Research Article

Zinc Deficiency in Dogs with Special Reference to its Effect on the Coat

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Abstract | This study aimed for recording the clinical and laboratory findings of Zinc (Zn) deficiency in dogs. The clinical study was conducted on two groups of dogs. The first group consisting of seven dogs which was clinically healthy and used as a control group, and the second group consisting of sixteen dogs "German Shephard" at different ages which was suffering from decrease appetite, stunt growth rate, as well as skin lesion in form of loss of hair, crust, scales and inflammation of skin "dermatitis". All dogs were subjected to clinical and laboratory examinations followed by special dermatological examination. Skin scrapings were examined under light microscope for the detection of fungal spores or mites. Blood samples were taken for hematological analysis, along with taking serum samples for biochemical analysis. Rectal temperature, heart, and respiration rates were not significantly differed between the two groups. Packed cell volume (PCV), total erythrothetic count (TEC), white blood cells (WBCs), serum glucose, total proteins and serum Zn were significantly decreased. Moreover, while copper (Cu) and iron (Fe) were significantly increased ($p<0.05$). All diseased dogs were treated with Zn sulphate @10mg/kg orally and daily for 14 days, and the treated dogs revealed a marked improvement in clinical signs and other different hematological and biochemical parameters.

Keywords | Dogs, Zn deficiency, Dermatosis, Skin affection

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INTRODUCTION

Dogs hold a special position in most human societies, not equaled by any other animal species. The extraordinary intelligence of dogs has been exploited by human beings for conducting various activities, including hunting, retrieving, herding, rescue operations, tracking and security. Zinc is one of the most significant trace elements found in living creatures, and it plays a role in a variety of biological processes, including carbohydrate, lipid, protein and nucleic acid metabolism (Al-Saad et al., 2010). It has a role in keratinization regulation, optimal reproductive function, wound healing, immune system function and maintenance normal sense of smell and taste (Miao et al., 2013).

Zinc is required for growth, cell formation, proliferation and differentiation (Underwood and Suttle, 1999). Zinc is a component of more than 70 metalloenzymes and found in muscle, bone, teeth, reproductive organs, liver, spleen and hair. It is a component of thymosin, a thymic hormone involved in the immunological response, and serves as a cofactor in cellular protein synthesis (Willense, 1995).

Skin stores about 2% of the total amount of Zn in the body, with the epidermis containing six times more zinc than the dermis. Zinc levels are higher in tissues with high epithelial proliferation rates, as well as normally parakeratotic sites like the nose and keratinized pressure areas like the footpads (Colombini, 1999).

Zinc deficiency can be caused by a lack of Zn in the diet or by genetic defects (Machado et al., 2011). It develops from eating diets that are low in Zn "primary deficiency" or diets high in phytates, which block Zn absorption, or high in minerals like calcium (which chelates Zn in the

food and decreases its absorption). Zinc absorption can be hampered by high levels of iron and Cu in the diet "secondary deficiency" (Olsen et al., 2004; Wu et al., 2016). Zinc-responsive dermatosis in dogs has been linked to the consumption of low-quality cereal or soy-based dry foods, which exacerbate in some animals with a concurrent Zn absorption defect.

Clinical symptoms differ based on the species and severity of the deficit. Loss of appetite; poor wound healing and skin lesions. Stunted growth are the main symptoms. Impaired reproductive function, weight loss, gastrointestinal lesions, decreased immunological response were also recorded (Colombini, 1999; Machado et al., 2011).

In mature animals, lack of this mineral causes skin abnormalities, poor wound healing, conjunctivitis, and keratitis (Tielsch et al., 1999; Takahashi et al., 2008). Initial erythema is followed by suppurative dermatitis with crusting, alopecia, and scaling. Furthermore, the lesions are mostly found on pressure sites such as palmar and plantar cushions, the area around the eyes and mouth, as well as the paws, ears, and ventral trunk (Prasad, 1993). Around the extremities, mucocutaneous junctions, nose and pressure points on the limbs, lesions develop symmetrically (Olsen et al., 2004), and the coat appears to be drab and brittle (Dillitzer et al., 2011).

