A New Era Under Soil Based Probiotics for Anti-Pruritic Combat Among Cats with Feline Atopic Skin Syndrome

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Abstract

Present research was conducted at the University of Aydin Adnan Menderes, Faculty of Veterinary. In a total of 10 cats with pruritic dermatoses were allocated, classified [Feline atopic skin syndrome (FaSs)] and adapted to the retrospective case controlled study on the basis of Polycheck in vitro Allergy Test, clinical signs, dermatoscopic and cytological examination. No prior drug prescription, nor immunosuppressive treatment were evident, which was an inclusion criteria. Complete blood count, serum biochemistry, and endocrine panels were all deemed available on days 0 and 21 for all cats involved. The Feline Dermatitis Extent and Severity Index (FeDESI) and a 10 cm visual analog scale (VAS) were deemed available as relevant prognostic parameters. A three strain invoving soil-based probiotic used via rectal route significantly decreased FEDESI and VAS pruritus scores after 10 days of rectal use. Pre-treament day 0 FEDESI scores (median \pm SD) (106.3 \pm 41.38), were significantly higher than scores on day 10 (15.3 \pm 10.53) switching the severity of the disease to mild status in all cases. Furthermore, day 0 VAS pruritus scores were 7.4 \pm 1.78 (mean \pm SD) (prior to treatment), whereas owner VAS pruritus score was decreased to 1.3 \pm 1.06 (mean \pm SD) significantly (p=0.005). It should not be unwise to draw preliminary conclusion that 3 chained soil-based Bacillus probiotic was capable of short term cure for FaSs. Bacillus probiotics with safety usage should be added to therapeutical armamentarium of FaSs.

Keywords: Atopic skin syndrome, feline, soil-based probiotic.

INTRODUCTION

Terminology in veterinary dermatology era has been changing time to time. Feline atopic syndrome (FaS), novel proposal remarking allergic dermatoses, composed gastorintestinal and respiratory issues among cats (Mueller et al., 2021). Under this classification Feline atopic skin syndrome (FaSs) denotes allergic cutaneous disorders in relationship with environmental allergy (Halliwell et al., 2021a,b; Santoro et al., 2021). Allergic reflection involving dermatitis in cats involve several cutaneous reactions in relationship with food, environmental or insect allergens. include self-induced The latter alopecia/hypotrichosis, miliary excoriation/ulcer on the head/neck and eosinophilic granuloma complex (Halliwell et al., 2021a,b; Santoro et al., 2021). Therefore, therapeutical approach should be directed to etiology. On the other hand, there is no time for unsatisfactory animal owner, rounding around several clinics with similar approaches. Due to unmet and satisfactory solutions, the aim of the present authors were to use rectal route for soil-based probiotics as an antipruritic combat among cats with FaSs.

MATERIALS AND METHODS

Diagnostic tree

Diagnosis was based on the diagnostic algorithm involving clinical signs with FaSs. The vast majority of cats with FaSs originally exhibit one/more cutaneous reaction patterns including as miliary dermatitis, alopecia or hypotrichosis, head and neck pruritis shown in Figure 1 (Santoro et al., 2021) below.

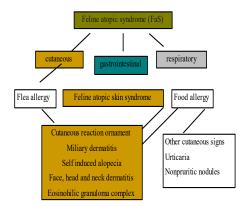


Figure 1. Algorithm showing the clinical signs associated with feline atopic syndrome (adapted from Santoro et al., 2021).

In an attempt to make specific (and thereof differential) diagnosis for FaSs, relevant literature was carefully elucidated (Santoro et al., 2021) in parallel line with other relevant/significant ones (Diesel et al., 2011; Favrot et al., 2014, Ravens et al., 2014).

In diagnosis of FASs, it should be considered that many the differential approaches due to variable clinical presentation of the disease (Fig. 1). Many other cutaneous and non-cutaneous diseases also may present with encrusted papules, alopecia, head/neck pruritus and

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cutaneous eroded plaques (Diesel et al., 2011; Favrot et al., 2014, Ravens et al., 2014).

