Clinical Outcomes of Oral Bisphosphonates Beyond Five Years – Should We do Automatic Osteoporosis Drug Holidays?

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**Background:** The long-term management of patients with osteoporosis and the rational use of bisphosphonates are growing concerns due to potential rare adverse effects. In the past decade, the concept of a “drug holiday” for bisphosphonate therapy has emerged, whereby the risk of adverse effects might be decreased and patients still benefit from anti-fracture efficacy. However, there are limited data to guide decision-making about the initiation and termination of “drug holiday”.

**Objective:** The aims of this study were to evaluate the clinical practice in patients with long-term oral bisphosphonates (≥ 5 yrs) prescription and to compare the treatment outcomes in both drug holiday and non-drug holiday patients.

**Materials and Methods:** We conducted a retrospective study from database of regular follow-up patients who were prescribed oral bisphosphonate for osteoporosis for a period of at least 5 years during 2001-2017. The characteristics of patients, indications of treatment, type of bisphosphonate, adverse effects, and changes in bone mineral density (BMD) at last follow-up were evaluated.

**Results:** A total of 85 cases with long-term prescribed oral bisphosphonates (≥ 5 yrs) were identified (mean age 71.5±9.5 years, female 95.3%, DM 32.9%, duration of treatment 7.2±2.5 years, low-risk osteopenic patients at baseline 29.4%, previous osteoporotic fracture 8.2%). No case of atypical fracture of femur or osteonecrosis of the jaw was observed. Drug holiday was offered in 54 patients (63.5%) during the study period (duration of drug holiday 4.7±2.4 years). Only 2/3 of these patients had a follow-up BMD, and paired BMD data revealed 46.7% of patients with worsening BMD values. Two cases of vertebral fracture occurred after drug holiday for 7 and 8 years.

**Conclusions:** This real-world study demonstrates the diversity of bisphosphonate usages in some patients at low risk. The usages have been started since the time when treatment may not have been indicated. While BMD testing tends to be over-utilized in low-risk patients, the follow-up BMD at proper timing could be done in less than half of osteoporosis patients. Hence, clinicians need to reconsider the assumption that a patient with oral bisphosphonate for 5 years should automatically start a drug holiday. Discontinuation of bisphosphonate is associated with worsening BMD and osteoporotic fractures in some patients with high risk of fracture.

**Keywords:** Drug Holidays, Oral Bisphosphonates, Osteoporosis