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Original article

Analysis of the carbon footprint of pharmacological treatments in advanced chronic kidney disease and peritoneal dialysis: Oral vs. subcutaneous administration

Análisis de la huella de carbono de los tratamientos farmacológicos en enfermedad renal crónica avanzada: administración oral vs. subcutánea

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ABSTRACT

Background: Carbon footprint quantification currently stands as the most accepted model for assessing the ecological impact of human activities.

Selecting the most environmentally friendly treatment for pathologies arising from advanced chronic kidney disease can reduce the carbon footprint.

Methods: We aimed to analyze the carbon footprint from using subcutaneous administration treatments versus oral medication in patients with the same medical condition: advanced chronic kidney disease (ACKD) (CKD stage 4 or 5 not in dialysis) or peritoneal dialysis (PD).

This is an observational, cross-sectional study with 41 patients, 19 receiving oral medication (cinacalcet), and 22 subcutaneously administered erythropoiesis-stimulating agent (darbepoetin alfa). Both treatments were dispensed at the Hospital Clínico Universitario de Valencia internal pharmacy.

The carbon footprint was calculated using analytical techniques from hybrid life cycle models of the studied medications. For this analysis, three groups were considered: patient and supplies transportation, energy, and waste disposal.

Results: A total of 41 patients were included, with a median age of 72 years (IQR: 63–80). No significant between-group differences were detected in analytical parameters. The overall carbon footprint derived from the subcutaneous treatment process with erythropoiesis-stimulating agents (ESA) was 95,512.93 kg of CO_2/year, compared to 12,199.85 kg of CO_2/year resulting from cinacalcet treatment ($p < 0.001$). Group-wise analysis did not detect significant differences in travel-related consumption. However, in waste generation and transportation, ESA use showed a significantly higher carbon footprint than oral medication use ($p < 0.001$), partly attributable to the refrigeration energy consumption of darbepoetin (inexistent for cinacalcet).

Conclusions: The use of drugs not requiring subcutaneous administration with syringes could significantly reduce healthcare-related carbon footprint.

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Palabras clave:
Huella de carbono
Enfermedad renal crónica
Estudio trasversal
Nefrología verde
Diálisis peritoneal

RESUMEN

Antecedentes: La cuantificación de la huella de carbono es actualmente el método con mayor aceptación para evaluar el impacto ecológico de las actividades humanas.

Seleccionar el tratamiento más respetuoso con el medio ambiente para las patologías derivadas de la enfermedad renal crónica avanzada puede ayudar a reducir la huella de carbono.

Métodos: Nuestro objetivo fue analizar la huella de carbono derivada del uso de tratamientos de administración subcutánea frente a la medicación oral en pacientes con la misma condición médica: enfermedad renal crónica avanzada (ERCA) (estadio de ERC 4 o 5 no en diálisis) o diálisis peritoneal (DP).

Se trata de un estudio observacional y transversal con 41 pacientes, 19 de los cuales recibían medicación oral (cinacalcet), y 22 un agente estimulante de la eritropoyesis administrado por vía subcutánea (darbepoetina alfa). Ambos tratamientos fueron dispensados en la farmacia hospitalaria del Hospital Clínico Universitario de Valencia.

La huella de carbono se calculó mediante técnicas analíticas de modelos híbridos de ciclo de vida de los medicamentos estudiados. Para este análisis se consideraron tres grupos: transporte de pacientes y suministros, consumo de energía y eliminación de residuos.

Resultados: Se incluyeron un total de 41 pacientes, con una mediana de edad de 72 años (rango intercuartílico: 63–80). No se detectaron diferencias significativas entre los grupos en los parámetros analíticos. La huella de carbono global derivada del proceso de tratamiento subcutáneo con agentes estimulantes de la eritropoyesis (AEE) fue de 95.512,93 kg de CO_2/año, en comparación con los 12.199,85 kg de CO_2/año resultantes del tratamiento con cinacalcet.

El análisis por grupos no detectó diferencias significativas en el consumo relacionado con los desplazamientos. Sin embargo, en la generación y transporte de residuos, el uso de AEE mostró una huella de carbono significativamente mayor que el uso de medicación oral, atribuible en parte al consumo de energía por refrigeración de la darbepoetina (inexistente en el caso del cinacalcet).

Conclusiones: El uso de fármacos que no requieren refrigeración ni procesos complejos de eliminación de residuos, reduce significativamente el impacto ambiental de las actividades sanitarias.

