

THERAPEUTIC MANAGEMENT OF CHRONIC KIDNEY DISEASE (CKD) IN CATS

MANEJO TERAPÊUTICO DA DOENÇA RENAL CRÔNICA (DRC) EM GATOS

MANEJO TERAPÉUTICO DE LA ENFERMEDAD RENAL CRÓNICA (ERC) EN GATOS



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ABSTRACT

Chronic Kidney Disease (CKD) is a highly prevalent condition in felines, especially among geriatric patients. This disease is characterized by progressive evolution and has a multifactorial nature, often associated with comorbidities such as hyperthyroidism. The present study aimed to review and synthesize the main recent scientific evidence regarding the therapeutic management of CKD in cats, with emphasis on nutritional, pharmacological, and diagnostic innovations. This study consists of a narrative literature review conducted in the PubMed database, including articles published in the last five years concerning innovations in the treatment of feline CKD. The research findings demonstrated that nutritional management remains the cornerstone of CKD treatment, particularly in controlling mineral metabolism, highlighting the importance of the calcium:phosphorus ratio and appropriate magnesium supplementation in preventing ionized hypercalcemia. A significant advancement was also observed in the treatment of non-regenerative anemia associated with CKD, with the use of hypoxia-inducible factor prolyl hydroxylase inhibitors, such as molidustat. The gut–kidney axis has also been a promising focus of studies, with the development of strategies aimed at modulating the intestinal microbiota to reduce uremic toxins. Staging according to the guidelines of the International Renal Interest Society (IRIS), and the use of CKD biomarkers such as creatinine and SDMA, are essential for the diagnosis and monitoring of the disease. Finally, it is concluded that modern management of feline CKD must be individualized, integrated, and based on continuous clinical and laboratory monitoring, aiming to slow disease progression, minimize systemic complications, and improve the patient's quality of life.

Keywords: Chronic Kidney Disease (CKD). Cats. Nutritional Management. Molidustat. Gut–Kidney Axis.

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RESUMO

A Doença Renal Crônica (DRC) é uma enfermidade com alta prevalência em felinos, principalmente dentre os pacientes geriátricos. Esta doença se caracteriza pela evolução progressiva, possuindo caráter multifatorial, estando frequentemente associada à comorbidades, como, por exemplo, o hipertireoidismo. O presente trabalho teve como objetivo revisar e sintetizar as principais evidências científicas recentes a respeito do manejo terapêutico da DRC em gatos, com ênfase nas inovações nutricionais, farmacológicas e diagnósticas. O estudo refere-se à uma revisão bibliográfica narrativa, realizada na base de dados PubMed, contemplando artigos publicados nos últimos cinco anos com relação às inovações no tratamento da DRC felina. Os resultados das pesquisas demonstraram que o manejo nutricional permanece como a base do tratamento da DRC, especialmente no controle do metabolismo mineral, destacando-se a importância da relação cálcio:fósforo e da suplementação adequada de magnésio na prevenção da hipercalemia ionizada. Observou-se, também, um avanço significativo no tratamento da anemia arregenerativa associada à DRC, com o uso de inibidores da enzima prolil hidroxilase do fator induzível por hipóxia, como o molidustat. O eixo intestino-rim também foi alvo promissor de estudos, havendo o desenvolvimento de estratégias voltadas à modulação da microbiota intestinal com redução de toxinas urêmicas. O estadiamento, conforme as diretrizes da IRIS (International Renal Interest Society), e a utilização de biomarcadores da DRC, como a creatinina e SDMA, são fundamentais para o diagnóstico e acompanhamento da doença. Por fim, conclui-se que o manejo moderno da DRC felina deve ser individualizado, integrado e baseado em monitoramento clínico e laboratorial contínuo, visando retardar a progressão da doença, minimizar complicações sistêmicas e melhorar a qualidade de vida do paciente.

Palavras-chave: Doença Renal Crônica (DRC). Gatos. Manejo Nutricional. Molidustat. Eixo Intestino-Rim.