Diagnosis approach for skin diseases depends on obtaining detailed history with thorough physical and dermatological examination (Beale, 2011). Diagnosis of Zn deficiency based on clinical symptoms, laboratory analysis, and treatment response (Beigh et al., 2017). So the goal of this research was to describe the clinical, haematological, and biochemical changes in Zn deficient dogs.

MATERIALS AND METHODS

Ethical approval

The research procedures were approved by the Ethics Committee of Egyptian Veterinary Medicine Authority.

Animals

This study enrolled 23 German dogs aged between 18 months and 3 years. The dogs were divided into two groups; the control group consisting of 7 (3 females and 4 males) apparently healthy dogs that came to the clinic for routine checkup, vaccination and deworming. The diseased group including 16 dogs (7 females and 9 males) with various dermatologic signs. Control dogs were dewormed and vaccinated against viral diseases (rabies and DHPP vaccines) according to the regulation of veterinary authorities. The dogs were selected from Faculty of Veterinary Medicine, Zagazig University, Others from shelter El-Obour city as well as from some private veterinary clinics.

A questionnaire was filled for each examined dog to cover most case history especially of dermatological importance, including owner's name, address, dog's name, age, sex, breed, reproduction data, along with the type of diet (current and previous), previous vaccination and treatment, itching or chewing behavior, otitis or ear licking, and environment (exercise, house, garden, flat). In contact pets, previous diseases and surgery and current non-skin-related problems are appeared. The sheet includes special dermatological history, including owner complaint, date of onset, pruritus, severity and time of onset (before or after lesions), first observed cutaneous lesions and their development, other affected animals or human beings in contact, presence of fleas and antiparasitic therapy given, shampoos, grooming, and previous treatment. Data of onset and specific clinical signs are also included according to Birchard and Sherding (2005).

Some diseased dogs were suffered from decreased appetite and growth rate, and dermatological abnormalities in other ill canines included a dry coat and easily removed hair. Redness and swelling were present on the affected skin with parakeratosis, varying degrees of alopecia and pruritus.

Each dog either healthy or diseased was subjected to thorough general clinical examination including medical history. General appearance, close inspection of entire skin, behavior, state of appetite, skin tent test, sunken eyes, urine and stool characters were noted during the preliminary general examination. Vital signs (pulse, respiration and body temperature) were monitored and examining the mucous membrane according to Birchard and Sherding (2005).

Hamatobiochemical studies

Two blood samples were taken from each dog by puncturing the saphenous vein or cephalic vein using hypodermic needles after clipping the hair in the area of puncture followed by disinfection with ethyl alcohol 85%. The first blood sample (2 ml) was taken into a clean, dry and labelled EDTA tube for hematological analysis. Complete blood picture including total erythrocytes count (TEC), total leukocytes count (TLC), hemoglobin (Hb) and packed cell volume (PCV) using fully automatic blood cell counter (Model: PCE-210N) according to Jain (1993). The second sample was taken (about 7 ml of blood) without anticoagulant to obtain clear sera for measuring serum glucose, total proteins and albumin (in g/dL spectrophotometrically) using special test kits. Serum globulin was estimated by subtraction of the amount of serum albumin from the amount of total serum protein. Serum Zn, Cu and Iron concentrations were determined by an atomic absorption spectrophotometer Model 210 VGP using special kits which supplied by Buck Scientific Co. USA. The analysis was performed as described previously

by Brown and Taylor (1995).

Skin scraping samples

Using a sharp scalpel, many skin scrapings were taken from the periphery of active lesions until a small amount of blood was oozing.

The scraped material was transferred to a test tube containing a 10% sodium hydroxide "NaOH" solution, the tube was immersed in a water bath at 60°C for 15 minutes then centrifuged for around 10 minutes, and the sediment was examined microscopically to confirm or exclude the presence of external parasites (Houston, 2000).

Stool examination

Fecal samples obtained directly from the rectum of healthy and diseased dogs and examined for presence of internal parasites.

