol/l	Ins, μ U/ml	GH, ng/ml
Healthy	8	14.3 \pm 1.58	3.35 \pm 0.24	0.63 \pm 0.48	1.9 \pm 0.17
Dysplastic	8	17.4 \pm 2.88*	3.58 \pm 1.58	1.17 \pm 0.60	2.1 \pm 0.19

* $p < 0.05$ **Table 3.** Coefficients of correlation (r) between parameters of coxometry (Norberg angle-NA, Distraction index -DI, Inclination angle- IA and Percentage of femoral head coverage -PC) and studied hormones, free thyroxine (fT4), free triiodothyronine (fT3), insulin (Ins) and growth hormone (GH)

Parameter	fT4	fT3	Ins	STH
Norberg angle (NA)	0.25	0.46	-0.56	0.46
Distraction index (DI)	-0.37	-0.52	0.51	-0.15
Inclination angle (IA)	-0.57	-0.64	0.62	-0.35
Percentage of femoral head coverage (PC)	0.28	0.31	-0.32	0.12

 $p < 0.05$ in $r > 0.65$

The first clinical and radiographic signs occur at the age of 4-12 months (14). Our study was performed on animals in these age limits (8 - 12 months).

Several investigators submitted data about disturbances in endochondral ossification (17, 18, 19). Allhands et al. (20) and Madsen et al. (21) found that the ossification of the femoral head was delayed in dogs with hip dysplasia. In the experimental study of Delgado-Baeza (22) it was shown that hip dysplasia could be reproduced by operatively induced confluence of the three acetabular bones. The disease occurs because of disproportion in the development of bones.

These results suggest that the disturbance in the dysplastic hip begins with a disproportionate ossification of the femoral head and the triradiate acetabular growth plate. It is not known yet how the mechanism of endochondral ossification is disrupted and hence, hip dysplasia develops.

Endochondral ossification is accomplished by the closely related processes of chondro- and osteogenesis, which are dependent on endocrine control (23). Metabolic factors also take part in the

complicated regulation of bone growth and they reflect the significance of resorption, use and elimination of nutrients for skeleton development. The most important during the growth period is protein metabolism. If there is a positive nitric balance, the osteogenesis will go on under conditions of disturbed chondrogenesis and the growth cartilage will narrow (9). The uniform feeding and housing conditions of our two groups of dogs made it possible to emphasize on hormonal changes.

The hormonal regulation of endochondral ossification involves mainly GH, Ins, T3 and T4. GH stimulates the division and growth of cells in the germinative and proliferative layer of growth cartilage, the synthesis of collagen and intercellular matrix. The influence of GH over the skeleton development is closely connected with diet (24). Overfeeding during the growth period leads to increased values of GH and fast skeleton development, whereas when there is malnutrition, the liver does not reply to somatotropin stimulus and the release of insulin-like growth factor from the liver decreases, accompanied by delayed growth. Denko & Boja (25) found increased values of growth hormone in children suffering from

hereditary hip dysplasia. In the present study, we did not observe any change with regard to GH and INS. It is considered that insulin takes part in maturation of cartilage and accumulation of glycogen. The thyroid hormones interfere with the last stages of endochondral ossification regulating chondrocyte growth to maturity and chondrocyte destroyed by connective-tissue complexes. Our results are in accordance with the investigations of Zenovko et al. (26), which evidenced high levels of T4 in patients with degenerative joint disease.

The cells from the hypertrophic layer are target for endocrine control of bone growth (27, 28, 29). Balance between hormonal values and endothelial signals in the subchondral vascular system is necessary for normal endochondral ossification (30).

These authors also indicate that chondrocytes release tissue factors with suppressing effect over cartilage maturity and in the same time endothelial proteases facilitate differentiation of chondrocytes. The thyroid hormones take part in maturity of chondrocytes directly as well as by stimulating release of proteases from endothelial cells of the new-formed capillaries. The elevated values of thyroxine observed in our study suggest premature maturity of chondrocytes, early ossification of the triradiate growth plate and is probably the reason for the subsequent irregular conformation of the joint.

According to Banovac & Koren (31) the thyroid hormones stimulate the release of membrane-bound alkaline phosphatase in osteoblasts, thus initiating the beginning of ossification of the triradiate growth plate.

The significant differences in NA and DI between dysplastic and healthy animals were similar to those of other investigators (32, 33, 34). Our results showed that the parameters indicating early presence of hip dysplasia were DI and NA. The DI was elevated at 6-10 weeks of age in affected dogs, whereas the NA was decreased a bit later - at 16-18 weeks of age (11). According to Smith et al. (35), DI was the most indicative sign of dysplasia in German Shepherd dogs. They also claimed that this breed was predisposed to the disease 4.95 times more compared to other breeds. In the present study, we did not determine any relationship between IA and the degree of dysplasia in agreement with the results of Banfield et al. (36). No significant difference in PC in the two groups was found. PC and NA had similar diagnostic value (12) but it

was smaller than DI (34).

Until now no data were available about the correlation of changes in hormonal values and the degree of dysplasia. The correlation analysis showed that there was no significant correlation between coxometric parameters and researched hormone blood levels.

In conclusion, canine hip dysplasia was accompanied by increased blood-free thyroxine levels. It could be involved in the pathogenesis of the disease by inducing premature maturation of chondrocytes and ossification of the triradiate acetabular growth plate. The indices of coxofemoral laxity were NA and DI. The disease was not accompanied by alterations in IA and PC. The variations in coxometric indices did not correlate with the changes in fT4, fT3, Ins and GH.

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