RESEARCH ARTICLE

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Intestinal Integrity Assessment with Diamine Oxidase Activity in Dogs with Atopic Dermatitis

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Abstract

Diamin oxidase (dAo) as a valuable biomarker, and a mirror of the integrity/mucosal function of the small intestine (sint). The levels of dAo in the serum and mucosa of the sint could be capable of determining as an assessment of sint barrier function. Given better understanding of gut-brain-skin axis in veterinary internal medicine field, relevant data is lacking through dogs with atopic dermatitis (atode) in which resarches focus and rely on skin changes. However more data is crucial, which prompted the present author to perform this study and analyzed the relationship between integrity/mucosal function of sint to those of dogs with atode. Dogs enrolled and classified as suggested criterion for mild (10), moderate (35) and severe (60) skin lesions scoring based on CADESI-04. Commercially available Canine Diamine Oxidase ELISA Kit were purchased for dAo analytes. As detected by Quantitave Competitive ELISA, dAo levels (ng/mL) were detected as 5,28±1,19, 2,594±0,76 and 1,28±0,22, with a statistical significance of Group III in contrast to Group I, suggesting that as severity of the atode elevates, circulating dAo levels were declined in correlation. It should not be unwise to draw preliminary suggestion that dAo levels could alter in relationship with disease activity in dogs with atode. This alterations, mainly deduction, should reflect diasease activity, in which dogs in Group III (severe atode) represented lowest dAo values in contrasto to other classfied groups of disease.

Keywords: Atopic dermatitis, diamine oxidase, dog, intestinal integrity.

INTRODUCTION

For many long years, it was suggested that several frequent dermatological issues presented no association with diet. Contrarily researches coming from recent years, highlightened that diet could be capable of influencing outcome (Katta and Desai, 2014; Shmalberg, 2017). Furthermore diet, round the clock adjust gene expression (Hunter et al., 2008; Livingstone et al., 2014), in which genes encoding certain proteins is capable of switching on/off by lifestyle choices (to the present authors knowledge not only for humanbeing but also for animals) i.e what people (animals) eat, and where/how they live (Anturaniemi et al., 2020; Geary et al., 2022). Diet could be capable of changing the game by gene expression through affecting gut microbiota (Singh et al.2017, Anturaniemi et al., 2020; Geary et al., 2022). Given the resident microbiota is vital for maintanence of both functional and structural integrity of the gut and regulation of immunity (Furusawa et al., 2013; Purchiaroni et al., 2013), it should not be unwise to recognize 'gut-skin-brain axis' on behalf of investigating atode and its relationship with sint, which prompted the present author performing this study. Gut-skin-brain axis' needs to be explored in much details, specifically in dogs in relationship with dermatlogical issues and atode.

The term atode has took place used in veterinary field denoted inflammatory dermatitis with itching, in which foremost recognized frequently by an IgE antibody-related reaction (Halliwell, 2006). Following diagnosis of atode has been clarified, an elimination diet should be performed for possible detection of food allergens play a role in the development of this disorder (Favrot et al., 2010). Proposed definitions through gut microbiota presented its effects on accompanying pathogenesis of atode were composed of i) immunity and inflammation (Bowe, 2011; Belkaid and Hand, 2014), ii) storage of blood lipids/fat (Musso et al., 2010 a,b) neuropeptide existence (Pincelli et al., 1990; Gueniche et al., 2010; Holzer and Farzi, 2014) and metabolic alterations Taking into account all aforementioned data, it should not be unwise to focus on the lack of literature for highlightining the association between intestinal integrity and atode among dogs, which was the purpose of this study.

MATERIALS AND METHODS

Diagnostic criterion and CADESI-04 scores

To those of dogs enrolled diagnosis was based on table 1 fullfilly meeting all necessary criterion for a full diagnosis of atode. Available diagnostic tree evolved clinical signs (Griffin and DeBoer, 2001; Favrot et al., 2010), exclusion of other relevant dermatoses based on Favrot Criteria (Favrot et al., 2010, CADESI-04 scoring based on proposed benchmarks for mild (10), moderate (35) and severe AD (≥60) skin lesions (Olivry et al., 2014). In an attempt to exclude other relevant etiology; skin scraping, cutaneous cytology, dermatoscopy, epidermal corneometric analysis, serum biochemistry, endocrine panel results were all deemed available (in which not necessary data to show herein). The present research was approved by HADYEK Aydın Adnan Menderes University Local Ethical Committee on Animal Experiments with number 64583101/2020/045 (9/7/2020).

