Experimental stem cell treatment leaves three women blind

March 17 2017, by Carmen Heredia Rodriguez, Kaiser Health News

An experimental treatment - which blinded three women after stem cells from abdominal fat were injected into their eyes - was advertised on a government-run clinical trial website but lacked proper safeguards, researchers reported Wednesday.

The report in the *New England Journal of Medicine* notes that the procedures were part of a national rise in the number of clinics harnessing stem cells from fat to treat a variety of diseases - even though many have not been proved to work. Two of the women thought they were getting treatment as part of a clinical trial because they learned about the procedure on clinicaltrials.gov, a database run by the National Library of Medicine that features thousands of studies, many of which are sanctioned by research organizations and have regulatory oversight.

Jeffrey Goldberg, professor and chairman of ophthalmology at the Byers Eye Institute at Stanford University and co-author of the study, said the report aims to highlight the ethical implications of how clinical research is defined for the public and the dangers of poorly regulated trials.

"I would emphasize it's a challenge and we can't expect patients to fully vet these options," he said. "And that's where the ethics of the doctors and oversight of regulatory agencies need to play a role in the public health of our community."

The women featured in the report sought treatment in 2015 for age-related macular degeneration, a common, progressive eye condition

characterized by blurriness in the center field of vision. Their ages ranged from 72 to 88, the report said, and they paid $5,000 for the procedure. Each had both eyes treated at the same time, a protocol that is "both atypical and unsafe," according to the researchers.

The report did not name the clinics involved in the study or its sponsor. Researchers said in a press release accompanying the study that the clinic is no longer performing the procedures but is still treating patients.

Clinicaltrials.gov shows the trial referenced in the article was sponsored by a stem cell company based in Sunrise, Fla., called Bioheart Inc., now known as U.S. Stem Cell. Dr. Shareen Greenbaum served as the trial's principal investigator, according to the company's press release. She is an ophthalmologist working at the Hollywood Eye Institute in Cooper City, Fla.

According to the journal report, clinicians used cells extracted from fat, and treated them with enzymes to obtain the stem cells. Blood was also drawn from the patient and then platelet-dense plasma was extracted. The cells were then mixed with plasma and injected into both eyes.

Within days, the three patients sought medical care for complications related to the procedure. Two patients suffered bleeding and each had retina detachments. The researchers said they are not expected to regain their sight.

The analysis said that the consent forms signed by the women did not mention a clinical trial. It also noted that the patients paid for the procedure and both eyes were treated at the same time, a protocol that is "both atypical and unsafe." The patients paid for procedures "that had never been studied in a clinical trial, lacked sufficient safety data and was performed in both eyes on the same day," the researchers wrote.

State insurance records show insurers for Greenbaum, U.S. Stem Cell and a registered nurse paid out more than $3 million in 2016 to patients harmed by stem cell procedures, although it is not clear if those patients are the same ones detailed in the study. U.S. Stem Cell said in a statement Wednesday that it could not comment on these cases but it is committed to "research and development of effective cell technologies." The statement noted that the company has "successfully conducted more than 7,000 stem cell procedures with less than 0.01 percent adverse reactions" since 2001. Greenbaum did not return calls for comment.

Stem cells have unique properties that researchers believe may hold promise for new treatments for a host of diseases such as diabetes and arthritis. These cells have the ability to change into different types of specialized cells and act as a repair system for tissues throughout the body.

Hundreds of stem cell clinics have sprung up across the nation offering therapies. But many of these medical interventions have not been vetted through federal protocols for safety and effectiveness. Because stem cells are harvested from the patient who will receive the treatment, many of these clinicians say they do not need the Food and Drug Administration's approval, said Karen Maschke, a research scholar at the Hastings Center, a bioethics research institute.

In the journal report, the authors hypothesize the adverse effects of the treatment were caused by stem cells transforming into myofibroblasts, or cells that can lead to scarring. Enzymes used to extract the stem cells could have also contaminated the solution.

But the report said even if the treatment had caused no adverse effects, there's little evidence showing that it would have worked.

Formal clinical trials have several safeguards to protect participants

against adverse effects, said Maschke. Biomedical trials are overseen by an institutional review board that is responsible for reviewing the study's research protocol to ensure participants are being protected. Patients are also required to sign consent forms that outline the risks associated with the experiment.

For large clinical trials, a separate oversight group called a data safety monitoring board conducts reviews throughout the trial to assess the risks and benefits of the experiment, Maschke said. Smaller and less dangerous trials rely on the research team and chief investigators to notify the institutional review board of any safety issues. Participants can also report their concerns to the Office for Human Research Protections within the Department of Health and Human Services.

Dr. Thomas Albini, one of the co-authors and an associate professor of clinical ophthalmology at the University of Miami, warned consumers that clinical trials with a fee should be carefully reviewed. "I'm not aware of any legitimate research, at least in ophthalmology, that is patient funded," he said in the press release accompanying the study.

The government website recently expanded its requirements for those wishing to register clinical trials on the site. However, Maschke said she isn't sure whether the new rules will lead to a more rigorous vetting process for prospective listings.

"It's unclear whether or not anyone is enforcing required postings and what's supposed to be in them," she said.