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Osteoporotic fractures associated with prolonged use of proton pump inhibitors in the geriatric population: a systematic review

Fracturas osteoporóticas asociadas al uso prolongado de inhibidores de la bomba de protones en población geriátrica: revisión sistemática

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Abstract

Proton pump inhibitors (PPIs) are widely used medications for the treatment of acid-related disorders; however, their prolonged use in the geriatric population has been associated with adverse effects on bone metabolism. Chronic suppression of gastric acid may interfere with the absorption of nutrients essential for bone health, which, together with age-related physiological changes, polypharmacy, and the presence of osteoporosis, increases the risk of fragility fractures. The objective of this systematic review was to identify the most frequent fractures associated with prolonged PPI use in older adults with osteoporosis and to analyze the relationship between treatment duration and fracture risk. A systematic review was conducted in accordance with the PRISMA 2020 guidelines, using databases such as PubMed, Scopus, Web of Science, and ScienceDirect. Following the screening process, nine studies published between 2019 and 2025 were included, and odds ratios, relative risks, and hazard ratios were analyzed. The results demonstrated a consistent association between prolonged PPI use and an increased risk of osteoporotic fractures, particularly hip and vertebral fractures. The risk was higher with exposures of 12 months or longer, in postmenopausal women, and in patients with comorbidities or concomitant treatments. These findings support the need to critically evaluate the indication and duration of PPI therapy in older adults at risk of osteoporosis

Keywords: osteoporotic fractures; proton pump inhibitors; osteoporosis; older adults; systematic review

Resumen

Los inhibidores de la bomba de protones (IBP) son fármacos ampliamente utilizados para el tratamiento de enfermedades ácido-pépticas; sin embargo, su uso prolongado en la población geriátrica se ha asociado con efectos adversos sobre el metabolismo óseo. La supresión crónica del ácido gástrico puede interferir con la absorción de nutrientes esenciales para la salud ósea, lo que, aunado a los cambios fisiológicos del envejecimiento, la polifarmacia y la presencia de osteoporosis, incrementa el riesgo de fracturas por fragilidad. El objetivo de esta revisión sistemática fue identificar las fracturas más frecuentes asociadas al uso prolongado de IBP en adultos mayores con osteoporosis y analizar la relación entre la duración del tratamiento y el riesgo de fractura. Se realizó una revisión sistemática conforme a las directrices PRISMA 2020, utilizando bases de datos como PubMed, Scopus, Web of Science y ScienceDirect. Tras el proceso de cribado, se incluyeron nueve estudios publicados entre 2019 y 2025, analizándose razones de momios, riesgos relativos y razones de riesgo. Los resultados mostraron una asociación consistente entre el uso prolongado de IBP y un mayor riesgo de fracturas osteoporóticas, especialmente de cadera y columna vertebral. El riesgo fue mayor en exposiciones iguales o superiores a 12 meses, en mujeres posmenopáusicas y en pacientes con comorbilidades o tratamientos concomitantes. Estos hallazgos respaldan la necesidad de evaluar de forma crítica la indicación y duración del tratamiento con IBP en adultos mayores con riesgo osteoporótico.

Palabras clave: fracturas osteoporóticas; inhibidores de la bomba de protones; osteoporosis; adultos mayores; revisión sistemática

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INTRODUCTION

Proton pump inhibitors (PPIs) are widely used medications for suppressing gastric acid secretion in various acid-related disorders, including gastroesophageal reflux disease, functional dyspepsia, and gastric and duodenal ulcers.Prolonged and inappropriate PPI use in the geriatric population has been associated with significant adverse effects on bone tissue. These effects are related to physiological changes associated with aging, polypharmacy, and the indiscriminate use of these medications, which can lead to chronic suppression of gastric acid and interfere with the absorption of key nutrients involved in bone metabolism.Together, these mechanisms, combined with the presence of osteoporosis, significantly increase the risk of fragility fractures in older adults.

OBJETIVE

General Objective
To determine the most frequent fractures associated with long-term PPI use in geriatric patients with osteoporosis.

Specific Objectives
To identify available evidence regarding the association between prolonged PPI use and bone complications in older adults with osteoporosis.
To analyze the effect of duration of PPI treatment on the risk of developing osteoporotic fractures in older adults.de presentar fracturas óseas en adultos mayores con osteoporosis.

METHODOLOGY

A systematic review was conducted following the PRISMA 2020 guidelines. Inclusion and exclusion criteria were established according to the research question structured under the PICO framework.Literature searches were performed in PubMed, Scopus, Web of Science, and ScienceDirect, using MeSH terms and Boolean operators.The search strategy identified 571 records, followed by screening (illustrated in Figure 1). After full-text review, nine studies published between 2019 and 2025 were included in the final analysis.From the selected studies, relevant data were extracted including odds ratios (OR), hazard ratios (HR), and relative risks (RR) to evaluate the association between exposure to PPIs and fracture risk. Particular emphasis was placed on studies evaluating participants diagnosed with osteoporosis.

RESULTS

Nine studies were included (cohort studies, case-control studies, nested case-control studies, systematic reviews, meta-analyses, and pharmacovigilance analyses) evaluating the association between PPI use and osteoporotic fracture risk in older adults.

Most studies involved populations aged ≥65 years, and many adjusted their analyses for osteoporosis diagnosis.

All studies reported a positive association between prolonged PPI use and fractures, particularly involving the:

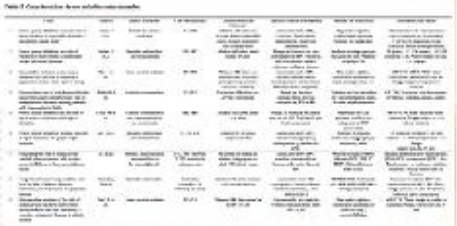
- Hip
- Vertebral columna
- Wrist
- Humerus

A dose–duration relationship was observed in multiple studies, with risk increasing in exposures ≥12 months.

Key findings include:
Kim et al. (2020): OR = 1.15 for osteoporotic fracture in women ≥65 years, increasing to 1.72 with ≥1 year of PPI use.
Meta-analyses (Robert et al.; Liu et al.):

- Hip fracture risk: RR 1.22–1.57
- Vertebral fracture risk: RR 1.38–1.49

Concomitant therapy with PPIs and glucocorticoids or bisphosphonates further increased fracture risk.
Pharmacovigilance data (Di et al., 2023) identified safety signals for esomeprazole and omeprazole, particularly among women and older adults.
Park et al. (2023) found higher fracture risk among PPI users compared with H_2 receptor antagonist users (aOR 1.13).



CONCLUSIONS

The results of this study consistently demonstrate that long-term proton pump inhibitor use is associated with an increased risk of osteoporotic fractures in the geriatric population.Hip and vertebral fractures were the most frequent and clinically relevant outcomes. A positive relationship was identified between treatment duration and fracture risk, particularly in patients exposed to PPIs for 12 months or longer.Postmenopausal women and older adults with comorbidities or concomitant treatments represent the most vulnerable groups.Overall, current evidence supports a consistent association between prolonged PPI use and osteoporotic fracture risk in older adults, especially in patients with osteoporosis or other chronic risk factors.

REFERENCE