Introduction

Climate change has been classified as "the greatest global threat to health in the 21st century".[1] The current most accepted model for assessing the ecological impact of businesses and healthcare systems is carbon footprint quantification.[2] This calculation is the sum of direct and indirect greenhouse gas emissions resulting from a specific activities and processes, and its result is expressed in kg of CO_2, as this gas represents 80% of emissions.[3]

Renal replacement therapies have a significant impact on the carbon footprint of healthcare systems, especially in terms of supply chains and waste management.[4] Hemodialysis is one of the main contributors to energy consumption, greenhouse gas emissions, water consumption, and waste generation within the healthcare system.[5] Even if peritoneal dialysis (PD) consumes less water/energy than hemodialysis, it also generates a significant amount of plastic waste (tubing, bags) and logistical transport emissions. Establishing new management strategies based on greener nephrology is therefore essential for carbon footprint reduction.[6]

Apart from renal replacement therapy, CKD patient care has a further environmental impact due to the need for periodic visits to centres and the use of refrigerated or injectable medications that require increased waste management and electricity compsumption.[7] Even though every drug has an environmental impact, oral option's footprint is primarily driven by manufacturing (pharmaceutical industry emissions) and packaging (blisters/boxes), rather than the frequent patient transport associated with hospital-administered injectables or the energy consumption linked to refrigeration. Erythropoiesis-Stimulating Agents (ESAs) like Darbepoetin alfa require cold storage, and subcutaneous administration with frequencies ranging from weekly to monthly, necessitating specific logistical arrangements (hospital pharmacy collection or administration visits) that contribute to the carbon footprint.

Choosing a more environmentally friendly treatment for ACKD-related pathologies can have a positive impact on the amount of waste generated and energy consumed. Our objective was to compare the carbon footprint derived from the use of oral medication and subcutaneous injectable treatments (darbepoetin alfa) in patients with ACKD or on peritoneal dialysis, aiming to prescribe treatments tailored to patient needs and reduce the carbon footprint in the future. We hypothesized that the carbon footprint associated with subcutaneous hospital-dispensed treatments would be significantly higher than that of oral pharmacy-dispensed treatments, primarily driven by transportation, energy consumption due to refrigeration and waste management, and patient mobility requirements.

Materials and methods

In this observational, cross-sectional, single-centre, non-interventional study we compared two cohorts (both including patients with either ACKD or on PD) receiving hospital-dispensed medication. One group received oral medication (cinacalcet) and the other group received a subcutaneously administered erythropoiesis-stimulating agent (darbepoetin alfa). Cinacalcet was indicated for treatment of hyperparathyroidism secondary to chronic kidney disease, while darbepoetin alfa was indicated for anaemia secondary to chronic kidney disease. The study was approved by the Institutional Review Board of the Hospital Clínico Universitario de València (2022/306), and informed consent was obtained from all patients.

Patients collecting medication between 1st February and 1st May 2023 were selected for study using the following inclusion criteria: patients on a PD programme or with ACKD (estimated glomerular filtration rate < 30 ml/min/1.73 m^2), aged 18 and above, and capable of signing informed consent (Fig. 1). Clinical and demographic data were obtained through patients' electronic health records, and carbon footprint-related data were collected through surveys with targeted questions (Supplementary material). We adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (**STROBE**) reporting guideline. A completed STROBE checklist is provided (Supplementary material).

Carbon footprint calculation

The carbon footprint was calculated using analytical techniques based on hybrid life cycle models of the medications under study. The

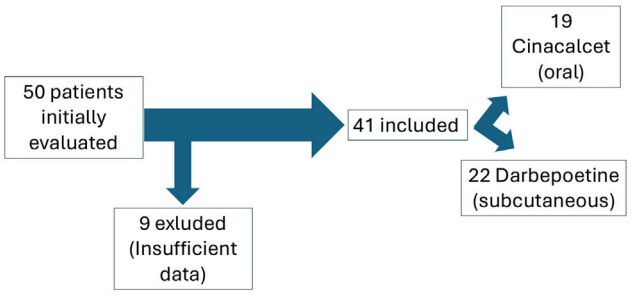

Fig. 1. Flowchart.

total carbon footprint for each treatment is the sum of the carbon footprint derived from three groups of variables: transportation, energy usage, and waste management.

According to GHG Protocol and relevant ISO 14040/14044 standards for Life Cycle Assessment (LCA), the carbon footprint was calculated for each group of variables using the formula *activity data* × *emission factor*, where the activity data is the parameter defining emission-generating activity, and the emission factor is the quantity of gases emitted per unit of activity.

