Supplement may protect against hearing loss

by Terri Somers

Cpl. John Shahin doesn't remember the sound of the bomb that hit his Humvee in Iraq three years ago, leaving the 22-year-old Marine with hearing loss and other lingering injuries.

He remembers feeling the pressure of the explosion before he was knocked unconscious. He remembers regaining consciousness as a buddy shook him. He remembers the blood. And he remembers a loud ringing in his ears. Almost three years later, loud noise makes the ringing return, which leads to migraines.

Shahin is just one of thousands of wounded service members who have Navy researchers and a San Diego company scrambling to further test and develop an antioxidant compound that has been shown to prevent hearing loss from traumatically loud noise.

And with further research, scientists are hoping that the compound, commonly used to treat Tylenol overdose, may win regulatory approval for restoration of hearing loss.

The compound, N-acetylcysteine, or NAC, is being marketed as an over-the-counter product known as the "hearing pill" by American BioHealth Group in San Diego.

Two-thirds of U.S. personnel wounded in Iraq have some kind of hearing loss, said Cmdr. Michael Hoffer, a doctor at San Diego Naval Medical Center who directs the hearing programs for the nation's military hospitals. That injury can create balance issues and make military life even more dangerous, he said.

One military study showed that if one in four people in a tank had hearing loss, he was twice as likely to miss his target and 25 percent more likely to be killed before knocking out the target, said Cmdr. Ben Balough, who runs the head-and-neck-surgery program at the Naval Medical Center.

NOW HEAR THIS - Marine Cpl. John Shahin, 22, undergoes a hearing test at San Diego Naval Medical Center. He is among those whose injuries include hearing loss from loud noise. CNS Photo by Nancee E. Lewis.

Such hearing loss is expensive, too. The Department of Veterans Affairs said last year that it spends about $1 billion annually in disability payments for hearing loss, Balough said. The Defense Department, which has spent $8 million developing NAC, has committed an additional $2 million for further clinical testing that it hopes may lead to regulatory approval for use as a restorative treatment after noise-related injuries.

Dr. Richard Kopke, a hearing specialist, first came across NAC when he was researching deafness caused by a chemotherapy drug. Kopke and other researchers at Albert Einstein College of Medicine in New York were testing the ability of different antioxidants to combat the chemical reaction brought on by a loud noise. The noise trauma causes the cells in the inner ear to release toxins that cause the death of cells in the cilia, the tiny, hairlike cells of the inner ear that vibrate and allow us to hear. There's another chemical in the body, glutathione, that defends the cells against toxins, but it's quickly depleted in a traumatic event. Kopke and his team decided to try NAC for hearing loss. They knew that it helps the body produce more glutathione to prevent cell death. It has been used for years to combat Tylenol overdose because it helps stop the death of liver cells. Through this application, there has been an accumulation of data showing the compound to be safe and effective.

In 1994, Kopke continued his NAC studies in San Diego, after he was recruited by Hoffer to join the research staff at the Naval Medical Center.

NAC worked in studies on chinchillas, whose ears are more sensitive to noise than those of humans. Kopke's lab documented a 50 percent to 80 percent reduction in hearing loss and a similar reduction in hair-cell loss.

Kopke has since retired from the military and is running the nonprofit Hough Ear Institute in Oklahoma City. The Navy patented NAC's use for hearing loss and began looking for a business partner to help commercialize it. David Karlman, a San Diego entrepreneur, read about the NAC patent in the Federal Register. Through Tech Link, a federally supported technology transfer office, he began discussions with the Navy. "My gut told me that this was a good product, considering the market and the incidence of hearing loss in the country," Karlman said. Then he did due diligence and found there was no therapeutic or preventive agent on the market for hearing loss or related balance disorders.

After completing a competitive process that included submission of a business plan for the pill, Karlman's new company, American BioHealth Group, licensed the Navy's patent and began their ongoing partnership.

Karlman's partner, Mark Mugerditchian, used his 27 years in the pharmaceutical industry to write the protocol for the next big clinical trial the Navy would perform with NAC. That late 2003 trial involved 566 Marines at the recruit depot in San Diego. Half the recruits were given a dose of NAC before and after going to the firing range with their M-16s, and half received a placebo. All of the recruits wore ear guards for protection. Permanent hearing loss was reduced by 25 percent to 27 percent in the NAC group compared with the placebo group.

Together, American BioHealth and the Navy presented their data on NAC to the Food and Drug Administration, with the plan of starting the process for further clinical trials and ultimately regulatory

approval. The FDA determined that NAC as a preventive measure, in a small dose, would be a nutraceutical - a term that refers to foods claimed to have a medicinal effect on human health - rather than a pharmaceutical. Therefore, it didn't need regulatory approval to be sold. While not having to perform expensive and time-consuming clinical trials may seem a positive development, being a nutraceutical has its downside.

Many consumers and physicians have more trust for a product that has undergone tough clinical and regulatory scrutiny. And the military, which American BioHealth sees as a huge chunk of its market, can't buy and stockpile compounds unless they've been approved by the FDA, Balough said.

Karlman said the company plans to lobby the government to change this policy in the case of the hearing pill. Meanwhile, he has licensed another patent from the Navy and signed another development agreement involving the commercialization of NAC in combination with other compounds, which he won't name, for enhanced preventive and restorative properties in hearing loss. These compounds don't have the same clinical history and accumulated safety and efficacy data as NAC, so it's expected to be a longer process. Karlman won't say how much his company has invested in the hearing pill.

Earlier in development, the company raised $250,000 from the San Bernardino Center for Commercialization of Advanced Technology, a California consortium of business, government and academic interests that provides funding and guidance to fledgling technology companies. "One thing I liked about (the hearing pill) was that its method of action is so clear and straightforward: you're taking a pill of antioxidants which happen to have a direct and fairly dramatic effect," said Stuart Gordon, who runs that CCAT program.

There's a huge market outside the military, including industries such as mining, construction and aviation, Gordon said. And personal lives are not exactly quiet these days, with people going home to loud and large televisions or iPods, he said.

Karlman estimates the market for the hearing pill at about $250 million and growing.

He now has competition, including Sound Pharmaceuticals in Seattle, which has a compound that has yet to be tested in humans. As Karlman moves forward in development of NAC and other compounds, he said he's looking for an established distribution partner that can help the hearing pill gain widespread acceptance before the competition arrives.

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