2019

Comparison of Pharmacologic Treatments for Postmenopausal Osteoporosis

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Abstract

- The prevalence of osteoporosis in the United States in adults ≥ 50 years of age is "more than 10 million people overall and 33 million have low bone mineral density (BMD) at the hip" (DynaMed Plus, 2018).
- To combat postmenopausal osteoporosis, two treatment options include bisphosphonates and the anti-receptor activator of nuclear factor kappa β ligand (RANKL) agent (denosumab).
- The purpose of this scholarly project is to determine if there is a statistical significance regarding safety, efficacy, and preference between bisphosphonates and denosumab.
- Three databases were searched: PubMed, CINAHL, and Cochrane Database of Systematic Reviews. Topics researched included: postmenopausal osteoporosis, bisphosphonates, anti-RANKL agent, treatment outcome, adverse effects, and efficacy. Research was conducted from September 12, 2018 to January 29, 2019. All works published within the last 10 years.
- The most effective treatment for postmenopausal osteoporosis is denosumab. It is just as safe, more efficacious, better adhered to, and more preferred than bisphosphonates.
- This scholarly project compares the treatment options available to providers and allows them to choose the best option based on the patient's needs, safety, efficacy, preference, and cost.

Introduction

- Osteoporosis is defined as a "generalized skeletal disorder and is characterized by compromised bone strength and deterioration of bone quality, often leading to fragility fracture" (DynaMed Plus, 2018).
- Most often affects: women ≥ 65 years of age, Asian and Caucasian descents, and those with a small body frame.
- Of these affected, one in two women will experience an osteoporotic fracture in their lifetime (International Osteoporosis Foundation, 2017).

Statement of the Problem

- United States Food and Drug Administration (U.S. FDA) approved the first bisphosphonate in 1995 and approved denosumab in 2010 (Food and Drug Administration, n.d.)
- This scholarly project will analyze both treatment options to uncover if there is a statistical significance regarding safety, efficacy, and preference due to different mechanism of actions (MOAs) for bisphosphonates and denosumab.

Research Question

- In the treatment of postmenopausal osteoporosis, is there a statistical difference in the safety, efficacy, and preference when using bisphosphonates versus denosumab?

Results/ Discussion

Theme 1: Safety of Bisphosphonates

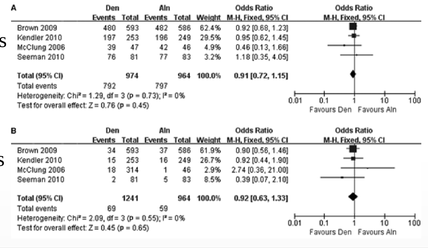
- Wang (2017) noted the safety of bisphosphonates versus placebo.
- Eriksen et al. (2014) focused on the long-term use of bisphosphonates which is crucial due to chronicity of disease.

Theme 2: Safety of the anti-RANKL agent

- Bone et al. (2008) and Keyserlingk et al. (2011) proved denosumab had a similar safety profile as placebo.
- Deeks (2018) and Lin et al. (2012) concluded no significant difference with denosumab versus bisphosphonates.

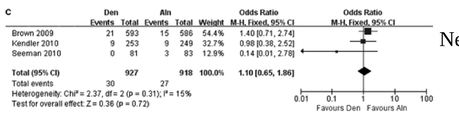
Adverse Events Risk (within 1-year)

Total AEs

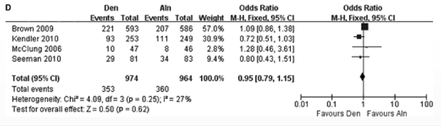


Serious AEs

Neoplasms



Infections



Note. Adapted from "Comparison of clinical efficacy and safety between denosumab and alendronate in postmenopausal women with osteoporosis: A meta-analysis," by Lin T., Wang, C., Cai, X.Z., Zhao, X., Shi, M.M., Ying, Z.M.… Yan, S.G, 2012, *The International Journal of Clinical Practice*, *66* (4), p. 406. Copyright 2012 by Blackwell Publishing.

