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Brittle bone disease: Drug research offers hope

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New research at the University of Michigan offers evidence that a drug being developed to treat osteoporosis may also be useful for treating osteogenesis imperfecta or brittle bone disease, a rare but potentially debilitating bone disorder that that is present from birth.

Previous studies have shown the drug to be effective at spurring new bone growth in mice and in humans with osteoporosis, and a U-M research team believes that it may spur new growth in brittle bone disease patients as well. This would be a significant improvement over current treatments, which can only reduce the loss of existing bone.

The new drug is an antibody to a protein called sclerostin, which normally signals the body to stop producing new bone. Previous studies have shown that inhibiting sclerostin through antibody therapy is effective at increasing bone formation and strength.

The new U-M study focused on the effects of the antibody in very young and very old mice with genetic features that mimic brittle bone disease. Researchers were particularly interested in studying the effects of the drug on young mice, which are still growing new bone and have much lower levels of sclerostin.

"The dynamics of bone growth in young mice and in children are very different from those in adults," said Ken Kozloff, associate professor of orthopaedic surgery and biomedical engineering. "Their bone structures are still forming, so it's important to understand how inhibiting sclerostin

may affect that. We were also concerned that the benefits of the drug would reverse themselves after treatment stopped."

The results of the study are encouraging, with no reduction in midshaft bone strength or mass in young mice six weeks after treatment stopped. While there was some loss in newly formed spongy bone, the researchers found that this could be remedied by using the sclerostin antibody in combination with other therapies.

Osteogenesis imperfecta is a genetic disease that affects an estimated 20,000 to 50,000 people in the United States, about 1 in 20,000 live births. It reduces the body's ability to form new bone and weakens the bone that does form. This leads to bones that fracture easily in everyday activities, causing a cycle of repeated fractures and hospitalizations.

There is no cure and current treatment options are limited. They include the use of bisphosphonate drugs to reduce the weakening of bone and the surgical implantation of steel rods in the bones to improve their strength.

"I envision a treatment that uses a precise combination of sclerostin antibodies to grow new bone, followed by bisphosphonates to lock in that bone growth," said Michelle Caird, associate professor of orthopaedic surgery who specializes in brittle bone disease. "The rodent studies we're doing right now are giving us a better understanding of how to optimize the timing and amounts of the two drugs. We have years of hard work ahead of us, but I think this could really improve quality of life for kids with this disease."

The research team still has an estimated two years of rodent studies to complete. They're hopeful that patients may have a new treatment option within the next five to six years. Amgen, the manufacturer of the drug and the provider of the drugs used in the U-M study, is currently testing

on osteoporosis patients.

Caird says the data gained from that testing may help a new treatment for brittle bone disease get through the testing and approval process more quickly. The team is also working on new study methods that may enable them to test the new drug in the lab on small samples of bone cells taken from patients.

Researchers believe that the therapy may also be useful for treating children who suffer from disuse osteopenia, a bone disorder that can result when bones don't bear normal amounts of weight. This is common among children who use wheelchairs as a result of diseases like cerebral palsy and spina bifida.

"Disuse osteopenia is the same disease that astronauts get when they're in microgravity environments for long periods of time," Caird said. "It affects many more children than brittle bone disease, so we're very hopeful that sclerostin antibody therapy will be a useful treatment for them as well. But we're focusing on brittle bone disease first because it's particularly debilitating and because there are so few other options for those kids."

More information: An abstract titled "Single Dose of Bisphosphonate Preserves Long-term Gains in Bone Mass Following Cessation of Sclerostin Antibody in Osteogenesis Imperfecta Model" will be presented March 31 at the annual meeting of the Orthopaedic Research Society.

Provided by University of Michigan