

COMPARISON BETWEEN ANABOLIC AND ANTIRESORPTIVE THERAPIES IN OSTEOPOROSIS: ANTIFRACTURE EFFICACY AND THERAPEUTIC STRATEGY

COMPARAÇÃO ENTRE TERAPIAS ANABÓLICAS E ANTI-REABSORPTIVAS NA OSTEOPOROSE: EFICÁCIA ANTIFRATURA E PLANO TERAPÊUTICO

COMPARACIÓN ENTRE TERAPIAS ANABÓLICAS Y ANTIRRESORPTIVAS EN LA OSTEOPOROSIS: EFICACIA ANTIFRACTURA Y PLAN TERAPÉUTICO



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ABSTRACT

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Osteoporosis is a metabolic bone disease characterized by reduced bone mineral density and deterioration of bone microarchitecture, which significantly increases the risk of fragility fractures. In this context, different pharmacological approaches have been used in the treatment of the disease, particularly antiresorptive and anabolic therapies. The present study aimed to compare the antifracture efficacy of these therapies and discuss their implications for therapeutic planning in patients with osteoporosis. This study is an integrative literature review conducted using the PubMed/MEDLINE, SciELO, and ScienceDirect databases. Articles published between 2016 and 2026, available in full text in Portuguese or English, addressing the effectiveness of anabolic and antiresorptive therapies in preventing osteoporotic fractures were included. After applying the inclusion and exclusion criteria, 15 scientific studies were selected to compose the final sample of the review. The results indicated that antiresorptive therapies remain widely used as first-line treatment due to their proven effectiveness in reducing the risk of vertebral, non-vertebral, and hip fractures. On the other hand, anabolic therapies have shown significant benefits in patients with severe osteoporosis or at high fracture risk, promoting greater increases in bone mineral density. In addition, recent evidence suggests that sequential therapeutic strategies, involving initial use of anabolic agents followed by antiresorptive drugs, may provide better clinical outcomes. It is concluded that both therapeutic classes play an important role in the management of osteoporosis, highlighting the importance of individualized treatment according to each patient's clinical profile and fracture risk.

Keywords: Osteoporosis. Anabolic Therapy. Antiresorptive Therapy. Fracture Prevention. Osteoporosis Treatment.

RESUMO

A osteoporose é uma doença metabólica óssea caracterizada pela redução da densidade mineral óssea e pela deterioração da microarquitetura do tecido ósseo, fatores que aumentam significativamente o risco de fraturas por fragilidade. Nesse contexto, diferentes abordagens farmacológicas têm sido utilizadas no tratamento da doença, destacando-se as terapias antirreabsortivas e as terapias anabólicas. O presente estudo teve como objetivo comparar a eficácia antifratura dessas terapias e discutir suas implicações na definição do plano terapêutico em pacientes com osteoporose. Trata-se de uma revisão integrativa da literatura realizada nas bases de dados PubMed/MEDLINE, SciELO e ScienceDirect. Foram incluídos artigos publicados entre 2016 e 2026, disponíveis na íntegra, em português ou inglês, que abordassem a eficácia das terapias anabólicas e antirreabsortivas na prevenção de fraturas osteoporóticas. Após a aplicação dos critérios de inclusão e exclusão, foram selecionados 15 estudos científicos para compor a amostra final da revisão. Os resultados indicaram que as terapias antirreabsortivas permanecem amplamente utilizadas como tratamento inicial, devido à sua eficácia comprovada na redução do risco de fraturas vertebrais, não vertebrais e de quadril. Por outro lado, as terapias anabólicas têm demonstrado benefícios relevantes em pacientes com osteoporose grave ou com alto risco de fraturas, promovendo aumento mais expressivo da densidade mineral óssea. Além disso, evidências recentes sugerem que estratégias terapêuticas sequenciais, envolvendo o uso inicial de agentes anabólicos seguido por medicamentos antirreabsortivos, podem proporcionar melhores resultados clínicos. Conclui-se que ambas as classes terapêuticas desempenham papel importante no manejo da osteoporose, sendo fundamental a individualização do tratamento de acordo com o perfil clínico e o risco de fratura de cada paciente.

