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A pilot study to evaluate alternative approaches for treatment of urinary tract infections in dogs.

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Abstract

Bacteria represent the most common cause of urinary tract infection. Antimicrobial drugs are the cornerstone of treatment of urinary bacterial infections. Because of the chronic nature of urinary bacterial infections urinary tract infection (UTI) and the potential for antibiotic resistance, a natural approach to prevention and treatment is desirable. This study evaluated the efficacy of a polyphenolic extract obtained from cranberries. The product was daily orally administered to 10 dogs with bacterial cystitis for a period of 60 days. The results obtained, despite of the small population under study, suggest a potential efficacy of the product in treating bacterial cystitis.

Keywords: Bacterial urinary infection, Dogs, Cranberry, Phytotherapy.

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Introduction

Complementary and alternative veterinary medicine can include the use of herbs, supplements and other products whose use is already supported by scientific evidence (i.e. alleviate physical symptoms, improve quality of life, prevent diseases in veterinary patients). These types of treatments are receiving increasing attention in the popular press and in professional circles, uncomplicated canine bacterial urinary tract infection (UTI) is a common clinical condition and occurs in approximately the 14% of dogs that visit a veterinarian in their lifetime [1].

UTIs are associated with a temporary or permanent breach in host defense mechanisms, and often (Bacterial UTIs) they occur as a consequence of ascending migration of pathogens through the genital tract and urethra to the bladder. Whilst the majority of simple infections resolves within a 2-3 weeks with conventional therapies (i.e. oral antimicrobials), persistent or recurrent UTIs, often involving refractory bacterial isolates, may be difficult to treat using a standard therapy [2].

In animals, cranberry has been found effective *in vitro* and *in vivo* for the prevention of UTI. The proanthocyanidins, the main active constituents of cranberry, is able to inhibit the adhesion of type I and P-fimbriated uropathogens to the uroepithelium, thus impairing bacteria colonization and subsequent bacterial infection [3]. Moreover, in the human literature cranberries showed a potential effect for the prevention and management of urinary infections through urine acidification [4].

The aim of this study is to evaluate the effect of a feed supplement given in powder form on dogs affected by simple uncomplicated UTI. This supplement contains a high concentration (35%) of polyphenolic extract from cranberry juice concentrate extract rich in flavonoids.

Materials and Methods

Ten dogs were recruited from the Veterinary Clinic Napolivet (2014-2015), in Naples (Italy). Dog's owners were verbally informed about the methods and objectives of the study and provided written consent before their dogs were treated with the feed supplement. Animals were conssidered for enrollment when showed clinical signs of UTI such as pollakiuria, dysuria, stranguria, hematuria, inappropriate urination and when found with bacterial cystitis after positive urine culture. Instead, the presence of relevant comorbidities as diabetes mellitus, urinary or reproductive tract conformational abnormalities and neoplasms of urinary tract were criteria for exclusion. Furthermore, animals treated with antibiotics were excluded from the study. A specific questionnaire focused on the evaluation of palatability of the supplement, presence of vomit and/or diarrhea, general health and vitality was provided to the owner.

The product was daily orally administered for 60 days. The evaluations were made at day 0 (D0), day 15 (D15), day 30

(D30) and day 60 (D60). After the beginning of the treatment, a complete urinalysis (including urine specific gravity, sediment examination and bacterial culture) of urines collected by cystocentesis were performed. Hematologic examination, biochemical analysis and a complete physical examination with right lateral abdominal radiograph were performed to exclude the presence of predisposing conditions for cystitis and to monitor the effects of the treatment.

Furthermore, at D0 and D60 ultrasonography (Biosound Esaote Megas ES) was performed on dogs, placed in right lateral recumbent position to minimize urinary bladder movement, in order to identify any urinary bladder disorder, and in particular to evaluate thickness and morphological conditions of mucosa, submucosa and serosa.

Graph Pad Prism® software was used to perform statistical analysis. Shapiro-Wilk test established the normality or non-normality distribution of data. The Wilcoxon-Mann-Whitney-Test was used to evaluate differences between the times; $p < 0.05$ was chosen as the significance level.