Inclusion Criteria

The present research was conducted at the Aydin Adnan Menderes University, Faculty of Veterinary, Department of Internal Medicine. In a total of 10 cats with pruritic dermatoses had presumably forced us for interpretation of allergy based on Polycheck in vitro Allergy Test, clinical signs, dermatoscopic and cytological examination through with microbiological laboratory work for exclusion of other relevant secondary diseases. Anti-parasitic routine application was evident in all cats. During trial, all cats were subjected to the lowest carbohydrate involving commercial cat food (Virbac Gastro-1- Digestive, Support, Virbac, Turkey) for at least 6 weeks. No prior drug prescription, nor immunosuppressive treatment were evident, which was an inclusion criteria. Complete blood count, serum biochemistry, and endocrine panels were all deemed available on days 0 and 21 for all cats involved.

Scoring system preferred

The Feline Dermatitis Extent and Severity Index (FeDESI) was preferentially optional in an attempt to make scoring of relevant clinical signs [excoriations/erosions, erythema and self-induced alopecia (Nuttall et al., 2004). The owners were shortly educated to assess pruritus by use of a 10 cm visual analog scale (VAS) (Hill et al., 2007) similar to previous study (Schmidt et al., 2012).

Probiotic enema treatment methodology

Soil based probiotic formulation (Figure 2) was prescribed as rectal enema involving 3 different Bacillus strains (Algeapro Triogermila-I, veterinary side distributor RDA Group, Istanbul, Turkey). Briefly each vial (6 x 10⁹ CFU) was poured and then dissolved in 10 ml sterile water, which was then rectally administered as an enema model. Therapeutical application involved 10 days, and each owner was advised to enter at the clinic everyday exactly at similar duration. Methodology of and proposed mechanism of efficacy was shown in Figure 3 below.

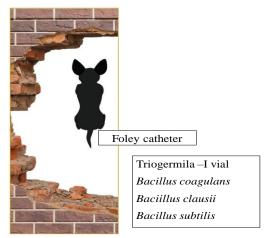


Figure 2. Cartoon depicting rectal enema usage of a soil based probiotic combination of 3 different *Bacillus* strains. Briefly foley catheter was inserted 15 cm from the rectum and one vial was prescribed in each session.

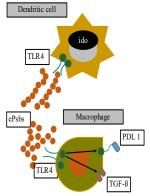


Figure 3. Probable molecular and cellular efficacy of antiinflammatory probiotic exopolysaccharide (ePs) exhibited by *B. subtilis* against disease induced inflammation, adapted from (Zamora-Pineda et al., 2022).

Statistical analysis

Descriptive statistics of the obtained data were tabulated to indicate the mean and standard deviations. Wilcoxon test was used to determine the statistical differences of FeDESI and VAS score before and after treatment. A p value of < 0.05 was considered significant by using the SPSS 26.0 program (IBM, USA) in all analyzes.

RESULTS

FEDESI and VAS pruritus scores

Both FeDESI and VAS pruritus scores were changed in FaSs cases. Pre-treament day 0 FeDESI scores (median \pm SD) (106.3 \pm 41.38), were significantly higher than scores on day 10 (15.3 \pm 10.53) switching the severity of the disease to mild status in all cases. Furthermore, day 0 VAS pruritus scores were 7.4 \pm 1.78 (mean \pm SD) (prior to treatment), whereas owner VAS pruritus score was decreased to 1.3 \pm 1.06 (mean \pm SD) significantly (p=0.005) (Table 1). Figures 4 and 5 showed FEDESI and VAS pruritus scores alterations before and after treatment. There were no side effects attributable to treatment applications. All cases were monitored for 6 months after completion of treatment in which no recurrence was observed.

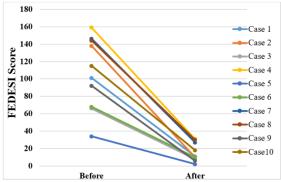


Figure 4. FEDESI score alterations before and after treatment.