Palavras-chave: Osteoporose. Terapias Anabólicas. Terapias Antirreabsortivas. Prevenção de Fraturas. Tratamento da Osteoporose.

RESUMEN

La osteoporosis es una enfermedad metabólica ósea caracterizada por una densidad mineral ósea reducida y un deterioro de la microarquitectura del tejido óseo, factores que aumentan significativamente el riesgo de fracturas por fragilidad. En este contexto, se han utilizado diferentes enfoques farmacológicos en el tratamiento de la enfermedad, destacando las terapias antirresortivas y anabólicas. Este estudio tuvo como objetivo comparar la eficacia antifractura de estas terapias y discutir sus implicaciones en la definición del plan terapéutico en pacientes con osteoporosis. Se trata de una revisión bibliográfica integradora realizada en las bases de datos PubMed/MEDLINE, SciELO y ScienceDirect. Se incluyeron artículos publicados entre 2016 y 2026, disponibles en texto completo, en portugués o inglés, que abordaran la eficacia de las terapias anabólicas y antirresortivas en la prevención de fracturas osteoporóticas. Tras aplicar los criterios de inclusión y exclusión, se seleccionaron 15 estudios científicos para conformar la muestra final de la revisión. Los resultados indicaron que las terapias antirresortivas siguen siendo ampliamente utilizadas como tratamiento inicial debido a su eficacia comprobada en la reducción del riesgo de fracturas vertebrales, no vertebrales y de cadera. Por otro lado, las terapias anabólicas han demostrado beneficios relevantes en pacientes con osteoporosis grave o con alto riesgo de fracturas, promoviendo un aumento más significativo de la densidad mineral ósea. Además, evidencia reciente sugiere que las estrategias terapéuticas secuenciales, que incluyen el uso inicial de agentes anabólicos seguido de medicamentos antirresortivos, pueden proporcionar mejores resultados clínicos. Se concluye que ambas clases terapéuticas desempeñan un papel importante en el manejo de la osteoporosis, y la individualización del tratamiento según el perfil clínico y el riesgo de fractura de cada paciente es fundamental.

Palabras clave: Osteoporosis. Terapias Anabólicas. Terapias Antirresortivas. Prevención de Fracturas. Tratamiento de la Osteoporosis.

1 INTRODUCTION

Osteoporosis is a bone metabolic disease characterized by decreased bone mineral density and deterioration of the microarchitecture of bone tissue, factors that significantly increase the risk of fragility fractures. It is an important public health problem, especially in aging populations, and is more prevalent in postmenopausal women due to the reduction in estrogen levels, which accelerates the bone resorption process. It is estimated that the disease is associated with high morbidity, mortality, and costs for health systems, especially as a result of vertebral and hip fractures, which significantly compromise the functionality and quality of life of patients (GATTI; FASSIO, 2019; LORENTZON, 2019; HASSAN; GREGSON; TOBIAS, 2021).

From a pathophysiological point of view, osteoporosis is related to an imbalance in the bone remodeling process, in which the resorption activity carried out by osteoclasts exceeds the bone formation promoted by osteoblasts. This process results in the progressive loss of bone mass and structural fragility of the skeleton. Bone remodeling involves a complex system of cellular and molecular regulation, controlled by hormones, cytokines, and growth factors that directly influence the balance between bone formation and resorption. When there is an alteration in this balance, bone strength is compromised and the risk of osteoporotic fractures is increased (SOEN, 2020; MINISOLA et al., 2019; HASSAN; GREGSON; TOBIAS, 2021).

Among the main pharmacological approaches used in the treatment of osteoporosis, antiresorptive therapies, such as bisphosphonates and denosumab, and anabolic therapies, represented mainly by teriparatide, abaloparatide, and romosozumab, stand out. Antiresorptive drugs work by reducing osteoclastic activity and, consequently, bone resorption, contributing to the increase of bone mineral density and to the reduction of the risk of osteoporotic fractures. Clinical studies show that these therapies can reduce vertebral fractures by approximately 40% to 70% and hip fractures by up to 53% in women with postmenopausal osteoporosis (LORENTZON, 2019; DAVIS et al., 2020; HÄNDEL et al., 2023).

