

Scientists discover way to jumpstart bone's healing process

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Rarely will physicians use the word "miraculous" when discussing patient recoveries. But that's the very phrase orthopaedic physicians and scientists are using in upstate New York to describe their emerging stem cell research that could have a profound impact on the treatment of bone injuries. Results from preliminary work being released todayshow patients confined to wheelchairs were able to walk or live independently again because their broken bones finally healed.

At the heart of the research is the drug teriparatide, or Forteo, which was approved by the FDA in 2002 for the treatment of osteoporosis. Astute observations led a team of clinicians and researchers to uncover how this drug can also boost our bodies' <u>bone</u> stem cell production to the point that adults' bones appear to have the ability to heal at a rate typically seen when they were young kids.

Baseline research presented in February at the Orthopaedic Research Society meeting revealed that of 145 patients who had an unhealed bone fracture - half of them for six months or longer - 93 percent showed significant healing and pain control after being on teriparatide for only eight to 12 weeks. These findings were enough to convince the National Institutes of Health to fund a clinical trial underway in Rochester, and if the preliminary data are any indication, researchers may have discovered a new, in-the-body stem cell therapy that can jumpstart the body's natural <u>healing process</u> in bones.

The clinical implication is significant, as orthopaedists can soon have a



new tool at their disposable to deal with many common, painful bone ailments including the tens of thousands of painful fractures for which there is no treatment (pelvic fractures, vertebral compression fractures, clavicle fractures), fractures that won't heal, fractures in patients that are either too sick to have surgery or chose not to have surgery, and even reduce the size of a incision in some surgeries.

Aging Bones Heal Slower

Of the estimated six million fractures in the United States each year, approximately five percent will have slow or incomplete healing. According to J. Edward Puzas, Ph.D., who heads up orthopaedic bone research at the University of Rochester Medical Center and is the principal investigator of the clinical trial, a large portion of non-healing fractures tend to occur in older adults.

"In many people, as they get older, their skeleton loses the ability to heal fractures and repair itself," Puzas said. "With careful application of teriparatide, we believe we've found a way to turn back the clock on fracture healing through a simple, in-body stem cell therapy."

Those especially hard hit are the nearly 60,000 Americans suffering from pelvic fractures, where bracing and immobilization are not an option for an injury that leaves people immobile and in pain before the bone fuses.

"It takes three to four months for a typical pelvic fracture to heal. But during those three months, patients can be in excruciating pain, because there are no medical devices or other treatments that can provide relief to the patient," said Susan V. Bukata, M.D., medical director of the Center for Bone Health at the University of Rochester Medical Center Bukata. "Imagine if we can give patients a way to cut the time of their pain and immobility in half? That's what teriparatide did in our initial



research."

Bukata said much more was at stake then just comfort and pain relief. Patients who would ordinarily be confined to nursing homes or require additional medical attention because of non-healing fractures might be able to live an independent life. Bukata and Puzas estimate that if this drug saved just one week in a nursing home, it would pay for itself - and beyond.

"Many people don't realize that pelvic fracture carries with them the same mortality as hip fractures - in one year, approximately one-quarter of all older women with pelvic fractures will die from complications," Bukata said. "And during that year of recovery, a patient typically puts a greater strain on our health care system, not to mention their pain and suffering."

Translational Research at Work

The impetus for the research began in Bukata's clinic, where she saw painful bone fractures in osteoporotic patients quickly heal within a few months of taking teriparatide. At the time, Bukata also served on a research team at the University's Center for Musculoskeletal Research, and she began to advocate that the team direct its efforts in an entirely new direction based on the results she was seeing with patients who were taking teriparatide.

"I had patients with severe <u>osteoporosis</u>, in tremendous pain from multiple fractures throughout their spine and pelvis, who I would put on teriparatide," said Bukata. "When they would come back for their followup visits three months later, it was amazing to see not just the significant healing in their fractures, but to realize they were pain-free - a new and welcome experience for many of these patients."



Puzas and Bukata developed a plan to focus attention in both the lab and clinic to understand if her observations were a fluke or if there was an underlying scientific process producing such life-changing results for patients.

"While we had come to understand how teriparatide builds bone more robustly than the body can on its own, up to that point, we had no clue how the drug would or could help with fracture healing," Puzas said.

Bukata began prescribing teriparatide to patients with non-healing fractures, and was amazed at her findings: 93 percent showed significant healing and pain control after being on teriparatide for only eight to 12 weeks. And in the lab, Puzas began to understand how teriparatide stimulates bone stem cells into action.

Closing the Gap

When a fracture occurs, a bone becomes unstable and can move back and forth creating a painful phenomenon known as micromotion. As the bone begins healing it must progress through specific, well-defined stages. First, osteoclasts - cells that can break down bone - clean up any fragments or debris produced during the break. Next, a layer of cartilage - called a callus - forms around the fracture that ultimately calcifies, preventing the bony ends from moving, providing relief from the significant pain brought on by micromotion.

Only after the callus is calcified do the bone forming cells - osteoblasts begin their work. They replace the cartilage with true bone, and eventually reform the fracture to match the shape and structure of the bone into what it was before the break.

According to Puzas, teriparatide significantly speeds up fracture healing by changing the behavior and number of the cartilage and the bone stem



cells involved in the process.

"Teriparatide dramatically stimulates the bone's stem cells into action," Puzas said. "As a result, the callus forms quicker and stronger. Osteoblasts form more bone and the micromotion associated with the fracture is more rapidly eliminated. All of this activity explains why people with non-healing fractures can now return to normal function sooner."

"The decreased healing time is significant, especially when fractures are in hard-to-heal areas like the pelvis and the spine, where you can't easily immobilize the bone - and stop the pain," Bukata added. "Typically, a pelvic fracture will take months to heal, and people are in extreme pain for the first eight to 12 weeks. This time was more than cut in half; we saw complete pain relief, callus formation, and stability of the fracture in people who had fractures that up to that point had not healed."

The new clinical research will study post-menopausal women and men over 50 who come to the Emergency Department at Strong Memorial Hospital with a low-energy pelvic fracture. Patients will be divided into two groups -- one offered teriparatide, the other a placebo -- and followed for 16 weeks to measure the fracture healing process in a variety of ways: pain levels, microscopic bone growth determined through CT scans and functional testing of bone strength, among others.

Source: University of Rochester Medical Center (<u>news</u> : <u>web</u>)

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