Acta Scientific Ophthalmology (ISSN: 2582-3191)

Volume 5 Issue 2 February 2022

Editorial

Bisphosphonates and Ocular Inflammation

Ali Nouraeinejad[1,2]*

[1]Ph.D. in Clinical Ophthalmology, Tehran University of Medical Sciences, Tehran, Iran

[2]University College London (UCL), London, United Kingdom

***Corresponding Author:** Ali Nouraeinejad, Ph.D. in Clinical Ophthalmology, Tehran University of Medical Sciences, Tehran, Iran.

Received: November 24, 2021

Published: January 01, 2022

Osteoporosis, as a musculoskeletal disease, is assigned by low bone mass and degradation of bone microarchitecture, culminating in an escalation in bone weakness and propensity to fracture [1,2]. When the cumulative effect of bone resorption is in excess of bone formation, osteoporosis is induced [1]. Osteoporotic fractures are linked to substantial morbidity, mortality, and high healthcare expenses [1].

Although men tend to show worse results after fractures, the prevalence of osteoporosis and the risk of osteoporosis-induced fracture are higher in women [3,4].

Bisphosphonates, which are applied orally or intravenously, are largely prescribed in the management of osteoporosis and highly effective at limiting the bone loss that occurs in many disorders known by increased osteoclast-mediated bone resorption [1,5]. Bisphosphonates inhibit bone resorption and are widely used to prevent osteoporotic fractures with relatively few side effects [6,7]. However, bisphosphonates have been found to be linked to some rare and severe adverse effects, such as atypical femur fractures, other atypical fractures, osteonecrosis of the jaw (ONJ), an increased risk of aseptic osteonecrosis (AON), atrial fibrillation, esophageal and colon cancer, bone and muscle pain, irregular heartbeat, gastrointestinal intolerance, upper gastrointestinal (GI) adverse effects, acute phase reaction, hypocalcemia, impaired fracture healing, renal complications, electrolyte imbalance, and ocular inflammation [1,2,5-17].

Although the mechanism of adverse ocular reaction is not clear yet [12,13], it has been proposed that bisphosphonates are secreted into the tears by the lacrimal gland and consequently could provoke transitory irritation to the mucous membranes with consequent release of inflammatory mediators [12,18,19]. In addition to the release of cytokines, this irritation may irritate the release of other acute phase proteins in the eye, or induce activation of gamma delta T cells within the orbit [12,14,20,21]. In this context, the resultant rise in the concentration of inflammatory mediators, especially among new users of bisphosphonates, may put them at a higher risk of scleritis or uveitis [8].

Bisphosphonate use has been documented to cause adverse ocular effects, such as uveitis, scleritis, episcleritis, nonspecific conjunctivitis, blepharitis, synechiae, subconjunctival hemorrhage, ocular hypertension, ischemic optic neuropathy, and optic neuritis [6-10,12-14,16,17]. Bisphosphonates can also precipitate orbital inflammation [6,7,9,11,16,17].

However, population-based cohort studies [8,10,22] concluded that the "underlying inflammatory disease" was the most likely determinant of the inflammatory eye reactions in patients taking bisphosphonates [12]. This was concluded due to their findings that the risk of inflammatory eye reactions was found to be at maximum among patients with underlying inflammatory diseases [12].

In most cases, symptoms started within days of initiating bisphosphonate administration and resolved upon stopping the

drug [8]. The technique of bisphosphonate administration affects the timing of the adverse ocular effects so that they usually occur within 48 to 72 hours after intravenous (IV) bisphosphonate administration and 2 to 3 months after oral bisphosphonate administration [17,23]. Others reported that the onset can be from a few hours after exposure up to more than 3 years, with an estimated median of 3 weeks [10,12,24].

In conclusion, although ocular side effects of bisphosphonate therapy are fairly rare, orbital and ocular inflammation are its possible vision-threatening side effects. The important message is to inform clinicians prescribing bisphosphonates and people using them about the risk of ocular inflammation in order to be familiar with the signs and symptoms of these conditions so that they can instantly look for proper treatment.

Conflict of Interest

The author declares no conflict of interest.

