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Euglena gracilis as an adjuvant for the treatment of a dog with chronic kidney disease – case report

[Euglena gracilis *como adjuvante no tratamento de um cão com doença renal crônica – relato de caso*]

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ABSTRACT

A young dog diagnosed with chronic kidney disease, based on clinical changes and sonographic findings (IRIS, 2023), was supplemented with 15mg per kg of body weight per day of inactive dried *Euglena gracilis* (henceforth called IDEG) as an adjuvant to standard treatments used for the management of chronic kidney disease in dogs. The treatments were divided into two stages, with a total duration of 120 days. At the end of the treatments, the patient showed improvement in vitality, interaction, weight gain, reduction in azotemia, and a 44% decrease in serum C-reactive protein levels.

Keywords: azotemia, dogs, algae extract, C-reactive protein

RESUMO

Um cão jovem diagnosticado com doença renal crônica, com base nas alterações clínicas e nos achados ultrassonográficos (IRIS, 2023), foi suplementado com 15mg por kg de peso corporal por dia de Euglena gracilis *seca inativa (doravante denominada IDEG) como adjuvante aos tratamentos normalmente usados para o manejo da doença renal crônica em cães. Os tratamentos foram divididos em duas etapas, com duração total de 120 dias. Ao final dos tratamentos, o paciente apresentou melhora da vivacidade, da interação e do ganho de peso, redução da azotemia e redução de 44% na proteína C reativa sérica.*

Palavra-chaves: azotemia, cães, extrato de alga, proteína C reativa

INTRODUCTION

Chronic kidney disease develops silently and manifests clinical signs when the kidney has lost a significant part of its function. The disease can be divided into four stages, according to the magnitude of metabolic changes (IRIS, 2023). The kidney performs excretory, regulatory, and endocrine functions, and the main metabolic consequences of the disease are azotemia, hyperphosphatemia, the increased serum PTH (parathyroid hormone), metabolic acidosis, non-regenerative anemia, isosthenuria, hypokalemia, hypercholesterolemia, hypercalcemia (or hypocalcemia), proteinuria, urinary tract infection, and arterial hypertension. The clinical manifestations are weight loss, dehydration, ulcerations in the oral cavity, halitosis, emesis, melena, polyuria, and polydipsia (Dibartola and Westropp, 2015).

Furthermore, it is known that important conditions of oxidative stress are present in different degrees in these patients, according to the stage of the disease, and it is inferred that this condition triggers and self-perpetuates the inflammatory cascade in them (Rosa, 2021). Within this context, the literature demonstrates interest in using potential antioxidant and anti-inflammatory substances, in conjunction with previously established therapies, in an attempt to minimize the effect of oxidative stress on the inflammatory cascade and promote renoprotection (Blandy, 2019).

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Beta 1,3-1,6 glucans, derived from cell walls of yeasts, fungi, and beta 1,3 glucans of *Euglena gracilis*, have been investigated for their potential immunomodulatory and antioxidant action (Barsanti *et al*., 2011). Inactive dried biomass of the microalga *Euglena gracilis* contains approximately 50% of beta 1,3 glucans (Barsanti *et al*., 2011) and has shown promising results in controlling a wide range of inflammatory pathologies in humans (Gissibl *et al*., 2019). Nagayama *et al*. (2020) observed a renoprotective effect in a chronic kidney disease rat model that was fed with 5% of purified *E. gracilis* beta 1,3 glucans (paramylon) for eight weeks. The results showed that paramylon attenuated renal function, glomerulosclerosis, and tubulointerstitial injury, podocyte injury, renal fibrosis, tubulointerstitial inflammatory cell infiltration. They also observed that proinflammatory cytokine gene expression levels tended to be suppressed with paramylon treatment.

The main objective of this study was to assess the use of IDEG as an adjuvant to alleviate physiological imbalances, improve clinical manifestations, delay disease progression, and consequently improve life quality.

MATERIALS AND METHODS

A male German Spitz dog, non-neutered, inactive, weighing 2.0kg and aged one year and two months, has been under the care of a veterinarian specialized in nutrition (the author) since the fifth month of age due to chronic kidney disease. The dog has been fed with a completely balanced homemade food with 30% DM, 5,495kcal/g/DM, 36.5% PB/DM, 28.3% total fat/DM, and 2.05% total dietary fiber/DM, with vitamin and mineral supplementation to meet the nutritional needs of healthy adult dogs (FEDIAF 2019). The exception was the restricted amount of phosphorus in the diet (0.3% in DM). It was also supplemented with EPA and DHA (300 mg/kg/day); lactulose (667 mg/meal), and aluminum hydroxide (15 mg/meal). This original diet (henceforth called OD) provided 211 kcal/day (NRC, 2006), totaling 132 grams per day, divided into 2 to 3 meals per day.