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Table 1. Diagnostic tree applied based on evidenced based veterinary medicine, at the present study.

Clinical signs	-Pruritus -Primary skin lesions [erythema), Secondary skin lesions (i.e. hyperpigmentation/lichenification) -Self-trauma (i.e. excoriations/self-induced alopecia) (Griffin and DeBoer, 2001).
-Excluding other pruritic dermatoses and active skin infection	Favrot et al. (2010)
CADESI-04 as a biomarker	-Proposed benchmarks for mild (10), moderate (35) and severe AD (≥60) skin lesions (Olivry et al 2014)

Intestinal integrity and mucosal function interpretation by use of Canine Diamine Oxidase ELISA Kit

This assay, as decribed by the available web site (https://www.mybiosource.com/dao-canine-elisa-its/diamine - oxidase / 739902) was purchased by Turkish side Distributor (RDA Group, Istanbul) from the specified website of distributor. The latter assay presented sensitivity:1.0 ng/mL and excellent specificity [Spike Recovery: 92-101% and Linearity 1:8 Range 994-109%]. There has been no significant cross-reactivity nor interference between dAo and its analogues (Mybiosource web site). The latter assay proven to have high sensitivity and specificity for detection of dAo. According to owner there was no prior cross-reactivity/interference between dAo and analogues. Samples included sera obtained from dogs with a diagnosis of atode. Assay Type was Quantitative Competitive, which was analyzed by ELISA Device available at RDA Group, Istanbul. Sensitivity was 1.0 ng/mL, with a detection range of 0.312-20 ng/mL. Prior to analysis preparation and storage conditions evolved were 2-8 degree Celcius, immediately forwarded to RDA Group, Istanbul Kruskal Wallis one way ANOVA test was preferred as a rank based nonparametric methodology. P value was set as 0.01.

RESULTS

Regarding dAo values (mean± standart deviation) statistical analytes showed p values set as p = 0,299 between Group II and III, p=0,008 between Group I and-III and p=0,158 between Group I and II as was shown in fig. 1 and table 2. During study test kits were purchased previously were all gave available results. There was no error nor analytical fault during methodology.

Table 2. a, b: dAo acticvity among dogs enrelled at this study with atode. Different letters in same lime are statistically significant. Due to proposed bencmarks for atode based on CADESI-04 (Olivry et al 2014) Group I to III were denoed as mild, moderate and severe.

	Group I Mild (10)	**Group II Moderate (35)**	**Group III Severe (≥60)**
dAo	5,28 ± 1,19a	2,594 ± 0,76ab	1,28 ± 0,22b
P value		0,030	

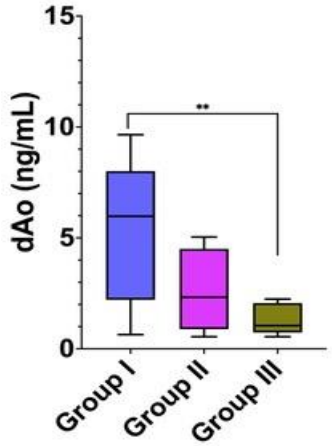

Figure 1. Boxplot analytes showing dAo levels among dog withg atode enrolled and classified as suggested criterion for Group I--mild (10), Group II--moderate (35) and Group III--severe (60) skin lesions scoring based on CADESI-04.

Selected clinical cases

All enrolled cases were daignosed with atode as was also shown as a diagnostic tree at table I. Entire clinical cases were fullfilly met the criteria shown at the latter table. Different cases were presented at each group showed different levels of circulating dAo levels, selectedly shown at fig 2. None of the dogs were excluded from the study during trial, nor analysis were fault.

