Reduced Dialysis Adherence and Greater Medication Use Associated with Increased Itch Severity

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Background

Individuals suffering from end-stage kidney disease encounter a wide range of physical and emotional symptoms associated with their condition. This substantial symptom load significantly disrupts their daily lives and has been linked to a decline in their overall health-related quality of life (HRQOL). One particularly common and distressing symptom is **chronic kidney disease–associated pruritus (CKD-aP)**, which affects approximately 50% of patients and ranks among the top ten most burdensome symptoms reported by individuals on dialysis [1].

There has been some interest in exploring the use of antidepressants as a potential treatment for patients with severe and unresponsive pruritus in various chronic health conditions [2], [3]. Additionally, gabapentinoids, typically prescribed for neuropathic pain, have shown promise in relieving pruritus [4]. Nevertheless, it's important to note that **neither antidepressants, antihistamines, nor systemic gabapentinoids have demonstrated consistent success in reducing the intensity of CKD-aP, and their utilization for this particular condition lacks a solid evidence base** [5], [6].

Objectives

CKD-aP is an underdiagnosed condition among patients on hemodialysis. As it is unclear whenever this has economic implications, the purpose of this analysis was to **investigate the healthcare resource utilization (HRU) in relation to the CKD-aP intensity** from patients-records from Fresenius Medical Care centers across five European Countries.

Methods

From September 2021 all clinics belonging to the FMC Nephrocare network in France, Ireland, Italy, Spain and UK, introduced a quality improvement program addressing HRQoL issues experienced by patients on dialysis (ePROM-CQI). The questionnaire pack included the KDQOL-36, the 5-D Itch questionnaire and an ad hoc, 12 item scale tapping intradialytic symptoms.

The present analysis is a **retrospective cohort study assessing medication prescription pathways for patients experiencing different degrees of CKD-aP** in the first screening wave of the ePROM-CQI program. The index date of the study was the survey administration. Healthcare utilization data and medication prescription for each patient were collected in the 12 months after the index date. Pruritus was classified in 5 severity classes (not present to very severe). Prescription of systemic pruritus medications, gabapentinoids, and antidepressants 3, 6 and 12 months after survey administration, was assessed by ATC codes. We assessed the association between CKD-aP level and HRU with mixed-effect generalized linear models adjusting for potential confounders such as age, vintage, gender, country of residence, comorbidities. Chi-square test was used for comparison between groups. All the statistical analyses were conducted using SAS 9.4.