Results and Discussion

All the animals included in the study completed the protocol. The median age of the dogs was 6.7 years old (range, 4-11 years), and their mean body weight was 19.5 kg (range, 44-47 kg). Eight owners out of ten (80%) reported a good palatability of the product tested during the study period. Vomit and diarrhea were observed at D0 in the 60% of the animals, at D60 only one case of sporadic vomit and diarrhea was reported. *Escherichia coli* were the only bacterial pathogen isolated in all our urine samples at D0. Our data showed a significative decrease in protein, epithelial cells, leukocytes and bacterial counts in urine at D60 compared to D0. All the dogs under study showed negative urine culture at D60. In addition, leukocytes and neutrophils counts had a significant decrease at D60. Moreover, ultrasonography revealed an improvement in the urinary bladder mucosal irregularity and thickening at D60 (Figure 1). UTIs are more commonly diagnosed in old female dogs, indicating that age is a relevant risk factor. The mean age at diagnosis, regardless of sex, is approximately 7-8 years [3,5]. The age and breeds of dogs with recurrent UTIs varies widely, this may reflect different lifespan and changes in the popularity of some breeds over time [2,6,7]. In our study, *E. coli* was isolated in all urine samples; this is in agreement with the literature. In fact, *E. coli* was reported to be the most common pathogen isolated from urine of humans, cats and dogs affected by urinary infections [2].

The mechanism of action of cranberries has not been completely elucidated yet, but it is known that cranberries contain an a-type proanthocyanidins which may inhibit the adherence of P fimbriae of E. coli to uroepithelial cells [1]. An *in vitro* study demonstrated that metabolites of the cranberry extract in the urine of six healthy dogs were sufficient to reduce adhesion of E. coli and in general, may be beneficial in preventing *E. coli*–associated UTIs in dogs [8]. In an *in vivo* study, Chou and colleagues reported that cranberry extract decreased *E. coli* adherence to Madin-Darby canine kidney cells but did not inhibit bacterial growth. This effect suggests that cranberry extract has a potential role in the prevention of UTIs in dogs.

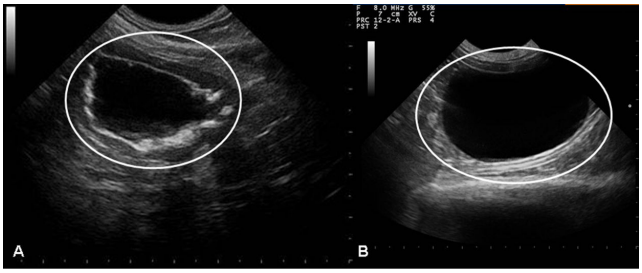

Figure 1. *(A) Image of ultrasonography of urinary bladder with mucosal irregularity and thickening at D0; (B) image of ultrasonography of urinary bladder with an improvement of mucosal irregularity and thickening at D60.*

The flavonoids contained have anti-inflammatory and antioxidant activities [9], potentially useful in preventing and controlling the main symptoms of UTIs together with alteration of micturition, such as dysuria, haematuria, stranguria, etc. The sediment characteristics of our samples were highly variable. Sediment analysis alone is considered inadequate for diagnosis of UTIs. It can report a variable quality of results interpretation, stain contamination, and false positive results. Nevertheless, an increased number of leukocytes clearly state the presence of urinary tract inflammation and the increased numbers of epithelial cells can be associated with infection, inflammation, irritation, and neoplasia of the urinary tract [10]. Both types of laboratory findings were reported in our samples at T0, but a decrease in values was highlighted starting from D15, thus demonstrating a positive response to the treatment with cranberries. In addition, the number of bacteria detected during the microscopic examination showed a significative reduction at D60. In literature, there is no consensus on the appropriate duration of treatment with antibiotics. Uncomplicated UTIs are usually successfully treated with a standard 7-14 day course of an appropriate antimicrobial agent [11]. In our study at day 15 only 4/10 animals showed a negative urine culture, but at day 30 and day 60 all the animals turned negative.

Conclusion

Lack of scientific data in veterinary medicine doesn't help supporting the routine use of herbs and probiotics in the treatment of urological diseases such as UTI. This study was a preliminary work aiming to evaluate the possibility to use alternative treatments as a replacement of the standard antimicrobial therapy. Our data suggest some findings even if include flaws as the low number of cats in the trial and the lack of a control group.

Therefore, adequate basic research as well as clinical research should be carried out to test the efficacy of the usage of herbs and probiotics in the prevention or treatment of UTIs.

Conflicts of Interest

Two of the authors are employees of Candioli Farmaceutici S. P. A.

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