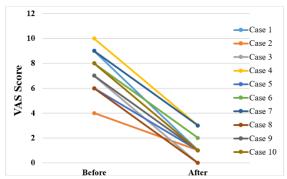


Figure 5. VAS score alterations before and after treatment.

Table 1. FEDESI and VAS pruritus scores of enrolled cats in the present study.

Score	Before Treatment (X ⁻ ± Sd)	After Treatment (X ^{-±} Sd)	P value
FEDESI	106.3 ± 41.38	15.3 ± 10.53	0.005
VAS	7.4 ± 1.78	1.3 ± 1.06	0.005

Demographic findings

Cutaneous patterns described miliary dermatitis (n=2), self-induced alopecia (n=2), head and neck pruritus (n=4) and eosinophilic granuloma complex (EGC) (n=2). Either alone or in combination, and after excluding other possible causes, these patterns are consistent with a diagnosis of FaSs. Clinical photographs of selected case were shown in Figures 6 and 7, denoting before and after treatment.



Figure 6. Head and neck dermatitis under FaSs respond to the probiotic treatment used in this study.



Figure 7. Eosinophilic granuloma complex in relationship with FaSs in a 2 years old British short hair cat. Evidence of proof involve before and after probiotic treatment. This case was additionally on oral same Bacillus strain probiotic consumption for additional 11 days.

DISCUSSION AND CONCLUSION

Direct-fed microbials (dFm) as was elucidated as the feed product composed of naturally-existing live microbes, [i.e. Bacillus genus, as was the subject of treatment in the present study], were given as subject of nutritional

strategies for improving dogs' intestinal functionality and faecal quality. Even if prescribed in the diet, these latter microorganisms may esteem non-pathogenic bacteria (Feliciano et al., 2009; Félix et al., 2010). Bacteria of the Bacillus genus, involving facultative anaerobic *B. subtillis* and B. licheniformis, are capable of sporulation, making them more resistant to acidic gastric pH (Hoa et al., 2000; Coppola and Gil-Turnes, 2004; Moir, 2006). B. subtilis and B. licheniformis are frequently detected as spores in the soil. The spores are dehydrated, even if disclose to proper nutrients and moisture, then would probably germinate in the small intestine, recommence their cell vegetative growth (Tam et al., 2006). Prior research presented that B. subtilis and B. licheniformis could alter faecal odour and decline gas formation in the intestine of dogs (Paap et al., 2016). Herein at the present study 3 different Bacillus strains were used which were all soil based probiotics. Mechanism of action was shown in fig.3 involving probable molecular and cellular efficacy of antiinflammatory probiotic exopolysaccharide (ePs) exhibited by those strains (Zamora-Pineda et al., 2022).

Bacillus species supply their beneficial effects originally through the production of digestive enzymes (Danilova and Sharipova, 2020). In a prior study the fungal activity of cyclic lipopeptides (cLpS) derived from B. subtilis for inhibiting M. canis growth, was analyzed. In vitro, Bacillus cLp exhibited an inhibitory effect on M. canis growth proposed it as an alternative strategy for controlling the growth of *M. canis* by use of metabolites obtained from B. subtilis as a biomedicine envoy with antifungal activity (Tunsagool et al., 2021). In the present study although fungal analytes were not available, preferred strains might exist antifungal efficacy. Another 11 years study analyzed efficacy of oral B. subtilis PTA 6737 usage on fecal microbial populations, in which researchers concluded study B. subtilis could be safely and orally administered to domestic cats (Kerr et al., 2011). There were no side effects observed at this study.