RESUMEN

La Enfermedad Renal Crónica (ERC) es una afección de alta prevalencia en felinos, especialmente entre los pacientes geriátricos. Esta enfermedad se caracteriza por una evolución progresiva y posee un carácter multifactorial, estando frecuentemente asociada a comorbilidades como el hipertiroidismo. El presente trabajo tuvo como objetivo revisar y sintetizar las principales evidencias científicas recientes sobre el manejo terapéutico de la ERC en gatos, con énfasis en las innovaciones nutricionales, farmacológicas y diagnósticas. El estudio corresponde a una revisión bibliográfica narrativa realizada en la base de datos PubMed, incluyendo artículos publicados en los últimos cinco años en relación con las innovaciones en el tratamiento de la ERC felina. Los resultados demostraron que el manejo nutricional continúa siendo la base del tratamiento de la ERC, especialmente en el control del metabolismo mineral, destacándose la importancia de la relación calcio:fósforo y de la suplementación adecuada de magnesio en la prevención de la hipercalemia ionizada. También se observó un avance significativo en el tratamiento de la anemia no regenerativa asociada a la ERC, con el uso de inhibidores de la enzima prolil hidroxilasa del factor inducible por hipoxia, como el molidustat. El eje intestino-riñón también ha sido un objetivo prometedor de investigación, con el desarrollo de estrategias orientadas a la modulación de la microbiota intestinal para reducir las toxinas urémicas. El estadiaje conforme a las directrices de la International Renal Interest Society (IRIS) y la utilización de biomarcadores de la ERC, como la creatinina y la SDMA, son fundamentales para el diagnóstico y seguimiento de la enfermedad. Por último, se concluye que el manejo moderno de la ERC felina debe ser individualizado, integrado y basado en un monitoreo clínico y de laboratorio continuo, con el objetivo de retrasar la progresión de la enfermedad, minimizar las complicaciones sistémicas y mejorar la calidad de vida del paciente.



Palabras clave: Enfermedad Renal Crónica (ERC). Gatos. Manejo Nutricional. Molidustat. Eje Intestino-Riñón.

1 INTRODUCTION

Chronic Kidney Disease (CKD) represents one of the most prevalent pathologies in the clinic of geriatric felines, characterized by a progressive and multifactorial course, which requires integrated therapeutic approaches (Geddes & Aguiar, 2022). The clinical management of these patients is complex, as CKD often coexists with other endocrinopathies common in senior cats, such as hyperthyroidism, which can mask loss of kidney function and complicate laboratory monitoring (Yu et al., 2022).

In addition to the progressive reduction of glomerular filtration, the disease triggers a series of systemic complications, including non-regenerative anemia, mineral and bone disorders (CKD-MBD), and the accumulation of uremic toxins derived from intestinal metabolism (Charles et al., 2024; Tang et al., 2024; Summers & Quimby, 2024).

In recent years, the understanding of the gut-kidney axis and the identification of new biomarkers have allowed the development of more refined nutritional and pharmacological strategies. These range from strict control of the calcium:phosphorus ratio in the diet for the management of ionized hypercalcemia to the use of hypoxia-inducible factor prolyl hydroxylase (HIF-PH) inhibitors for the treatment of anemia associated with renal failure (Ehrlich et al., 2024; Charles et al., 2024). Thus, the modern therapeutic approach to CKD in felines seeks not only to slow the progression of kidney injury, but also to mitigate the deleterious effects of comorbidities and optimize the metabolic homeostasis of geriatric patients.

2 METHODOLOGY

The present study is characterized as a narrative literature review, developed with the objective of synthesizing and analyzing the most recent scientific evidence related to the therapeutic management of chronic kidney disease in cats. The search was carried out in the PubMed database, using the descriptors "Chronic Kidney Disease", "Cats" and "Treatment", combined using the Boolean operator AND, according to the terminology of Medical Subject Headings (MeSH).

Articles published in the last five years, available in full in Portuguese or English, that directly addressed innovations in the treatment of feline CKD, were included. Studies without a direct relationship with the central theme, duplicate publications, and reviews with low methodological rigor were excluded. The selection of studies was conducted in two stages: initial screening of titles and abstracts, followed by careful evaluation of full texts to confirm scientific relevance. The information extracted was organized and discussed in a descriptive way.