Therapeutic trails

The dogs were given 10 mg/kg B.wt. Zn sulphate (ZnSO4) (Tab Zinfate, Yash Pharma) orally every day for 14 days. Regular bathing with keratolytic shampoos like sulphur and salicylic acid, as well as antimicrobial therapy, may be indicated. Oral Zn supplementation, in combination with dietary changes and the cessation of calcium supplementation is recommended.

Statistical analysis

All data were analyzed using one-way analysis of variance (ANOVA), using Statistical Package for Social Sciences software, version 16.0 (SPSS Inc., Chicago, IL). The level of significance between groups was determined by Duncan's post hoc test. Results are expressed as mean± standard error, a p-value of less than 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

All diseased dogs were suffered from lack of appetite, stunted growth, and lethargy as in (Figure 1a). In 13 patients (59%) there are dermatological signs in form of erected hair (Figure 1b) erythema (Figure 1c and d), hypotrichosis, alopecia as shown in (Figure 1e) scales as in (Figure 1f), excoriations and parakeratosis (Figure 1g and h) severe itching, fleas were not observed.

Vital signs of the diseased patients revealed normal mucus membranes, temperature, pulse and respiration rates as explained in (Table 1). Hematological observation revealed significant decrease of Hb. concentration, PCV, TEC $P \leq (0.01)$ in Zn deficient dog. Leucocytic count was significantly decreased in Zn deficient animals and these hematological parametrs were improved after treatment as in (Table 2).

Figure 1: Emaciated and lethargy dog as in (a), erected hair (b) erythema (c and d), hypotrichosis, alopecia as shown in (e) scales (f) and excoriations (g and h).

Biochemical parameters revealed significant lower values of total proteins, albumin and glucose in Zn deficient dogs (Table 3). A numerical decrease in globulin in diseased patients compared with the control dogs. There was a significant decrease of serum Zn and significant increase of iron and Cu in diseased dogs compared to the control ones. The direct microscopic examination of hair and scales revealed neither spores nor hyphae of dermatophytes nor mites.

Dogs had been administered Zn replacement therapy and had a clinical follow-up, either by examination or via telephone. Response to Zn supplementation was graded as excellent (total resolution of lesions), good (greater than 50% but less than 100% resolution of lesions), or poor (less than 50% resolution or no change). The length of time treated when evaluated and determined as either (4 weeks to 8 weeks at maximum).

Table 1: Vital parameters in Zn deficient patients compared with the control group.

Parameter	Control group	Zn responsive dermatosis group		P-value
		Before treatment	After treatment	
Temperature °C	38.24 ± 0.15	38.24 ± 0.17	38.28 ± 0.086	0.889
Heart rate/ min.	111.0 ± 2.92	107.0 ± 5.15	107.0 ± 5.148	0.390
Respiration/ min.	24.20 ± 1.39	25.40 ± 3.19	24.40 ± 0.510	0.859

Table 2: Hematological alterations in Zn deficient patients compared with the control group.

Parameter	Control group	Zn responsive dermatosis group		P-value
		Before treatment	After treatment	
Hb. (gm%)	12.69 ± 0.484[a]	10.42 ± 1.140[b]	10.62 ± 0.220[b]	< 0.001
PCV (%)	37.11 ± 0.947[a]	29.43 ± 1.026[b]	31.70 ± 0.660[b]	< 0.001
RBCs (× 10^6/µL)	5.976 ± 0.209[a]	4.136 ± 0.302[b]	4.400 ± 0.142[b]	<0.001
WBCs (×10^3/µL)	10.93 ± 0.247[a]	06.36 ± 0.30[c]	9.480 ± 0.213[b]	<0.001
MCV (fl)	79.25 ± 1.916	66.44 ± 6.936	69.40 ± 5.546	0.150
MCH (pg)	27.18 ± 0.746	23.23 ± 2.599	25.34 ± 1.647	0.542
MCHC (%)	34.22 ± 0.351	26.36 ± 3.805	28.14 ± 2.698	0.164

Hb: Hemoglobin; PCV: Packed cell volume; RBCs: Red blood cells; WBCs: White blood cells; MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration.

Table 3: Biochemical alterations in Zn deficient patients compared with the control group.