On the other hand, anabolic therapies directly promote bone formation through the stimulation of osteoblastic activity, contributing to the reconstruction of bone microarchitecture and to a more expressive increase in bone mass. Randomized controlled trials have shown that teriparatide can significantly reduce the risk of vertebral and clinical fractures when compared to risedronate in women with severe osteoporosis (GEUSENS et al., 2018; BODY et al., 2020). In addition, clinical studies have shown that romosozumab promotes a faster increase in bone mineral density and a significant reduction in vertebral

and nonvertebral fractures in postmenopausal women at high risk of fracture (LANGDAHL et al., 2017; MCCLUNG et al., 2023).

In view of this evidence, the scientific literature has emphasized the importance of individualizing treatment and choosing the most appropriate therapeutic strategy according to the patient's risk profile. Comparative studies and meta-analyses indicate that anabolic therapies may be more effective in reducing fractures in certain groups of patients, especially those with severe osteoporosis or very high risk of fracture, while antiresorptive therapies continue to be widely used as a first line of treatment and in maintaining the gains made with bone-forming therapies (HÄNDEL et al., 2023; SILVA et al., 2022; CALAF-ALSINA et al., 2023). In this context, understanding the differences between these therapeutic approaches becomes essential to guide clinical decision-making and optimize the management of osteoporosis.

In view of this scenario, it is relevant to systematically analyze the available evidence on the efficacy of the different therapeutic strategies used in the treatment of osteoporosis. Thus, the present study aims to perform an integrative review of the literature on the anti-fracture efficacy of anabolic and antiresorptive therapies in the treatment of osteoporosis, as well as to discuss its implications in the definition of the therapeutic plan in patients at increased risk of osteoporotic fractures.

2 METHODOLOGY

The present study is characterized as an integrative literature review, a method that enables the synthesis of available scientific knowledge on a given topic, allowing the critical analysis of previously published studies and the identification of gaps in knowledge. This type of review allows the gathering of research results with different methodological designs, contributing to a more comprehensive understanding of the phenomenon investigated and assisting in evidence-based clinical decision-making. The integrative review follows systematic steps that include the definition of the research question, the search in the literature, the evaluation of the selected studies and the synthesis of the results (SOUZA; SILVA; CARVALHO, 2010).

The bibliographic search was carried out in internationally recognized scientific databases, including PubMed/MEDLINE, SciELO (Scientific Electronic Library Online) and ScienceDirect, selected for their relevance in the health area and for bringing together scientific journals of high impact in the production of biomedical knowledge. The search strategy was structured through the combination of controlled descriptors and keywords in English, based on the terms of the Medical Subject Headings (MeSH). The main descriptors

used were: *osteoporosis*, *anabolic therapy*, *antiresorptive therapy*, *teriparatide*, *romosozumab*, *denosumab*, *bisphosphonates*, and *fracture prevention*. These terms were combined using Boolean operators, especially the AND operator, in order to refine the results and identify studies related to the comparison between anabolic and antiresorptive therapies in the treatment of osteoporosis. An example of the search strategy used was: ("osteoporosis") AND ("anabolic therapy" OR "teriparatide" OR "romosozumab") AND ("antiresorptive therapy" OR "bisphosphonates" OR "denosumab") AND ("fracture prevention").

Inclusion and exclusion criteria were established for the selection of studies. As inclusion criteria, we considered scientific articles published in the last ten years (2016–2026), available in full, written in English or Portuguese, and addressing anti-fracture efficacy or the comparison between anabolic and anti-resorptive therapies in the treatment of osteoporosis. Randomized controlled trials, systematic reviews, meta-analyses, and observational studies relevant to the topic were included. As exclusion criteria, duplicate studies, articles that did not have a direct relationship with the research objective, case reports, editorials, letters to the editor, and studies with insufficient methodology or without access to the full text were discarded.

The article selection process took place in stages. Initially, the studies identified in the databases were screened by reading the titles and abstracts, with the objective of verifying their relevance in relation to the research theme. Then, the potentially eligible articles were submitted to full reading, in order to confirm the adequacy of the previously established inclusion criteria. After this screening and eligibility process, 15 scientific articles were selected, which composed the final sample of this integrative review.