The patient has been fed with OD since the fifth month of age, which was responsible for stabilizing the general picture of the disease, as observed by the parameters T0 in Table 1. Before the trial, it was dewormed, vaccinated, and treated with ectoparasiticide. The nutritional anamnesis showed normal appetite, urination, water ingestion, and defecation ECF 2/7 (Carciofi *et al*., 2008). The physical examination showed ECC 4/9 (Laflamme, 1997), EMM 3/3 (Michel *et al*., 2011), and no changes in vital parameters. At this point, the patient had no clinical manifestations, proteinuria, anemia, normophosphatemia, or azotemia (Table 1).

This patient underwent a treatment in which food was supplemented with 15mg per kg of body weight per day of IDEG in two stages; 60 days of IDEG supplementation to the OD without EPA, DHA, and lactulose, followed by 60 days of IDEG supplementation to the OD. Clinical and biochemical monitoring were performed at times 0, 30, 60, and 120. The parameters evaluated were body condition score **(ECC),** blood count, creatinine (always), serum phosphorus, urinalysis, UPC (except at time 60), and C reactive protein (at times 0 and 120).

RESULTS AND DISCUSSION

The results (Table 1) demonstrate a significant improvement in hematological parameters, creatinine, urea, and C-reactive protein levels with IDEG supplementation. Based on the serum creatinine levels at the beginning of treatment, this patient would be classified at stage III chronic kidney disease (creatinine between 2.9 and 5mg/dL), according to IRIS (2023). However, after the introduction of IDEG, creatinine decreased to levels below 2.9mg/dl, suggesting that the patient should be classified as stage II chronic kidney disease. Regarding C-reactive protein, before the treatment, it was 18 mg/L, and, after 120 days of IDEG intake, its value was under 10mg/L, indicating an improvement in this biomarker of acute inflammation.

It was not possible to infer the response of IDEG to proteinuria, once the patient remained non-proteinuric during the treatment period, suggesting the EPA & DHA effects. Considering the second period (IDEG + EPA & DHA), the results did not demonstrate a negative interaction between the active ingredients, once the UPC level at T120 was near the UPC level at T0. The use of IDEG did not regenerate nephrons or renal

function, once phosphatemia did not change. However, it showed an indirect positive effect on the patient, improving the body condition score, since weight loss and cachexia are commonly associated with chronic kidney disease.

Table 1. Evolution of physiological parameters during treatment

Parameter	Reference values	T 0 (3/22)	T 30 (4/22	T 60 (5/22)	T 120 (7/22)
Hematocrit (%)	40-47	46.4	39.8	42	47.1
Red blood cell (M/mm3)	6 – 7	7.42	6.9	7.45	8.04
Hemoglobin (g/dl)	14 – 17	17	13.5	13.5	14.9
Total protein (g/dL)	5.5 – 8.0	7.3	6.6	7.4	6.8
Serum urea (mg/dL)	21 – 60	207	132.2	112.3	139
Serum creatinine (mg/dL)	0.5 – 1.5	3.86	2.16	2.1	2.45
Total serum phosphorus (mg/dL)	2.6 – 6.2	3.5	4.21	-	4.99
UPC (Urinary Protein to Creatinine ratio)	< 0.5	0.157	0.37	-	0.18
Urinary sediment	Absence	Absence	Absence	-	Absence
C-reactive protein	< 20 mg/L	18 mg/L	-	-	< 10 mg/L
ECC	5/9	4/9	5/9	5/9	5/9
EMM	3/3	3/3	3/3	3/3	3/3

Results observed at 0, 30, 60 and 120 days in a chronic renal patient. Before IDEG (T0), during treatment with IDEG + Aluminum hydroxide (T30 and T60) and after the treatment with IDEG + Aluminum hydroxide + Omega 3 + Lactulose (T120)

Nagayama *et al*. (2020) demonstrated the renal protection effect of paramylon (E. gracilis purified beta 1,3 glucans) in chronic kidney disease rat models fed with 5% of paramylon for 8 weeks. The authors suggest that the observed beneficial effect is due to the prebiotic effect of the agent and the modulation of the intestinal microbiota.

Castillho-Rodrigues *et al*. (2018) suggest a relationship between the microbiota of dogs with chronic kidney disease and circulating uremic toxins.

In our study, we administered 15mg per kg of body weight per day of IDEG, which represents a dietary inclusion of approximately 0.02% beta-glucan 1.3.

Phillips *et al*. (2019) developed the immunological characterization "in vitro", showing greater activation of IDEG to NKT (suggesting a stronger modulatory effect of the whole microalga), where beta 1,3 glucans demonstrated an important ability to regulate ROS production and the aqueous fraction showed a great antioxidant capacity. On the other hand, Vetvicka and Oliveira (2014) observed that the dosage of 15mg/kg of purified yeast β-glucan was effective in improving biological and immunological conditions in a model of diabetes in dogs (Vetvicka and Oliveira, 2014). Altogether, the chosen active ingredient and dosage seemed suitable for the intended application.

CONCLUSION

To the best of our knowledge, although this study is a case report, it is pioneering in demonstrating the potential of the application of inactive dried *Euglena gracilis* as an adjuvant to existing treatments for alleviating physiological imbalances in dogs with chronic kidney disease.

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