Parameter	Control group	Zn responsive dermatosis group		P-value
		Before treatment	After treatment	
Glucose mg/l	56.00 ± 1.581[a]	51.60 ± 0.927[b]	45.04 ± 1.335[c]	< 0.001
Total protein g/l	7.050 ± 0.130[b]	5.700 ± 0.322[c]	6.140 ± 0.108[c]	< 0.001
Albumin g/l	3.394 ± 0.075[a]	2.640 ± 0.093[b]	2.880 ± 0.058[b]	< 0.001
Globulin g/l	3.656 ± 0.196[b]	3.080 ± 0.364[b]	3.260 ± 0.087[b]	< 0.001
Cu mmol/l	17.17 ± 0.820[b]	22.38 ± 1.191[a]	11.27 ± 0.658[c]	< 0.001
Fe mmol/l	20.27 ± 0.816[b]	24.95 ± 1.647[a]	17.89 ± 1.278[b]	0.002
Zn mmol/l	26.97 ± 3.177[a]	11.06 ± 0.398[c]	23.04 ± 0.972[b]	< 0.001

Oral zinc supplementation, together with dietary correction and the suspension of calcium supplementation, where appropriate, brings rapid resolution of signs in most cases. Supplementation with Zn sulfate (10 mg/kg per day) is usually adequate, and this therapy is generally sufficient for the resolution of the lesions within 2 to 6 weeks and improvement of biochemical parameters as shown in (Table 3).

Good nutrition is essential for healthy coat especially protein, trace elements as Cu, iron, Zn and vitamins which promote healthy growth. In addition, hair growth can be affected by age and overall health, so growing puppies and adults under stress associated with pregnancy, lactation, or illness may require two to three times the NRC recommended level (National Research Council, 1985). Dermatologic problems are the most commonly seen disorders in pet's clinic (Kehrer and Klotz, 2015; Kubesy et al., 2020).

Our clinical signs in our patients were agreed with Mozaffari and Derakhshanfar (2007) who recorded that Zn deficiency is associated with reduced growth rate, poor immune function, decrease reproductive performance, as well as affecting skin in severe cases. A reduced appetite is often seen and thought to result from the decreased senses of taste and smell food (Droke et al., 1993). Although changes in appetite are linked to changes in the concentration of amino acid-derived neurotransmitters in the brain, Zn deficiency may reduce appetite by impairing taste, as the sense of taste is thought to be mediated through the salivary zinc-dependent system (Failla, 2003).

Regarding dermatological signs, the clinical signs recorded in our patients were consistent with those cited by White et al. (2001) and Beigh et al. (2017) who consider the presence of crusts and periocular hyperkeratosis as suggestive of Zn deficiency. The first sites which affected are nose and pressure points as Zn concentrations tend to be higher in tissues with high epithelial proliferation rates, and normally parakeratotic sites such as nose, as well as keratinized pressure areas, as footpads which contain the largest Zn concentrations (Colombini, 1999). Redness as a result of congestion in the capillaries in the lower layers of the skin will be present at the mucocutaneous junction and pressure points. In addition, scaling, crusting, hair loss, pyoderma.

The skin has the third highest abundance of Zn in the body (approximately, 2% of the total body store of Zn is found in the skin). In the skin, Zn concentration is higher in the epidermis than in the dermis, owing to Zn requirement for the active proliferation and differentiation of epidermal keratinocytes (Ogawa et al., 2016) that may

explain the dermatological changes "alopecia, redness, and parakeratosis" observed in this study. Zinc plays an important role in regulating various aspects of cellular metabolism, principally through its incorporation into enzymes (Watson, 1998). Alkaline phosphatase is a Zn-dependent enzyme which is essential for healthy skin. Although skin biopsy with histopathological examination is considered conclusive for diagnostic purposes (White et al., 2001), but the owner did not allow this examination. Dermatitis is typically associated with redness, swelling, skin lesions, blisters and/or rashes of the skin. The accompanying discomfort causes the dog or cat to lick, bite, or scratch the affected region excessively, which can develop to a secondary bacterial infection.