1. Transportation

This item includes supplies transportation and patient travel to hospital.

The activity value for transport by car and taxi was litres of fuel consumed across all trips in a year. The emission factor value was obtained from the Ministry for Ecological Transport official database and varied according to whether the fuel was diesel (B7) or gasoline (E5).[8]

For public transport, the activity value was the number of kilometres travelled multiplied by the corresponding emission factor published by the Ministry of Health. Cases of patients not travelling to hospital by any vehicle were recorded as 0 kg CO_2.

Finally, the total calculation was reached by adding the CO_2 values emitted during patient travel.

For supplies transportation we included data on vehicle type and refrigeration requirements obtained from the pharmacy department.

2. Energy usage:

Calculations were performed using energy storage and usage data provided by the pharmacy department, following the same methodology of multiplying the activity value (KW/h) by the corresponding emission factor.

3. Waste:

The waste variable was based primarily on patient waste management and transportation for disposal.

Calculations for waste transportation were made using hospital pharmacy department data (distance in km from the supplier, trips/year, and vehicle type), while waste disposal values were determined via data obtained in the patient survey and from the pharmacy department (frequency of waste disposal, company responsible, and disposal method). Incineration data were obtained using the SCOPE CO_2 application (https://www.scopeco2.org/tool/).

Statistical analysis

Qualitative variables are expressed as frequencies, and quantitative variables as mean and standard deviation (SD) or median and interquartile range (IQR), depending on the distribution. Between-group differences were assessed with the Student *T* or Mann–Whitney *U* test for quantitative variables and the Chi-square or Fisher's exact test for qualitative variables. A p-value < 0.05 was defined as significant.

Results

Of the 50 patients initially evaluated, 41 patients were included (Fig. 2). Patients included had a median age of 72 years [IQR 63–80]; 65% were male, 66% (28) were on peritoneal dialysis, 34% (13) were

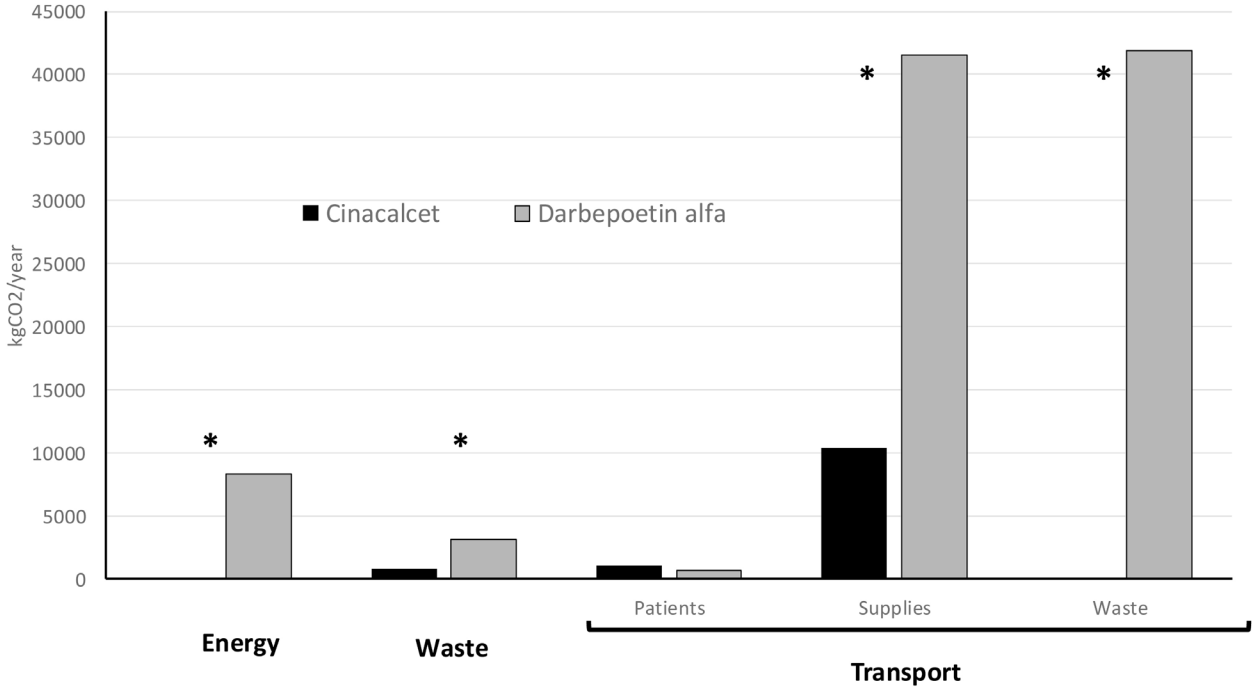

Fig. 2. Global carbon footprint of darbepoetin alfa and cinacalcet. * $p < 0.05$.