Theme 3: Efficacy of Bisphosphonates

- Wang (2017) identified the reduced risk of fractures and increased BMD with bisphosphonates versus placebo.
- Eriksen et al. (2014) reported long-term use of bisphosphonates had persistent beneficial effects on fracture risk and BMD beyond three years of treatment.

Theme 4: Efficacy of the anti-RANKL agent

- Keyserlingk et al. (2011) reported significant reductions in relative fracture risk with denosumab versus placebo.
- Beck et al. (2008) identified the superiority of denosumab versus alendronate or placebo in improving BMD.
- McClung et al. (2013) recorded the sustained effects of increased BMD with denosumab over eight years.
- Deeks (2018) confirmed the superiority of denosumab in improving BMD and believed it was possibly due to the differing MOAs.

Percent Change from Baseline in BMD and Bone Geometry Parameters at Month 24

Parameter	Placebo (n= 533)	Alendronate (n= 538)	Denosumab (n= 536)
Femoral Neck: DXA-BMD	1.40 (0.88)	2.99 (0.80)**	4.52 (0.85)**
Narrow Neck: HSA-BMD	2.11 (0.99)	2.53 (0.92)**	3.85 (0.89)**
Intertrochanter: HSA-BMD	1.16 (0.90)	4.43 (0.82)**	6.99 (0.82)**^
Shaft: HSA-BMD	0.27 (0.69)	1.59 (0.63)*	5.73 (0.63)**^^

Abbreviations: DXA (Dual-energy X-ray absorptiometry); BMD (bone mineral density); HSA (hip structure analysis)
*p< 0.05 vs. placebo; **p<0.01 vs. placebo; ^p< 0.05 vs. alendronate; ^^p< 0.001 vs. alendronate

Note. Adapted from "Effects of Denosumab on the Geometry of the Proximal Femur in Postmenopausal Women in Comparison with Alendronate," by Beck, T.J., Lewiecki, E.M., Miller, P.D., Felsenberg, D., Liu, Y., Ding, B., & Libanati, C., 2008, *Journal of Clinical Densitometry: Assessment of Skeletal Health*, *11* (3), p. 354. Copyright 2008 by The International Society for Clinical Densitometry.

Theme 5: Preference, adherence, and satisfaction between bisphosphonates and the anti-RANKL agent

- Freemantle et al. (2012), Kendler et al. (2011), and Palacios et al. (2015) recognized the increased adherence and preference of denosumab versus alendronate.
- Keyserlingk et al. (2011) stated denosumab could present as an effective new treatment for osteoporosis with fewer adherence barriers than present options.
- Therefore, from a clinical standpoint of adherence and preference, denosumab is clearly superior.

Conclusion

- Similar safety profiles exist between bisphosphonates and denosumab.
- Denosumab is more efficacious in increasing BMD; however, denosumab and bisphosphonates have similar fracture risk incidence.
- Denosumab has a much stronger adherence and preference profile than bisphosphonates.
- Therefore, the treatment of choice when managing the chronic condition of postmenopausal osteoporosis is denosumab.

Applicability to Clinical Practice

- Due to increasing prevalence of postmenopausal osteoporosis, the need for a safe, effective, and adhered to treatment is more important than ever before.
- Providers are faced with the choice to select either the historic first line treatment, bisphosphonates, or use the newer, safer, more effective and better adhered to treatment, denosumab.
- The patient's needs must be taken into consideration and each decision must be on an individual basis. Therefore, clinicians should be well-versed on the treatment options for postmenopausal osteoporosis available and be able to educate patients on the different factors of each medication.

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Acknowledgements

- My advisor, Jeanie McHugo, Chair of the Physician Assistant Program and PA-C who always went above and beyond to enhance this project by answering questions, providing critique, and encouraging me through this journey.
- My scholarly project team: Stephanie Gagelin, Ashley Pommer, and Amy Quinn. Your insight and feedback has been gratefully appreciated through this process.
- To the patients who were diagnosed with postmenopausal osteoporosis, caring for you during this chronic disease inspired me to research and analyze the best line of treatment.