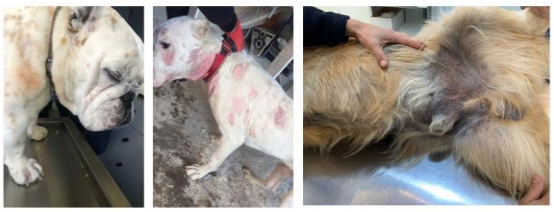

Figure 2. Serum dAo activities (ng/mL) were represented as 4.345, 3.210 and 0.765 to those of dogs with atode in groups I to III, respectively.

DISCUSSION AND CONCLUSION

The patho-physiological mechanisms underlying atode -related intestinal mucosal injury (inmi) have yet to be entirely elucidated in dogs. Prior researches denoted that inmi is a complex pathophysiological condition composed of multifactorial reasons [i.e. intestinal hypoperfusion, oxidative stress and inflammatoric mediators] (Capurso et al., 2012; Rahman et al 2003). Hence, from a clinical point of view it is essential to analyze the association between injury of the intestinal mucosal barrier and atode ip herein.

Intestinal mucosal barrier could be damaged by i) ischemic reperfusion injury, ii) overwhelming production of inflammatory mediators, iii) microcirculatoric alterations and iv) apoptosis (Zhang et al., 2007). Altough this was not an etiological study, the present author did not evaluate predisposing factors or underlying reasons. Among those aforementioned factors microcirculation disorder causes intestinal barrier dysfunction through reactive oxygen species existence via xanthine oxidase/ hypoxanthine buildup in intestinal environment (Tian et al., 2013). In humans with atode elevated intestinal permability (Ukabam et al., 1984; Pike et al., 1986; Caffarelli et al., 1993) without clear evidence was reported. Alterations among intestinal barrier functioning could represent mucosal damage as a probable consequence of local inflammatory respond (Rosenfeldt et al., 2004). The latter valuable hypothesis prompted the present author to elucidate and establish the present study. Thus obtained results should be discussed cautiously, in which as the severity of the atode increases, circulating dAo levels were decreased at the present study (fig. 1 and table 2).

It was well recognized that high-fat dietary conditions deduce biodiversity of intestinal microbiota along with elevated levels of lipopolysaccharides, consequently resulting with systemic inflammation via i) altering colonic epithelial integrity and barrier function, ii) diminishing mucus layer thickness, and iii) elevating pro-inflammatory cytokine levels (Morales et al., 2016; Deng et al., 2018). Interestingly 12 out of 17 dogs enrolled herein were receiving hight fat and carbonhydrate diet with an unknown origin (brand name) which could have hasten inmi to those of dogs.

The present author found that the decline in plasma dAo activity was associated with the severity of probable (without any histopathological evidence) mucosal injury. In the current study, in paralell line with the purpose, it was sought to determine the usefulness of plasma dAo activity level in estimating the severity of atode in relationship with the small intestinal changes.

Given dAo adjsut cell proliferation via degradation of polyamine, an essential substance for mitosis/meiosis (Kusche et al., 1975; Jänne et al., 1978; Baylin et al., 1978) it quickly detoxifies dietary histamine, preventing the allergy-like symptoms of histamine excess. dAo is peculiarly exist in enterocytes [through tip of small intestinal villi] (Baylin et al., 1978), there which it is libetared into the peripheral circulation into liver for inactivation (D'Agostino et al., 1986). dAo activity at the top level is presented within the small intestine, whereas lowest activity in the large intestine/stomach (Shakir et al., 1977; Bieganski, 1983) Plasma dAo activity decreased with inmi (Luk et al., 1980, Nakao et al., 2002), in which was the probable case obtained at this study. Circulating dAo levels (ng/mL) were detected as 5,28 ± 1,19, 2,594 ± 0,76 and 1,28 ± 0,22, with a statistical significance of Group III in contrast to Group I, denoting that as the severity of the atode increases, circulating dAo levels were decreased at the present study (fig. 1 and table 2). Further studies are warranted in larger dog populations for better understanding the relationship.

Conflict of Interest

The present author has competing interest.

Authorship contributions

Concept: K.U., Design: K.U., Data Collection or Processing: K.U., Analysis or Interpretation: K.U., Literature Search: K.U., Writing: K.U

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Ethical Approval

This study was conducted with the permission of the Aydın Adnan Menderes University Local Ethics Committee for Animal Experiments with the decision No. 64583101/2020/045 - 16 dated 09.07.2020.

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