# Alzheimer's drug could prevent bone fractures

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The most common drug used to treat Alzheimer's disease increases bone mass in mice, according to one of the first research articles published in the new open access journal *Heliyon*. The authors of the study, from Saitama Medical University in Japan, say this means the drug could also be used to treat bone loss diseases like osteoporosis and periodontitis, following further clinical research.

Alzheimer's disease is the most common form of dementia and the incidence is increasing in our aging population. In the early stages of Alzheimer's disease, bone density decreases, putting patients at a higher risk of bone fractures.

The new *Heliyon* study suggests that treating Alzheimer's disease with a drug called donepezil not only improves cognitive function but also increases bone density, reducing the risk of fractures.

"We think that donepezil can improve cognitive function and increase bone mass, making it a very useful drug for patients with dementia and osteoporosis," said lead author Dr. Tsuyoshi Sato, Associate Professor in the Department of Oral and Maxillofacial Surgery, Saitama Medical University. "From the viewpoint of medical economics, this dual purpose could reduce the cost of treating these diseases."

Two different kinds of cell control the bone mass and density in our bodies: osteoblasts make bone and osteoclasts absorb it. A molecule called acetylcholine causes osteoclasts to die in vitro. Although an

enzyme called acetylcholinesterase breaks this molecule down, the effect of this enzyme on osteoclasts remains unclear.

The most common drug used to treat Alzheimer's disease, donepezil, stops acetylcholinesterase from working, leading to an increase in the amount of acetylcholine in the brain. Recent retrospective clinical studies have suggested that patients being treated with donepezil for Alzheimer's disease have a lower risk of hip fracture, and that risk was dependent on the dose they were taking.

The researchers wanted to understand how donepezil prevents bone degradation. They looked at the drug's activity in vitro using mouse bone marrow cells, and found that more acetylcholinesterase is produced when osteoclasts are being made, which leads to even more osteoclasts being made. Donepezil stops acetylcholinesterase from working, therefore preventing osteoclasts from being made.

The team also looked at the effect of the drug in a mouse model with bone loss. They found that donepezil increases bone mass in mice by preventing the production of osteoclasts.

"We were surprised to see that donepezil directly inhibits the production of osteoclasts and subsequently increases bone mass in vivo," said Dr. Sato. "This is very surprising point - donepezil directly controls the molecule that is responsible for macrophages becoming osteoclasts."

Previous research has shown that acetylcholinesterase activity increases continuously with age, and may accelerate the risk of bone loss in elderly people. The researchers noted that the concentration of acetylcholinesterase in macrophages was higher when the tissue was inflamed. This suggests that inflammation causes bone to be degraded in part due to acetylcholinesterase production.

"Our findings are very promising and suggest that there is a role for donepezil in increasing bone mass in elderly patients with inflammation and dementia," said Dr. Sato. "There is still work to be done and we look forward to observing the effect of this drug in patients."

The team now plans to work with the Department of Neurology at Saitama Medical University on clinical research. They plan to study whether taking donepezil reduces patients' risk of bone fracture by looking at its effect in a group of patients compared to a control group.

**More information:** "Donepezil prevents RANKL-induced bone loss via inhibition of osteoclast differentiation by downregulating acetylcholinesterase" by Sato et al. (DOI: 10.1016/j.heliyon.2015.e00013). The article appears in Heliyon (September 2015)

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