Comparing Prevalence of Medication-Related Osteonecrosis of the Jaw (MRONJ) due to Denosumab and Bisphosphonates as a Side Effect of Osteoporosis Treatment

Kendra Apland

University of North Dakota

Follow this and additional works at: https://commons.und.edu/pas-grad-posters

Part of the Endocrine System Diseases Commons

Recommended Citation


https://commons.und.edu/pas-grad-posters/2
As the baby boomer generation continues to age, the diagnosis of osteoporosis and its side effects will continue to increase. Denosumab and bisphosphonates (BPs) are some of the most common medication classes used to treat osteoporosis and osteoarthritis, but it is believed that both medications have the possible side effect of medication-related osteonecrosis of the jaw (MRONJ). The purpose of this paper is to uncover if MRONJ is a side effect of osteoporosis treatment and which medication carries the highest incidence rate. Through a review of several electronic databases and several peer-reviewed research articles, a wide range of reported incidence rates of MRONJ for both medications were uncovered, along with many complicating possible risk factors. There is a wide range of reported incidence rates and differences in reported data were found. The research found that denosumab carries a slightly higher risk of MRONJ versus bisphosphonates, but the difference was found to be statistically insignificant. Uncovered risk factors include increasing age, gender, recent dental procedures, history of oral disease, and corticosteroid use. My research is impactful in the fact that as providers, we can be better informed about the differences between denosumab and bisphosphonates and the possible risk factors of MRONJ. We can use the information, along with possible other risk factors and our patient’s history, to make joint decisions about what osteoporosis medication is right for our patient.

Keywords: osteonecrosis, jaw, medication-related, bisphosphonates side effects, denosumab side effects, abnormal fracture, osteoporosis.

Introduction

• The world’s population is ageing: two factors — longer life spans and aging baby boomers — will combine to double the population of Americans aged 65 and older during the next 25 years to about 72 million (CDC, 2013).
• This will have a significant impact on age-related health care; a loss of bone mineralization and mass in the forms of osteopenia and osteoporosis being a major issue.
• Worldwide, osteoporosis causes more than 8.9 million fractures annually, resulting in an osteoporotic fracture every three seconds (International Osteoporosis Foundation, 2017).
• In addition to the personal burden and impact on quality of life, the costs associated with fracture treatment and rehabilitation are enormous.
• A study from 2002 estimated national health care expenditures due to osteoporotic fractures to be about $22 billion annually, with about 75% of the costs going to direct medical care (Deas, Duncan, Sloan, 2003).

Abstract

As the baby boomer generation continues to age, the diagnosis of osteoporosis and its side effects will continue to increase. Denosumab and bisphosphonates are some of the most common medication classes used to treat osteoporosis and osteoarthritis, but it is believed that both medications have the possible side effect of medication-related osteonecrosis of the jaw (MRONJ). The purpose of this paper is to uncover if MRONJ is a side effect of osteoporosis treatment and which medication carries the highest incidence rate. Through a review of several electronic databases and several peer-reviewed research articles, a wide range of reported incidence rates of MRONJ for both medications were uncovered, along with many complicating possible risk factors. There is a wide range of reported incidence rates and differences in reported data were found. The research found that denosumab carries a slightly higher risk of MRONJ versus bisphosphonates, but the difference was found to be statistically insignificant. Uncovered risk factors include increasing age, gender, recent dental procedures, history of oral disease, and corticosteroid use. My research is impactful in the fact that as providers, we can be better informed about the differences between denosumab and bisphosphonates and the possible risk factors of MRONJ. We can use the information, along with possible other risk factors and our patient’s history, to make joint decisions about what osteoporosis medication is right for our patient.

Keywords: osteonecrosis, jaw, medication-related, bisphosphonates side effects, denosumab side effects, abnormal fracture, osteoporosis.