Zinc affects the immune system through energy production, protein synthesis, stabilization of membranes against bacterial endotoxins, antioxidant enzyme production and maintenance of lymphocyte replication and antibody production (Engle et al., 1998), so dogs are also immunocompromised and develop respiratory infections and nasal discharge and decrease their resistance to infections (Prasad, 1993).

Hematological alterations were similar to that of Beigh et al. (2017). Reduction in the Hb. content may be due to increased rate of disruption or reduction in the rate of formation of erythrocytes, and significant decrease in RBC and Hb. content in Zn deficient dogs reflected anemia. This may be attributed to impairment of cell replications and protein synthesis and thus the generations of blood cells, which commence with condition of Zn deficiency. The decrease in PCV was obviously due to the decreased cellular count in affected dogs.

Because it affects the inflammatory/immune response, metabolic equilibrium, and antioxidant activity, Zn is one of the most important nutritional components for an organism's entire life (Mocchegiani et al., 2013). Even in cases of moderate Zn deficiency, the immune system function is compromised (Shahraz and Ghaziani, 2005). Immune system function is affected by severe Zn deficiency. T lymphocyte growth and activation require Zn, and a lack of it leads to a decline in cellular immunity (Yousefichaijan et al., 2016). This explains the significant reduction of WBCs in affected dogs and its increase after treatment.

Decrease glucose in affected dogs may be attributed to decreased appetite, which is often seen and thought to result from the decreased senses of taste and smell. Decreased total protein and albumin in affected dogs were agreed with Johnson (2011). The decreased globulin observed in Zn deficient dogs could be due to decreased production of gamma globulins as Zn deficient dogs had lower TLC values Beigh et al. (2017).

Plasma Zn represents 0.2% of total body Zn content (Lowe et al., 2009), although Zn concentration responds to temporary intake over short period. Infection, inflammation, stress, and trauma can all cause a drop in plasma Zn concentration that is independent to Zn status or dietary Zn intake. Tissue degradation during famine, on the other hand, can release Zn into the circulation, resulting in a brief increase in circulating Zn levels (Hambidge et al., 1989).

Zinc deficiency may be related to poor absorption of Zn, which necessitates supplementation throughout life, or a diet with low values of Zn due to high concentrations of phytates or calcium, considered a transient change responsive to providing a balanced commercial diet (White et al., 2001). A significant decrease of Zn in the diseased patient were in agreement with Vicente et al. (2013) which recorded that Zn deficiency can be diagnosed by measuring Zn concentration in plasma or hair. An increase in Cu and iron concentration may be responsible for decreased Zn level Uchida et al. (1997) as they chelate Zn and prevent its absorption. The response of the dogs in this report to Zn supplementation, improvement of hematological and biochenmical parameters confirms the diagnosis of Zn deficiency and Zn responsive dermatosis.

Oral zinc supplementation is the treatment of choice in dogs. An initial oral dosage of 1mg/kg of elemental Zn per 24 hours is the usual recommended starting dose. This is given for four to six weeks to determine the response to treatment. If the response is poor, the dose may be increased by 50% per month until a response is produced. Anti-inflammatory doses are normally recommended to relieve inflammatory reactions (Vicente et al., 2013).

CONCLUSIONS AND RECOMMENDATIONS

Zinc is involved in many aspects of body metabolism. Zinc responsive dermatosis is an uncommon disease in dogs resulting from a defect in zinc absorption/metabolism or feeding an inappropriate diet. The prognosis is good, but life-long supplementation is usually required. Thus, veterinarians should be aware of these conditions for giving the proper diagnosis, and undergoing the appropriate therapy.

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NOVELTY STATEMENT

This study showed the importance of Zn in Dog nutrition. Its deficiency affect growth rate, immune status of the animal in addition cutaneous lesion. Animal respond to Zn sulphate therapy but may take long course (4-8 weeks).

AUTHOR'S CONTRIBUTION

All authors planned and conducted the study. MS collect the sample NEA analyzed the data, AE discussed the results. All authors wrote the manuscript and contributed to the final version of the manuscript.

Conflict of interest

The authors have declared no conflict of interest.

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