Finally, the selected studies were analyzed systematically, considering information such as author, year of publication, type of study, population analyzed, therapeutic intervention, and main results related to anti-fracture efficacy and therapeutic strategies in the management of osteoporosis. The data extracted from the studies were organized and synthesized in a descriptive way, allowing the comparison between the different therapeutic approaches and the discussion of the scientific evidence available in the literature.

3 RESULTS

The search carried out in the PubMed/MEDLINE, SciELO and ScienceDirect databases initially resulted in the identification of several studies related to the pharmacological treatment of osteoporosis. After applying the established inclusion and exclusion criteria, as well as removing duplicate studies and analyzing eligibility by reading

titles, abstracts, and full texts, 15 scientific articles were selected, which made up the final sample of this integrative review.

The included studies presented different methodological designs, including randomized clinical trials, systematic reviews, meta-analyses, and observational studies, all aimed at evaluating the efficacy of pharmacological therapies used in the treatment of osteoporosis. Most of the studies analyzed focused on postmenopausal women, a population considered to be at higher risk for the development of the disease and for the occurrence of osteoporotic fractures.

With regard to antiresorptive therapies, several studies have shown that drugs such as bisphosphonates and denosumab act by reducing osteoclastic activity and, consequently, bone resorption, contributing to the increase of bone mineral density and to the reduction of the risk of vertebral, non-vertebral and hip fractures. Systematic reviews and meta-analyses show that these therapies have significant efficacy in preventing osteoporotic fractures, being widely used as a first-line treatment in patients with osteoporosis (DAVIS et al., 2020; HÄNDEL et al., 2023).

Regarding anabolic therapies, the studies analyzed indicated that drugs such as teriparatide, abaloparatide, and romosozumab act by directly stimulating bone formation through the activation of osteoblastic activity. Randomized controlled trials have shown teriparatide to be more effective than some bisphosphonates in reducing the risk of vertebral and clinical fractures in patients with severe osteoporosis (GEUSENS et al., 2018; BODY et al., 2020). In addition, more recent studies indicate that romosozumab promotes a faster increase in bone mineral density and a significant reduction in the risk of fractures in postmenopausal women at high risk of fracture (LANGDAHL et al., 2017; MCCLUNG et al., 2023).

In general, the analysis of the studies showed that anabolic therapies tend to promote a greater increase in bone mineral density and a more significant reduction in the risk of fractures in patients with severe osteoporosis or very high risk of fracture, while antiresorptive therapies remain widely used as an initial treatment strategy and in maintaining the gains obtained after bone-forming therapies. In this context, recent literature has highlighted the importance of sequential therapeutic strategies, in which anabolic treatment is followed by the use of antiresorptive drugs to maintain the benefits obtained in bone metabolism (HÄNDEL et al., 2023; SILVA et al., 2022).

4 DISCUSSION

The analysis of the studies included in this integrative review showed that anabolic and antiresorptive therapies play an important role in the treatment of osteoporosis, although they act by different mechanisms in the bone remodeling process. In general, the selected studies indicated that antiresorptive therapies remain widely used as an initial treatment, while anabolic therapies have been progressively indicated in patients with severe osteoporosis or at high risk of fractures (DAVIS et al., 2020; HÄNDEL et al., 2023; SILVA et al., 2022).

With regard to antiresorptive therapies, the studies included in this review have shown that drugs such as bisphosphonates and denosumab work by reducing osteoclastic activity, resulting in decreased bone resorption and increased bone mineral density. Systematic reviews and meta-analyses have shown that these therapies have significant efficacy in reducing the risk of vertebral, nonvertebral, and hip fractures, and are widely used as first-line treatment in patients with osteoporosis, especially in postmenopausal women (DAVIS et al., 2020; SILVA et al., 2022). Additional evidence from clinical trials has also demonstrated that denosumab is able to significantly reduce the incidence of vertebral, nonvertebral, and hip fractures in women with postmenopausal osteoporosis, reinforcing the role of this therapeutic class in the prevention of osteoporotic fractures (CUMMINGS et al., 2009).

