

The use of bisphosphonate drugs is associated with an increased risk of atypical hip fractures

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The use of bisphosphonates, a group of drugs used to prevent hip breakages in women with osteoporosis, is associated with an increased risk of atypical fractures in this joint, understood as those that occur in less frequent locations. It has been established thus in the PhD thesis by Javier Gorricho-Mendívil, a graduate in pharmacy, and read at the NUP/UPNA-Public University of Navarre. The author advocates encouraging other preventive measures such as "strategies to reduce falls and an active lifestyle to improve bone density and health".

"Hip fracture is the most common cause of admittance to hospital in the traumatology and orthopaedics departments," points out Javier Gorricho. "These fractures are associated with a high rate of mortality and loss of quality of life together with significant costs. It is estimated that in the European Union in 2010, there were 620,000 hip fractures and the cost of [osteoporotic fractures](#) amounted to over 37,000 million euros."

Most fractures occur in people over 65 and are more frequent in women. "In Spain the population over 65 has increased considerably in recent years rising from 14.92% in 1997 to 16.62% in 2008. This increases the significance of this health problem even further," pointed out Gorricho, whose thesis is entitled "Eficacia de los bisfosfonatos orales en la prevención de las fracturas de cadera en mujeres mayores de 65 años en la práctica clínica habitual" (Effectiveness of oral bisphosphonates in preventing hip fractures in women over 65 in regular clinical practice).

According to Javier Gorricho, in Navarre the average age of women who suffer hip fractures is over 80 and with fracture rates among those over 85 in excess of 20 per 1,000 inhabitants per year.

Trials using a placebo

To prevent hip fractures in women who have osteoporosis and who have a high risk, one of the main drugs used are the oral bisphosphonates class of drugs (alendronate, risedronate and ibandronate). "These drugs have been consistently found to increase the levels of bone mineral density, and reduce vertebral fractures detected in X-rays. When trials using a placebo were carried out, in those among whom a proportion of the target sample in the study did not take any medication, the reduction in the number of hip fractures was much smaller", said Javier Gorricho, whose thesis supervisor was Juan Erviti-López, researcher at Navarrabiomed-Fundación Miguel Servet.

In recent years the European, American and Spanish Drugs Agencies, among others, have issued "various warnings owing to the correlation detected between the use of these drugs and various problems linked to correct bone regeneration: osteonecrosis of the jaw and atypical hip fractures. In the most recent warning, doctors were asked to review after five years of treatment with these drugs whether it was appropriate or not to continue with the pharmacological treatment," pointed out Gorricho.

As studies had been carried out on North American and Scandinavian populations in the case of atypical hip fractures and there were no data on countries in the south of Europe, Javier Gorricho focussed his PhD thesis on Spain.

To do this he used the Database for Pharmaco-epidemiological Research in Primary Healthcare (BIFAP), with 4.8 million clinical records of the

National Healthcare Service of Spain provided by over 18,000 doctors, which signifies nearly 25 million people at one-year follow up. "This longitudinal population base, which began in 2001, includes information from the clinical records that has been rendered anonymous, so researchers cannot identify the patients and absolute confidentiality about the health details of these individuals is maintained," he explained. This database is designed and managed by the Spanish Agency for Drugs and Healthcare Products (AEMPS) to be able to conduct studies of this type and have the support of the autonomous communities (regions) and the main scientific societies involved.

Data covering three years

Gorricho's study, which received a grant from the Spanish Ministry of Health, Social Services and Equality in 2009, includes the hip fractures in women over 65 in the period between 1 January 2005 and 31 December 2008. Javier Gorricho identified 2,009 women with typical hip fractures and 44 with [atypical fractures](#), and whose average age was 82.

Among the conclusions of the thesis he stresses that the use of oral bisphosphonates was not associated with a reduction in hip fractures in women of 65 but it was associated with a greater risk of atypical hip fractures (subtrochanteric or diaphyseal fractures). "This risk increases when the time exposed to bisphosphonates is increased. The longer the treatment time was, the greater the risk of atypical fracture," as Javier Gorricho sums up.

According to Javier Gorricho, this study, which has found for the first time the same correlation between atypical hip fractures and the use of bisphosphonates in our population as that found in other countries (the United States and northern Europe), reinforces the monitoring measures adopted by the Spanish Drugs Agency with respect to these drugs.

Furthermore, as Javier Gorricho explained, the average age of hip fractures (82) and the lack of correlation between the use of the drug and a benefit in hip fractures indicate that "it is very important for studies to be conducted on this population, that of people over 75-80 years old, to check the effectiveness of the drugs since no benefit was detected in hip fractures according to a recent study in the United States, for example".

The study, in the author's view, also underlines the idea that it is necessary "to encourage other measures" to try to reduce hip fractures, such as "encouraging strategies to prevent falls or the maintenance of an active lifestyle to improve [bone density](#) and health". In fact, Javier Gorricho and his thesis supervisor, Juan Erviti, have had an article published in the *BMJ (British Medical Journal)*, together with Scandinavian and Canadian researchers advocating this fresh approach.

More information: "Overdiagnosis of bone fragility in the quest to prevent hip fracture." *BMJ* 2015;350:h2088. doi: [dx.doi.org/10.1136/bmj.h2088](https://doi.org/10.1136/bmj.h2088)

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