3 RESULTS AND DISCUSSION

3.1 NUTRITIONAL MANAGEMENT AND MINERAL METABOLISM

Nutritional management remains the central pillar in the treatment of feline CKD, with significant advances in the control of electrolytes and mineral metabolites. Dietary magnesium supplementation has shown benefits in stabilizing fibroblast growth factor 23 (FGF23) and preventing iatrogenic ionized hypercalcemia in cats fed phosphorus-restricted diets, since magnesium acts as a potent inhibitor of vascular and tissue calcification, contributing to the maintenance of mineral homeostasis (Tang et al., 2024). This effect is related to the fact that magnesium acts as a potent inhibitor of vascular and tissue calcification, reducing ectopic calcium deposition and contributing to the stability of mineral metabolism.

The alterations in mineral metabolism observed in felines with chronic kidney disease reflect the interdependence between renal function, nutritional management, and systemic homeostasis. The dysregulation of these mechanisms favors the development of secondary metabolic disorders, such as hypercalcemia, which are often described in patients undergoing phosphorus-restricted diets (Tang et al., 2024; Ehrlich et al., 2024).

Hypercalcemia is commonly associated with CKD, presenting with often nonspecific clinical signs, such as anorexia, weight loss, gastrointestinal and urinary disorders. Factors that lead to hypercalcemia concomitantly with Chronic Kidney Disease include decreased glomerular filtration, increased renal tubular reabsorption, and increased intestinal and bone absorption (Ehrlich et al., 2024).

At the same time, in felines that already have ionized hypercalcemia (which can be defined as a calcium value above the reference range of the laboratory analyzed) — either due to CKD or idiopathic causes — the transition to diets with controlled calcium concentrations (below 200 mg/100 kcal) and a calcium:phosphorus ratio of less than 1.4:1 has been shown to be effective in restoring normocalcemia in 60% of cases. However, in cats that had partial or no response to nutritional treatment, the addition of chia seeds (1 to 2 grams per day) was shown to be effective in decreasing serum calcium concentration (Ehrlich et al., 2024).

Although phosphorus restriction is widely recommended in feline CKD because it slows the progression of the disease, recent evidence indicates that this strategy may increase the risk of ionized hypercalcemia, especially when associated with diets with low magnesium concentration. These findings reinforce the need for dietary individualization and frequent biochemical monitoring (Ehrlich et al., 2024).

The progression of chronic kidney disease in felines has repercussions on multiple organ systems, reflecting the multifactorial character of the disease. Alterations in mineral metabolism, hematological disorders, and changes in the intestinal environment occur interdependently, reinforcing the need for an integrated therapeutic approach in the follow-up of these patients (Charles et al., 2024; Summers; Quimby, 2024).

3.2 HAEMATOLOGICAL COMPLICATIONS AND EMERGING THERAPIES

In the field of hematological complications, CKD anemia, traditionally treated with recombinant erythropoietin, now has new perspectives with the use of molidustat. This HIF-PH inhibitor stimulates the endogenous production of erythropoietin and has demonstrated the ability to significantly increase hematocrit and cell volume in anemic cats after 21 to 28 days of daily oral administration, presenting itself as a promising alternative to conventional erythropoiesis-stimulating agents, especially by reducing the risk of formation of anti-erythropoietin antibodies; however, long-term studies evaluating its safety and impact on the progression of CKD are still needed (Charles et al., 2024).

3.3 GUT-KIDNEY AXIS AND UREMIC TOXINS

The interaction between the gut microbiome and kidney health, called the gut-kidney axis, has emerged as a crucial therapeutic target. Gut dysbiosis in cats with CKD contributes to the accumulation of uremic toxins, such as indoxyl sulfate, which exacerbate systemic inflammation and renal fibrosis (Summers & Quimby, 2024). Strategies using soluble fiber, probiotics, and specific enteric adsorbents have been explored to reduce the burden of these toxins and preserve residual kidney function (Summers & Quimby, 2024).

3.4 STAGING AND DIAGNOSTIC CONSIDERATIONS

It is recommended that domestic felines (cats) be classified according to the CKD staging system of the Society of Renal Interest (IRIS), initially according to serum creatinine, which may be accompanied by symmetrical serum dimethylarginine concentration, as well as systolic blood pressure and urine protein/creatinine ratio (UPC) (Geddes & Aguiar, 2022).

