

Long-term use of bisphosphonates in osteoporosis

To the Editor

I read with interest the article written by Alwahhabi & Alsuwaine¹ and appreciate they took time to address this important issue. Unfortunately I have some major and some minor concerns with this manuscript.

1) The title does not reflect what the authors have described. They have described the complications of long term complications of bisphosphonates therapy and how they have managed. The title probably should have been "Complications of long term use of bisphosphonates in osteoporosis and management".

2) The major concern is the incidence of atypical femoral fractures (AFF). The authors have not given details of how many patients in these 16 plus years, they have treated to get these 34 patients with AFF. After radiographic adjudication and large database studies, the incidence of AFFs in the United States revealed that AFFs was 5.9 per 100,000 person years [95% confidence interval (CI) 4.6-7.4], with 1,271,575 person years observed² and in Europe incidence of AFFs was 3.2 cases per 100,000 person years.³ If we compare with the present study it gives an incidence of 15.45/100,000 person years which is too high. The calculation of 15.45/100,000 years was arrived at by the following method:

a) Total female Saudi Arabian population ≥ 55 years of Riyadh is 1,25641.⁴

b) If 10% of the whole female population of 1,25,641 followed up at one hospital, which is still not possible for 16 plus years (2009-2016), the number will be 12,564. Thirty-three patients of AFF in 17 years for population of = $17 \times 125,641 = 213,589$ person years gives an incidence of 15.45/100,000 person years. If this number is true then it is possible that the ethnic Saudi Arabian females has a very high risk of developing AFF, which need to be proved. In our own institution which is a tertiary center in the eastern province has seen only 6 cases in last 20 years.

3) Figure 1B, 1E, & 1M does not fit the description of as AFF.⁵

4) Figure 1D is not with a plate, but with an external fixator.

5) Figure 1K: is not a comminuted fracture with total knee replacement, but a stress fracture of a single cortex.

6) Figure 1N & 1O is not in the published manuscript. (The authors may have hind sighted, we

are surprised how this was missed by the referees and the editorial staff).

7) The authors have discussed about the use of the anabolic agent, fair enough but it should be emphasized that no medication will heal these fractures if they are not fixed appropriately and adequately.

8) Lastly, we feel that the authors should have stated that the risk of AFF is small, can happen even in patients who are not on bisphosphonates⁶ and other factors also influence the development AFF.⁷ This is not to alarm the GPs and other internists who might withhold the routine use of bisphosphonates, which is important in the prevention of fragility fractures

Mir Sadat-Ali,

Department of Orthopaedic Surgery

College of Medicine

Imam AbdulRahman Bin Faisal University

Dammam

King Fahd Hospital of the University

Al-Khobar

Fawaz M ALAnii

Department of Orthopaedic Surgery

King Fahd Hospital of the University

Al-Khobar, Saudi Arabia

Reply from the Author

Thank you for your detailed comments. This research was conducted in a single center. Our aim was not to report the incidence of AFF among Saudi alendronate users. The patients we reported have been treated in different departments, some even in other hospitals. We receive them only after they develop fracture.

Weather ethnic Saudi Arabian females have a very high risk of developing AFF is unknown. Finding the exact risk is out of the scope of this research. We are just reporting our real life experience with long term use of bisphosphonates.

We are not suggesting at all that anabolic therapy alone can heal AFF. Surgery will always remain the main management protocol. This is not for discussion by any means. Considering the risk of delayed healing of AFF even after surgery we are suggesting that teriparatide may accelerate the process.

Other related facts such as risk of AFF in non-bisphosphonates users is also out of the scope of this article. All AFF patients we reported are BPs users.

We do not (at all) advise against use of BPs in osteoporosis. We are just increasing the awareness of AFF risk among BPs users. This is in keeping with the

recent recommendations on drug holiday.

Figures 1N & 1O are not in the manuscript. We apologize for this.

Regarding Figure 1M which is a spiral fracture. We suggested to include spiral fractures under AFF. A similar case was reported by Schneider.

I hope we answered at least some of your concerns.

Basmah K.S. Alwahhabi

*Department of Endocrinology and Diabetes
Prince Sultan Military Medical City
Riyadh, Kingdom of Saudi Arabia*

References

1. Alwahhabi BK, Alsuwaine BA. Long-term use of bisphosphonates in osteoporosis. *Saudi Med J* 2017; 38: 604-608.
2. Feldstein A, Black D, Perrin N, Rosales A, Friess D, Boardman D, et al. Incidence and demography of femur fractures with and without atypical features. *J Bone Miner Res* 2012; 27: 977-986.
3. Meier R, Perneger T, Stern R, Rizzoli R, Peter R. Increasing occurrence of atypical femoral fractures associated with bisphosphonate use. *Arch Intern Med* 2012; 172: 930-936.
4. General Authority for Statistics. Central Department of Statistics [cited 2017 June 2017]. Available from URL: <http://www.cdsi.gov.sa>
5. Shane E, Burr D, Ebeling PR, Abrahamsen B, Adler RA, Brown TD, et al. Atypical subtrochanteric and diaphyseal femoral fractures: report of a task force of the American Society for Bone and Mineral Research. *J Bone Miner Res* 2010; 25: 2267-2294.
6. Tan S, Koh S, Goh S, Howe T. Atypical femoral stress fractures in bisphosphonate-free patients. *Osteoporos Int* 2011; 22: 2211-2212.
7. Mahjoub Z, Jean S, Leclerc JT, Brown JP, Boulet D, Pelet S, et al. Incidence and characteristics of atypical femoral fractures: Clinical and Geometrical Data. *J Bone Miner Res* 2016; 31: 767-776.

Statistics

Excerpts from the Uniform Requirements for Manuscripts Submitted to Biomedical Journals updated November 2003.
Available from www.icmje.org

Describe statistical methods with enough detail to enable a knowledgeable reader with access to the original data to verify the reported results. When possible, quantify findings and present them with appropriate indicators of measurement error or uncertainty (such as confidence intervals). Avoid relying solely on statistical hypothesis testing, such as the use of *P* values, which fails to convey important information about effect size. References for the design of the study and statistical methods should be to standard works when possible (with pages stated). Define statistical terms, abbreviations, and most symbols. Specify the computer software used.