Table 1
Baseline characteristics of patients by treatment group.

	Cinacalcet (n = 19)	Darbepoetin alfa (n = 22)	p-Value
Age, years (median, IQR)	73 (65–83)	64 (58–80)	**0.02**
Male sex, n (%)	13 (68)	14 (64)	0.74
Clinical status, n (%)			0.17
Peritoneal dialysis	15 (79)	13 (59)	
ACKD	4 (21)	9 (41)	
Creatinine (mg/dl)	5.42 (4.2–6.6)	3.37 (2.8–3.9)	0.19
eGFR (ml/min/1.73 m^2)	11.0 (7–11.7)	13.6 (12.1–15.3)	0.86
Phosphorus (mg/dl)	5.9 (4.1–6.2)	4.1 (3.6–4.7)	0.22
Parathyroid hormone (pg/ml)	208 (182–317)	185 (149–273)	0.44
Haemoglobin (g/dl)	12.4 (11.9–13.2)	12.0 (11.4–12.4)	0.35

Data represented as median, interquartile range (IQR), frequency or percentages. ACKD: advanced kidney disease. eGFR: estimated glomerular fitltration rate.

ACKD patients. 19 were undergoing treatment with cinacalcet (oral), and 22 were treated with darbepoetin alfa (subcutaneous).

Patients baseline characteristics according to treatment group are presented in Table 1.

The carbon footprint derived from the subcutaneous treatment process with darbepoetin alfa was 95,512.93 kg of CO_2/year, compared to the 12,199.85 kg of CO_2/year generated from treatment with cinacalcet (p-value 0.00). The contribution of each analyzed group to the carbon footprint is shown in Fig. 2.

The group with the greatest impact on the carbon footprint was transportation of erythropoiesis-stimulating agents (ESA), at 42,224.55 kg CO_2/year compared to 11,399.85 kg CO_2/year derived from cinacalcet consumption.

There were no significant between-group differences in carbon footprint from patient travel to the hospital for medicine collection (Table 2).

The second-largest contribution to the carbon footprint was derived from darbepoetin waste management, resulting in 55,001.42 kg CO_2/year, compared to just 800 kg CO_2/year with cinacalcet, due to sharps and needle processing and disposal (Fig. 2 and Table 2).

The median carbon footprint in waste generation for patients taking cinacalcet was lower, at 36.4 kg CO_2/year (IQR 36.3–36.5) compared to patients treated with darbepoetin alfa at 132 kg CO_2/year (IQR 93.5–143) with a p-value < 0.00 (Table 2).

Finally, the only energy-related variable calculated was darbepoetin alfa refrigeration, with total emissions amounting to 8286.96 kg CO_2/year (Fig. 2).

Discussion

Our results show that the carbon footprint of darbepoetin alfa (subcutaneously administered medication) is significantly higher than that of cinacalcet treatment (oral medication), largely driven by refrigerated transport and waste disposal, indicating a lower environmental impact for the oral administration route.

Carbon footprint modelling is a potentially fundamental tool in hospital management to reduce the environmental impact of medical treatments. The healthcare sector should take the lead in promoting sustainable practices, since changes in high-volume procedures could have a particularly significant impact on emissions.[7]

However, research on this area is scarce. Our findings align with existing literature comparing different drug administration pathways. For instance, Bouvet et al. MC highlight that oral administration results in significantly lower carbon emissions and water consump-

Table 2
Differences in carbon footprint stratified by groups.