The diagnosis of chronic kidney disease in cats can be carried out by different methods, mainly based on the reduction of the glomerular filtration rate (GFR). Although there is the possibility of direct measurement, this method can be financially burdensome to the responsible person and stressful to the animal. For this reason, GFR biomarkers such as urea, creatinine, and SDMA are widely used in routine clinical practice (Geddes & Aguiar, 2022).

3.5 CKD AND HYPERTHYROIDISM

Management of cats with CKD and concomitant hyperthyroidism requires extreme caution. Hyperthyroidism creates a hemodynamic and metabolic state that increases the glomerular filtration rate and reduces creatinine due to loss of muscle mass, leading to the disregard of the presence of CKD when creatinine alone is used. In this way, SDMA presents itself as a more promising biomarker because it is less dependent on muscle mass, but its behavior in hyperthyroid cats can be masked by increased glomerular filtration rate in the hyperthyroid state (Yu *et al.*, 2022).

Treatment of hyperthyroidism can "unmask" an underlying CKD by reducing the artificially elevated glomerular filtration rate due to the thyrotoxic state. (Geddes & Aguiar, 2022). In addition, the development of iatrogenic hypothyroidism after radioiodine or methimazole therapy is harmful as it further reduces renal blood flow and is associated with shorter survival times in azotemic cats (Yu *et al.*, 2022). In these cases, levothyroxine replacement is recommended to keep kidney function as stable as possible (Geddes & Aguiar, 2022).

4 CONCLUSION

The present study aimed to analyze and discuss the therapeutic management of CKD in felines, addressing nutritional, pharmacological and complementary strategies based on contemporary scientific evidence. Thus, nutritional intervention constitutes the therapeutic foundation in feline CKD. Diets with controlled phosphorus restriction, balance of calcium:phosphorus ratio and absolute calcium concentration, associated with magnesium supplementation, have been shown to be effective in stabilizing mineral metabolism and reducing the risk of hypercalcemia. Dietary personalization should consider the clinical and biochemical status of the patient, through the analysis of the monitoring of the ionogram, serum phosphorus, and magnesium. Thus, the prescription should be adjusted according to physiological responses.

In the context of hematological complications, non-regenerative anemia associated with CKD requires a pharmacospecific approach. Hypoxia-inducible factor prolyl hydroxylase inhibitors, exemplified by molidustat, emerge as a promising alternative to treatment with exogenous erythropoietin, due to the stimulation of endogenous erythropoiesis, reducing the risk of immunogenicity. However, there are limitations to the clinical incorporation of this agent, as studies are needed to evaluate the safety, effects on blood pressure, renal progression, and long-term outcomes.

Modulation of the gut-kidney axis represents a complementary therapeutic strategy with the potential to reduce the burden of uremic toxins, modulating systemic inflammatory processes. Therefore, interventions involving soluble fibers, specific probiotics, and enteric adsorbents may decrease the production and absorption of toxic uremic metabolites, preserving renal function and reducing renal inflammation and fibrosis. However, studies are needed to define strains, doses, and administration protocols that are effective and safe in felines with CKD.

Laboratory follow-up should follow standardized guidelines, such as those of IRIS, integrating serum creatinine count, SDMA, systolic blood pressure, and urine protein/creatinine ratio. The combined use of these biomarkers allows for greater diagnostic accuracy, minimizing interference from secondary diseases, such as hypothyroidism and hyperthyroidism. In addition, there is a guarantee of precise therapeutic adjustment, improving sensitivity for initial changes in the glomerular filtration rate.

The coexistence of CKD and hyperthyroidism imposes diagnostic and therapeutic challenges, given that the thyrotoxic state can mask renal failure by increasing GFR and reducing creatinine due to loss of muscle mass. In contrast, treating hyperthyroidism can "unmask" an underlying CKD. Therefore, SDMA has advantages in that it is less dependent on muscle mass, although its behavior may be influenced by physiological changes in the hyperthyroid state. Therefore, clinical management should include careful observation before and after treatment, avoiding iatrogenic hypothyroidism, and instituting levothyroxine replacement.

In short, it is recommended that the veterinary clinic adopt personalized therapeutic plans for each case with periodic reassessments. In addition, attention is focused on research, which should prioritize studies capable of validating refined nutritional interventions, confirming the safety and efficacy of new pharmacological therapies, and establishing protocols that result in measurable clinical benefits for the long-term treatment of CKD in felines. CLICK

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