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POSITIVA OCH NEGATIVA EFFEKTER AV BISFOSFONATER

- en observationsstudie

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Akademisk avhandling

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Title

Benefits and Harms of Bisphosphonates – An Observational Study

Abstract

Background: Bisphosphonates are first-line treatment for osteoporosis, but osteoporosis is considered an undertreated disease. The general aim of this dissertation was to further study the benefits and harms of bisphosphonates. There were four specific research questions: (1) Do bisphosphonates reduce the risk of new fractures in older adults who have a history of fracture? (2) Do bisphosphonates reduce the risk of fracture in people taking glucocorticoids? (3) Does confounding explain why bisphosphonates are associated with lower mortality in observational studies? (4) Do bisphosphonates increase the risk of non-jaw osteonecrosis?

Methods: To answer these questions, we used Swedish register data on deaths, diagnoses, and prescription medications to conduct four matched cohort studies of bisphosphonate users and nonusers. The cohorts were selected from patients registered in the Hip Fracture Register and from all residents of Sweden who were aged 50 years or older on December 31, 2005.

Results: (1) Bisphosphonate users had an initially increased risk of sustaining new fractures, which appeared to be due to an underlying high risk of fracture. This increased risk diminished over time, which is consistent with a gradual treatment effect, but it is also consistent with a bias known as depletion of susceptibles. (2) Bisphosphonate users had a lower risk of fracture during glucocorticoid therapy. (3) Bisphosphonate users had a lower mortality rate from day 2 of treatment. Although such an early treatment effect cannot be ruled out, this finding is consistent with confounding. (4) Bisphosphonate users had an increased risk of developing non-jaw osteonecrosis.

Conclusion: Most of the results were difficult to interpret as true benefits or harms of bisphosphonates because alternative explanations, arising from bias or confounding, were likely. The exception was the results of Study 2, where alternative explanations are more difficult to find. Therefore, Study 2 suggests that bisphosphonates reduce the risk of fractures in glucocorticoid-treated patients. Further research is needed to clarify the potential effects of bisphosphonates on mortality, non-jaw osteonecrosis, and new fractures after a previous fracture.

Keywords

osteoporosis, fracture, alendronate, risedronate, zoledronic acid, glucocorticoid, mortality, osteonecrosis, register, registry, real-world evidence, epidemiology

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