PHARMACOTHERAPY

Increased stroke risk associated with osteoporosis drugs

Patients receiving certain treatments for osteoporosis could be at increased risk of fatal stroke, according to the findings of an observational cohort study published in *Osteoporosis International*. The risk of death within 30 days of a diagnosis of stroke was found to rise with increasing doses of the bisphosphonates alendronate and etidronate. By contrast, no increased stroke risk was associated with raloxifene use in patients with osteoporosis.

Previous studies have hinted at a relationship between the use of raloxifene (a selective estrogen-receptor modulator) and risk of stroke and fatal stroke; however, no detailed analyses exist on either the dose-response or the stroke risk in patients using other antiosteoporosis drugs, such as bisphosphonates.

To address these points, Peter Vestergaard and colleagues made use of registers kept by the Danish health-care system that include detailed information on daily clinical practice with respect to the use of osteoporosis medications and the incidence of stroke in people treated with these drugs. Vestergaard's research team compared registry data from 103,562 patients who received pharmacotherapy for osteoporosis between 1996 and 2006 with 310,683 age-matched and sex-matched control individuals, who were randomly selected from the same time period. Osteoporosis medications assessed by the study investigators included several bisphosphonates (for example, alendronate, clodronate and etidronate); raloxifene; strontium ranelate; and parathyroid hormone or its analogs.

In general, the patients with osteoporosis had more comorbidities and previous use of medications for various conditions than those in the control group. The researchers observed a significantly increased risk of overall stroke and fatal stroke following treatment with alendronate or etidronate; surprisingly, the risk of overall stroke significantly decreased with increased dose of alendronate, which suggests that the interaction of this bisphosphonate with stroke risk should be investigated further. By contrast, raloxifene use produced no increase in risk of stroke or fatal stroke, regardless of dose.

Vestergaard comments that for the bisphosphonates alendronate and etidronate "an increasing risk of fatal strokes was seen with increasing doses, but no association for overall stroke risk was found. These associations have not been studied previously and thus need confirmation." Vestergaard concludes that, although raloxifene does not seem causally related to the risk of fatal stroke, "more studies are needed to see if the association for alendronate and etidronate is real."

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Original article Vestergaard, P. *et al.* Stroke in relation to use of raloxifene and other drugs against osteoporosis. *Osteoporosis Int.* doi:10.1007/s00198-010-1276-4