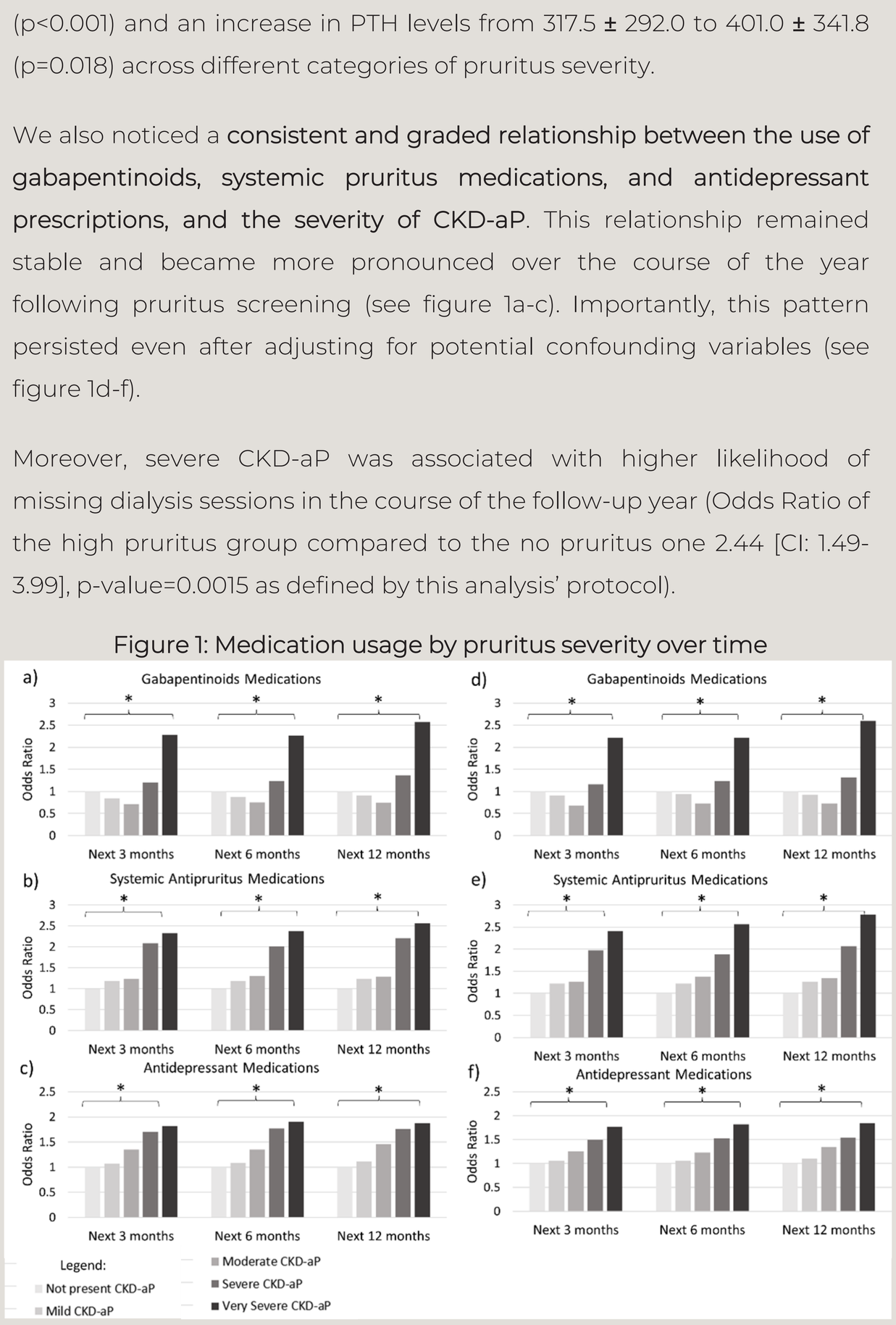
Results

The study included data from 6,262 patients, with an average age of 68.7 ± 13.9 years and a dialysis vintage of 5.4 ± 5.9 years. Approximately 63% of the patients were male, and around 62% of them received hemodiafiltration as their treatment. We observed a notable trend of increasing calcium-phosphate product from 39.3 ± 12.2 to 42.4 ± 13.2 ($p<0.001$) and an increase in PTH levels from 317.5 ± 292.0 to 401.0 ± 341.8 ($p=0.018$) across different categories of pruritus severity.

We also noticed a **consistent and graded relationship between the use of gabapentinoids, systemic pruritus medications, and antidepressant prescriptions, and the severity of CKD-aP**. This relationship remained stable and became more pronounced over the course of the year following pruritus screening (see figure 1a-c). Importantly, this pattern persisted even after adjusting for potential confounding variables (see figure 1d-f).

Moreover, severe CKD-aP was associated with higher likelihood of missing dialysis sessions in the course of the follow-up year (Odds Ratio of the high pruritus group compared to the no pruritus one 2.44 [CI: 1.49-3.99], p-value=0.0015 as defined by this analysis' protocol).

Figure 1: Medication usage by pruritus severity over time



Conclusions

CKD-aP is associated with increased use of gabapentinoids, antidepressants and other systemic anti-pruritus medications. While we cannot rule out the possibility that gabapentinoids and antidepressants have been prescribed to address legitimate medical conditions, existing evidence indicates that physicians may also prescribe these medications in an effort to alleviate CKD-aP. These findings underline the **need to educate on treatment strategies to address CKD-aP and the need to disseminate evidence-based treatment pathways for this condition.**

References: 1. E. van der Willik et al., Itching in dialysis patients: impact on health-related quality of life and interactions with sleep problems and psychological symptoms—results from the RENINE/PROMs registry, NDT, Volume 37, Issue 9, September 2022, Pages 1731–1741; 2. X. Hu et al. Prevalence of chronic kidney disease-associated pruritus among adult dialysis patients A meta-analysis of cross-sectional studies, Med. (United States), vol. 97, no. 21, p. e10633, 2018; 3. T. A. Kouwenhoven et al. Use of oral antidepressants in patients with chronic pruritus: A systematic review, J. Am. Acad. Dermatol., vol. 77, no. 6, pp. 1068-1073.e7, Dec. 2017; 4. Z. M. Lipman et al. Clinical management of chronic kidney disease-associated pruritus: current treatment options and future approaches, Clin. Kidney J., vol. 14, no. Suppl 3, p. i16, Dec. 2021; 5. E. Simonsen et al. Treatment of Uremic Pruritus: A Systematic Review, Am. J. Kidney Dis., vol. 70, no. 5, pp. 638–655, Nov. 2017.

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