Despite the proven efficacy of antiresorptive therapies, the recent studies included in this review have shown growing interest in the use of anabolic therapies in the treatment of osteoporosis. These drugs work by directly stimulating bone formation through the activation of osteoblastic activity, promoting an increase in bone mass and improving the microarchitecture of bone tissue. Randomized controlled trials have shown that teriparatide is more effective than some bisphosphonates in reducing vertebral and clinical fractures in patients with severe osteoporosis (GEUSENS et al., 2018; BODY et al., 2020). Similar results were observed in meta-analyses and comparative studies included in this review, which demonstrated a more significant increase in bone mineral density in patients treated with anabolic therapies when compared to antiresorptive treatments alone (YANG et al., 2020; VITHRAN et al., 2024).

Another anabolic agent identified in the selected studies was romosozumab, a monoclonal antibody that acts by inhibiting sclerostin, simultaneously promoting increased bone formation and reduced bone resorption. Clinical trials have shown that the use of this drug is associated with a significant increase in bone mineral density and a significant reduction in the risk of vertebral and non-vertebral fractures in postmenopausal women with osteoporosis (LANGDAHL et al., 2017; MCCLUNG et al., 2023). Additional studies have also

shown a significant reduction in the risk of vertebral fractures in women treated with romosozumab when compared to placebo, reinforcing the efficacy of this anabolic agent in the treatment of osteoporosis (COSMAN et al., 2016). In addition, comparative studies have shown that romosozumab followed by alendronate was associated with a lower risk of vertebral and hip fractures when compared to treatment with alendronate alone, highlighting the potential of this therapeutic approach in the management of patients at high risk of fracture (SAAG et al., 2017). Structural studies included in this review also indicated that romosozumab may promote improvement in the cortical and trabecular structure of bone tissue, contributing to increased bone strength and fracture prevention (DAMM et al., 2025).

Another relevant aspect identified in the analyzed studies refers to sequential therapeutic strategies in the treatment of osteoporosis. The evidence selected in this review suggests that the initial use of anabolic therapies, followed later by the administration of antiresorptive drugs, may result in greater gains in bone mineral density and a more significant reduction in the risk of fractures over time. This strategy has been particularly described in patients with severe osteoporosis or at very high risk of fracture (HÄNDEL et al., 2023; HAUSER; ALONSO; RICHES, 2021).

In addition to the clinical efficacy of pharmacological therapies, the studies analyzed also indicated that the choice of the most appropriate treatment should consider additional factors, such as the safety profile, cost of the drugs, therapeutic availability, and individual clinical characteristics of the patients. In many clinical settings, anti-resorptive therapies continue to be widely used due to their proven efficacy and increased availability compared to anabolic agents. Thus, the studies included in this review highlight the importance of an individualized approach to the management of osteoporosis, considering the patient's risk profile, history of fractures, and bone mineral density at the time of therapeutic decision (PATEL; LYERLY; HORLEN, 2020; SILVA et al., 2022).

Despite the relevant findings of this review, some limitations should be considered. Among them, the heterogeneity of the methodological designs of the included studies stands out, as well as possible differences in the characteristics of the populations evaluated, in the therapeutic regimens used and in the follow-up periods analyzed. In addition, the limited number of direct comparative studies between anabolic and antiresorptive therapies may make it difficult to generalize the results.

Thus, the findings of this review reinforce the importance of using therapeutic strategies based on the risk of fracture and the clinical characteristics of patients with osteoporosis. Understanding the differences between anabolic and antiresorptive therapies

can contribute to optimizing the clinical management of the disease and reducing the incidence of osteoporotic fractures, especially in high-risk populations.

5 CONCLUSION

It is concluded that anabolic and antiresorptive therapies play a fundamental role in the treatment of osteoporosis, contributing to the reduction of the risk of fractures through distinct mechanisms in the bone remodeling process. While antiresorptive therapies remain widely used as an initial treatment, especially in postmenopausal women, anabolic therapies have shown important benefits in patients with severe osteoporosis or at high risk of fractures, due to their ability to directly stimulate bone formation.

In addition, the evidence analyzed indicates that sequential therapeutic strategies, involving the initial use of anabolic agents followed by antiresorptive drugs, can enhance bone mineral density gains and contribute to reducing the risk of fractures over time. Thus, the importance of individualizing osteoporosis treatment is highlighted, considering the clinical profile and fracture risk of each patient, in order to optimize therapeutic results and improve disease management.

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