Bibliography

1. Lewiecki EM. "Bisphosphonates for the treatment of osteoporosis: insights for clinicians". *Therapeutic Advances in Chronic Disease* 1.3 (2010): 115-128.
2. Garriga C., *et al*. "Oral bisphosphonate use and age-related macular degeneration: retrospective cohort and nested case-control study". *Annals of the New York Academy of Sciences* 1415.1 (2018): 34-46.
3. Cawthon PM. "Gender differences in osteoporosis and fractures". *Clinical Orthopaedics and Related Research* 2011 469(7):1900-1905.
4. Alswat KA. "Gender Disparities in Osteoporosis". *Journal of Clinical Medicine Research* 9.5 (2017): 382-387.
5. Kennel KA and Drake MT. "Adverse effects of bisphosphonates: implications for osteoporosis management". *Mayo Clinic Proceedings* 84.7 (2009): 632-638.
6. Nouraeinejad A. "Handbook of ocular drugs, and ocular side effects of systemic drugs". Tehran: Tabib Publication (2000).
7. Nouraeinejad A. "Differential Diagnosis in Optometry and Ophthalmology". Second Edition. Iran: Noruzi Publication (2017).
8. Etminan M., *et al*. "Inflammatory ocular adverse events with the use of oral bisphosphonates: a retrospective cohort study". *Canadian Medical Association Journal* 184 (2012): E431-E434.
9. Rahimy E and Law SK. "Orbital inflammation after zoledronate infusion: an emerging complication". *Canadian Journal of Ophthalmology* 48 (2013): e11-e12.
10. Pazianas M., *et al*. "Inflammatory eye reactions in patients treated with bisphosphonates and other osteoporosis medications: cohort analysis using a national prescription database". *Journal of Bone and Mineral Research* 28 (2013): 455-463.
11. Pirbhai A., *et al*. "Bisphosphonate-induced orbital inflammation: a case series and review". *Orbit* 34 (2015): 331-335.
12. Clark EM and Durup D. "Inflammatory eye reactions with bisphosphonates and other osteoporosis medications: what are the risks?". *Therapeutic Advances in Musculoskeletal Disease* 7.1 (2015): 11-16.
13. Martin Guillén S., *et al*. "Uveitis Due to Bisphosphonates: A Rare Side Effect?". *Reumatología Clínica* 12 (2016): 119.
14. Mammo Z., *et al*. "Oral Bisphosphonates and Risk of Wet Age-Related Macular Degeneration". *American Journal of Ophthalmology* 168 (2016): 62-67.
15. Godkhindi Vishwapriya M and Basade Maheboob M. "Zoledronic Acid Induced Orbital Cellulitis-Case Report and Literature Review". *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)* 15.4 (2016): 75-79.
16. Umunakwe OC., *et al*. "Diffuse ocular and orbital inflammation after zoledronate infusion—case report and review of the literature". *Digital Journal of Ophthalmology* 23 (2017): 109-112.
17. Gomez Escobar LG and Devia DG. "Possible ocular adverse effects attributed to bisphoshonate therapy: Two care reports". *Revista Colombiana de Reumatología* 24 (2017): 54-59.
18. Fraunfelder FW and Fraunfelder FT. "Adverse ocular drug reactions recently identified by the National Registry of Drug-Induced Ocular Side Effects". *Ophthalmology* 111 (2004): 1275-1279.
19. Peterson JD and Bedrossian EH. "Bisphosphonate-associated orbital inflammation—a case report and review". *Orbit* 31 (2012): 119-123.

20. Hewitt RE., *et al*. "The bisphosphonate acute phase response: rapid and copious production of proinflammatory cytokines by peripheral blood gd T cells in response to aminobisphosphonates is inhibited by statins". *Clinical and Experimental Immunology* 139.1 (*20*05): 101-111.

21. Kassi G., *et al*. "Cytokines and insulin resistance after zoledronic acid-induced acute phase response". *Immunological Investigations* 43.6 (2014): 544-555.

22. French D and Margo C. "Postmarketing surveillance rates of uveitis and scleritis with bisphosphonates among a national veteran cohort". *Retina* 28 (2008): 889-893.

23. Patel DV., *et al*. "The incidence of acute anterior uveitis after intravenous zoledronate". *Ophthalmology* 120.4 (2013): 773-776.

24. Jones DG., *et al*. "Synovitis induced by alendronic acid can present as acute carpal tunnel syndrome". *BMJ* 330.7482 (2005): 74.