Literature Review

• Incidence rates of MRONJ:
  • General population:
    • 0.000066% to 0.001% (Syjda et al., 2016) and (DyMed Med Plus, 2017)
  • BP:
    • Between 0% to 2%: up to 6.7% (Loejon, et al., 2017)
    • 13.1 times greater in patients on BP therapy vs placebo group (Dodon, 2014)
  • Denosumab:
    • 0.04% to 10% (Loejon et al., 2017)
    • 15.5% after BP and then denosumab (Loejon et al., 2017)
    • Higher risk of MRONJ early after switching from BPs to denosumab compared to patients remaining on BPs
  • Based on global incidence rates, the switch from BPs to denosumab can be considered as safe as initially starting denosumab therapy (Loejon et al., 2017).
• Contributing factors:
  • Cancer treatment: The risk in cancer patients is about 50-100 times greater than in patients exposed to placebo (Dodon, 2014).
  • Duration of treatment: incidence is higher with longer duration of treatment, particularly when therapy exceeds four years (Up to, Date 2017).
  • Operative treatment: dental procedures that invade bone increase risk (DePaola, Black, & Rosen, 2016).
  • 52 to 61% of MRONJ patients reported tooth extraction as the precipitating event (Ruggiero et al., 2014).
• Demographics, systemic, other factors:
  • Age and gender are variably reported as risk factors.
  • Tobacco use has been inconsistently reported as a risk factor.
  • Corticosteroids are associated with an increased risk as they can further weaken bones (Ruggiero et al., 2014).
  • Patients with a single nucleotide polymorphism (SNP) in a specific gene associated with bone density and collagen formation were 5.8 times more likely to develop MRONJ (Ruggiero et al., 2014).
  • Studies suggest a likely genetic link between MRONJ and BP therapy.

Statement of the Problem

There are many different approaches to treating osteoporosis. Denosumab and bisphosphonates are two of the most common pharmacologic treatments prescribed. However, both are not without their various side effects. Both medications are believed to have the possible side effect of osteonecrosis of the jaw, but this is believed to be very rare.

Discussion

Is the incidence rate of MRONJ greater in those patients treated with denosumab or bisphosphonates?

Are there any precipitating factors or conditions that increase incidence rates of MRONJ with treatment of denosumab or bisphosphonates?

Applicability to Clinical Practice

• As potential future providers, a large proportion of our patients will most likely be elderly, so it is imperative to be aware of common conditions that could affect this population, like osteoporosis.
• Both conditions can be debilitating and cause significant physical impairment and fractures if left untreated, a major concern being hip fractures.
• Hip fractures in particular are associated with significant increased risk of mortality, loss of independence, and financial burden.
• In one study, the reported one-year mortality after sustaining a hip fracture was as high as 13% (Brodsky et al., 2010).
• There are many different treatment options for osteoporosis, among them BPs and denosumab, and there is not a one-size-fits-all solution.
• In any situation, we as providers have to be able to weigh the benefits of treating versus the possible risks of treating.
• We will need to take each patient’s preference and personal medical history into account to make a joint decision about osteoporosis treatment.

References

• Grbic et al (2010)
• Coleman et al (2009)
• Scagliotti et al (2008)
• Vahtsevanos et al (2007)
• Grbic et al (2006)
• Currey et al (2009)
• Bedford et al (2009)
• Ruggiero et al (2014)
• Geusens et al (2010)
• Chen et al (2009)
• Ruggiero et al (2013a)
• Ruggiero et al (2013b)
• Ruggiero et al (2013c)
• Ruggiero et al (2013d)
• Ruggiero et al (2013e)
• Ruggiero et al (2013f)

Acknowledgements

I would like to thank the UND faculty for their continued support and dedication to the education of their PA students. I would like to thank my advisor, Daryl Sieg, for his insight and direction throughout my PA education. I would also like to thank all of my preceptors who have helped guide my education and learning experiences. A sincere thank you to Emily Hanley, PA and Chad Speer for their assistance and input into this final project. Lastly, I cannot thank my family and fiancé enough for their love, support, and patience through this extensive yet rewarding journey.

Table 1: Disease frequency of MRONJ reported by various studies

<table>
<thead>
<tr>
<th>Treatment Type</th>
<th>Study design</th>
<th>Incidence rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buccal mucosal flap</td>
<td>Systemic review</td>
<td>0.04% (5459)</td>
</tr>
<tr>
<td>Implant-supported prosthesis</td>
<td>Systemic review</td>
<td>0.1% (775)</td>
</tr>
<tr>
<td>Vestibuloplasty</td>
<td>Prospective cohort study</td>
<td>0.04% (9500)</td>
</tr>
<tr>
<td>Le et al (2014)</td>
<td>Cross-sectional</td>
<td>0.5%</td>
</tr>
</tbody>
</table>

Figure 2: Mode of failures of BPs and denosumab treatment

Figure 3: MBIs of patient demonstrating osteonecrosis of the jaw.