	Cinacalcet (n = 19)	Darbepoetin alfa (n = 22)	p-Value
Transport			
Distance (km) Median (IQR)	10 (4–40)	10 (6.7–26)	0.66
Number of journeys per year. Median (IQR)	3 (2–4)	3 (2–4)	0.88
Drug collection + visit, n (%)	14 (74)	16 (73)	1
Drug collection only, n (%)	19 (100)	22 (100)	1
Journey by car, n (%)	7 (36)	6 (27)	0.75
Car fuel type			0.19
Diesel, *n* (%)	4 (57)	6 (100)	
Gasoline, *n* (%)	3 (43)	0 (0)	
Public transport, n (%)	8 (42)	11 (50)	0.56
Walking, n (%)	2 (10.5)	1(4.5)	0.58
Taxi, n (%)	2 (10.5)	4 (18)	0.66
CF, kg CO_2/year (median)	10.20 (2.08–24.5)	15.97 (5.25–28.66)	0.45
Waste disposal			
Waste container	Organic: 0 Plastic: 5 (26.3%) Cardboard:10 (52.6%) Sanitary container: 0 Unknown:4 (21.0%)	Organic: 1(4.5%) Plastic: 3 (13.6%) Cardboard: 6 (27.3%) Sanitary container: 9 (40.9%) Unknown: 3 (13.6%)	0.02
CF (Energy) kg CO_2/year (median)	36.4 (36.3–36.5)	132 (93.5–143)	<0.001
Electric energy consumption			
CF (Energy) kg CO_2/year (median)	0	355.1 (251.5–384.7)	<0.001

Data expressed as median and interquartile range or frequencies and percentages.
CF: carbon footprint.

tion.[9] A randomized noninferiority trial found that emissions for comparable phosphate replacement in critically ill patients, were 60-fold less for the enteral route (14.2 g of CO_2e) compared to the IV route (843 g of CO_2e).[10]

To date, this is the first study to compare the carbon footprint of subcutaneous and oral administration treatments in patients with ACKD or on PD. The comparison refers strictly to the environmental footprint of the administration process, not the clinical equivalence of the drugs.

Although no studies have calculated the carbon footprint of patients in pre-dialysis-phase CKD, several have analyzed this problem in patients on hemodialysis due to the great impact of this treatment, particularly the high water use. Studies of ways to reduce carbon footprint in haemodialysis units are centred mainly in the United Kingdom, where a list of guidelines for more sustainable practices has been published, focused on patient, staff, and supplies transportation, reducing energy expenditure and improving waste management via reduction, reuse, and recycling.[11] In addition to reducing the carbon footprint of the British healthcare system, implementing these guidelines would result in a saving of one billion pounds.[12] Our study shows that the use of oral medication, even if dispensed by hospitals, can reduce the carbon footprint of each of these variables and improve the sustainability of renal treatments.

The main limitations of this study are the lack of national-level studies on carbon footprint in the healthcare sector, the difficulty in obtaining data, and that emissions from medication production were likely underestimated due to the absence of available data for carbon footprint calculation. Nonetheless, the clear difference in carbon footprint between the two treatment types strongly suggest that oral treatments are more sustainable.

Another limitation is the small simple size. While the observational nature of the study and the absence of exceptional interventions could theoretically have allowed for a larger cohort, this work was conceived as a pilot study intended to explore the feasibility and applicability of hybrid life-cycle assessment models in nephrology practice.

This study should be regarded as a pilot study for comprehensive carbon footprint calculation from the ground up, with the objective of analysing and standardizing this parameter, thereby initiating measures to curb the acceleration of climate change. These measures are aimed at reducing the carbon footprint of renal treatments in hospital nephrology departments. Multicentre prospective studies, preferably using a similar methodology to that of our research, are imperative to validate our findings.

In conclusion, choosing an oral administration treatment in patients with ACKD or PD can reduce the carbon footprint derived from their medical treatment by as much as 85%. The overarching goal is to establish environmentally sustainable practices that contribute towards the ultimate target of net-zero carbon emissions. Focused not only on economic considerations and advancing eco-friendly medical practices, this initiative also strives to enhance clinical care and improve patient outcomes.

Key learning points

- Given the significant impact of kidney replacement therapies on the carbon footprint of healthcare systems, selecting the most environmentally friendly treatment for pathologies arising from advanced chronic kidney disease is crucial.
- The use of drugs not requiring subcutaneous administration with syringes could significantly reduce healthcare-related carbon footprint.
- Our results shed light on the environmental impact of a common medical practice in nephrology, and provide valuable insights for healthcare professionals, policy-makers, and researchers aiming to develop more sustainable approaches to patient care.

Conflicts of interest

The authors have no conflicts of interest to declare. All co-authors have seen and agree with the contents of the manuscript and there is no financial interest to report. We certify that the submission is original work and is not under review at any other publication.

The data underlying this article will be shared on reasonable request to the corresponding author.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.nefro.2026.501504.

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