Bioactive probiotic molecules possessing antiinflammatory efficacy compose i) exopolysaccharides, ii) cell envelope molecules, iii) secreted proteins. In a recent and interesting review article the authors briefly denoted cell envelope-associated probiotic molecules, along with secreted protein and carbohydrate probiotic molecules, and discussed anti-inflammatory exopolysaccharide (ePs) exhibited by B. subtilis (Zamora-Pineda et al., 2022). B. subtilis exhibited antiinflammatory efficacy and caused protection in several T cell-mediated diseases, alleviated disorders related to enteric/blood-borne pathogens, allergic eosinophilia etc. and also for prophylaxy (Jones and Knight, 2012; Jones et al., 2014; Paynich et al., 2017; Paik et al., 2019; Swartzendruber et al., 2019; Zamora-Pineda et al., 2022). The latter ePs inhibited C. rodentium induced colitis, (Paynich et a., 2017), denoting that ePs might play a therapeutic role, also in acute diarrhea. We may claim that ePs, as exhibited by probiotic strains used at this study, could be of beneficial for displaying anti-inflammatory efficacy at least for cats involved.

Homogenously to Lactobacillus, *B. coagulans* displayed immunoregulatoric efficacy preferiantly alter skin health. Peripheral blood mononuclear/polymorphonuclear cells were incubated with *B. coagulans* particles boosted antigen-presenting cells and suppressed inhibited reactive oxygen species formation (Jensen et al., 2010; Benson et al., 2012). Given reactive oxygen species and oxidative stress participate within the

pathogenesis of acne, the latter hypothesis could be of benecial for treatment of acne (Bowe and Logan, 2010). Apart from acne, as FaSs cases were involved in this study, *B. coagulans* strain augment antigen-presenting cells and probably conquer reactive oxygen species formation (Jensen et al., 2010; Benson et al., 2012).

Integumentary system, specifically the skin, shares traits within the gut, for instance being merged into the overall immune system. It should therefore not be unwise to draw the idea that skin co-morbidities with gut disorders (O'Neill et al., 2016) should participate. Intriguingly perception of skin-gut connections goes back to 1930s even if Dr. Pillsbury and Dr. Stokes hypothesized gastrointestinal mechanism for skin alterations like acne (Stokes and Pillsbury, 1930; Bowe and Logan, 2011). Accoding to them intestinal microflora alterations caused by stress resulted in skin inflammation (Bowe and Logan, 2011). Today at 21st century, several aspects of "gut-skin axis" have been well reconized with both murine and human studies. Regarding atopic dermatitis in humans impaired intestinal mucosal barrier seemed to be involved within the pathogenesis (Majamaa and Isolauri, 1996; Rosenfeldt et al., 2004). In children with atopic dermatitis increased transfer of intact and degraded proteins against the barrier, was a proof of elevated antigenic load (Majamaa and Isolauri, 1996). Selected triggers of zonulin release are i) small intestinal exposure to bacteria and gluten (Fasano, 2011), wheat ingestion (Varionen et al., 2000), and coeliac disease (Ciacci et al., 2004). It is not surprising that dermatological lesions, in general, were more incident in people with coeliac disease (Saarialho-Kere, 2004; Ojetti et al., 2006; Fasano and Catassi, 2012). On the other hand, small intestinal bacterial overgrowth has aroused interest for probably causing dermatological disorders (Bowe, 2011). Supposed etiology for skin lesion development associated to composed i) disabled immunesystem functioning, ii) altered lipid metabolism, iii) damaged gut associated lymphoid tissue, iv) nutritional insufficency, v) elevated intestinal permeability, and bacterial translocation damaging epidermal structure and barrier function (Guo et al., 2013; Kell and Pretorius, 2015). Diseased epidermal barrier function and immune system functioning participated for disase activity in human and canine AD (Nimmo Wilkie et al., 1991; Marsella et al., 2011). All aforementioned data herein supported the efficacy of soil based probiotic strains used succesfully in this study. Evidenced gut-brain-skin axis was also supported within this results, as selected Bacillus strains firstly and probably corrected intestinal barrier damage, even if existed, in the present cats of this study. As underlying small intestinal bacterial overgrowth was withdrawn, via rectal enema soil based probiotic combination in this study.

Conflict of Interest

The authors declare that they have no competing interests.

Authorship contributions

Concept: K.U., Data Collection or Processing: K.U., H.E., S.E., Analysis or Interpretation: K.U., H.E., S.E., Literature Search: K.U., H.E., Writing: K.U., H.E., S.E.

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