Standing up to Gravity: Drug Shows Promise as Treatment for Orthostatic Intolerance in Astronauts

NASA has long sought a safe and effective countermeasure for orthostatic intolerance—the dizzy spells and feelings of faintness that often affect returning astronauts, a consequence of their bodies' adaptation to the microgravity of space. Studies by NASA-supported researchers suggest that a drug used to treat these symptoms in sick people on Earth may help astronauts, too.

On their return to Earth after a space mission, many astronauts feel dizzy and lightheaded—a condition known as orthostatic hypotension or orthostatic intolerance. The problem is more severe after long-duration space missions. In an emergency, orthostatic intolerance could hinder an astronaut's ability to exit a landed spacecraft without assistance.

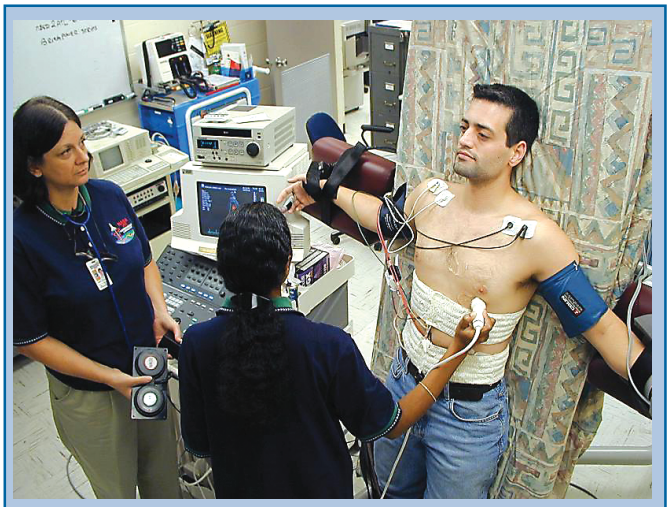
Recent findings by NASA-supported researchers suggest that a drug approved by the U.S. Food and Drug Administration (FDA) to treat orthostatic intolerance associated with disease may also alleviate the problem in astronauts returning to Earth from space.

Counteracting Gravity

When a person stands upright on Earth, the force of gravity pulls his or her blood and other body fluids toward the feet. However, the cardiovascular system has evolved an extensive set of mechanisms to counteract gravity.

"When you go from a lying to a standing position, your heart starts to pump faster to increase blood flow," explains Richard J. Cohen, Ph.D., of the Massachusetts Institute of Technology, who leads the cardiovascular research team at the National Space Biomedical Research Institute. "The large veins in your legs constrict, forcing more blood back toward the heart, and your small arteries also constrict. In healthy people, a whole network of reflexes help to maintain appropriate blood pressure so we don't feel dizzy when we stand up."

Standing up too quickly can cause brief periods of dizziness even in healthy individuals, but in most cases the condition is transient and requires no treatment. However, some people with conditions such as diabetes or Parkinson's disease suffer orthostatic intolerance as a result of nerve damage that impairs their cardiovascular reflexes.



Tilt testing in the NASA JSC Cardiovascular Laboratory to study the effects of orthostatic tolerance preflight and postflight. Recordings obtained include ECG, automatic blood pressure, beat-to-beat finger pressure, echocardiographic measurements, and respiratory tracing. Left to right: Janice Meck, Donna South, and Dominick D'Aunno.

When astronauts go into space, the absence of gravity means their cardiovascular reflexes are no longer being used. Their blood volume declines slightly and blood and other fluids shift toward the head.

"The cardiovascular system adapts remarkably well to microgravity," says Cohen. "However, when you return to Earth, your blood volume is somewhat lower, your cardiovascular reflexes have diminished, your veins and arteries constrict less than they otherwise would, and your heart's pumping ability is reduced."

As a result, insufficient blood flows to the brain, causing dizziness, lightheadedness, and sometimes fainting. These symptoms diminish within a few days as the body re-adapts to gravity and those cardiovascular reflexes kick back in.

Drug Stimulates Blood Vessel Constriction

Janice Meck, Ph.D., director of the cardiovascular laboratory at the NASA Johnson Space Center in Houston, wondered whether midodrine—the first FDA-approved drug for treating orthostatic intolerance—might also relieve the condition in astronauts returning from space. Midodrine acts on receptors in the nervous system that stimulate the blood vessels to constrict.

Meck suggested to Cohen that, as a first step in testing this hypothesis, his team study midodrine's effect in healthy male volunteers taking part in a bedrest study. Prolonged bedrest produces many of the same effects on the human body as exposure to microgravity does, including muscle deconditioning and orthostatic intolerance. For this reason, bedrest studies are an accepted way of modeling the effects of microgravity on the ground.

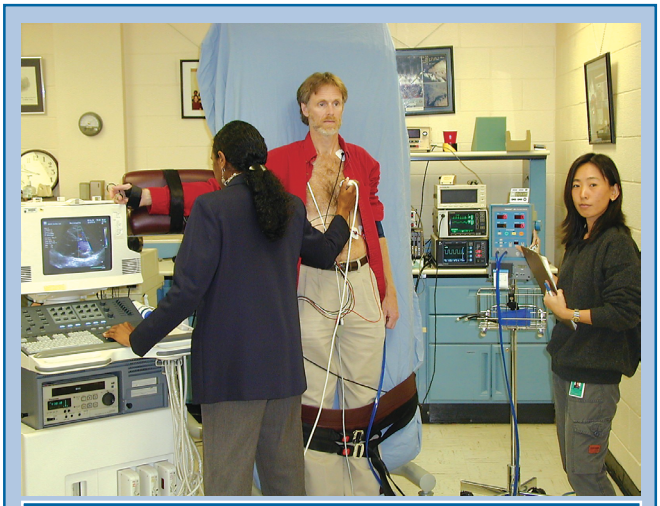
Fifteen subjects spent between nine and 16 days lying prone in bed with their heads tilted slightly downward. On the last day, they were randomly assigned to take either a low dose of midodrine or a placebo. The study was double-blinded, meaning neither the researchers nor the subjects knew who received the drug and who received the placebo.

Midodrine is a short-acting drug that reaches its peak effectiveness about one hour after it is taken. An hour after taking either the drug or the placebo, the subjects underwent a test of orthostatic tolerance known as a tilt-stand test. They lay flat on a table, one end of which was slowly raised until they were standing upright. Their blood pressure was monitored continuously. The test was halted immediately if a subject's blood pressure dropped suddenly or if a subject showed signs of dizziness or lightheadedness.

"We found that about 75 percent of subjects in the placebo group could not complete the tilt-stand test," says Cohen. "Among the subjects who received midodrine, only 29 percent were unable to tolerate the test. These results were achieved using a very small dose of the drug."

Encouraging Results in Astronauts

Midodrine has also shown encouraging results in testing on seven returning shuttle astronauts. All seven had flown in space before; two had suffered orthostatic intolerance on returning from their previous mission. All seven took midodrine immediately after landing. An hour later, they underwent the same tilt-stand test given to the subjects in the bedrest study.



Tilt testing with ultrasound being performed in the JSC Cardiovascular Laboratory. Left to right: Donna South, David Martin, and Yuho Hayashi.

"In both astronauts who had a history of orthostatic intolerance, midodrine corrected the problem," says Meck, who was the principal investigator for this study. "The drug caused no significant adverse effects in the five astronauts who did not have a history of orthostatic intolerance."

Several characteristics of midodrine make it a promising candidate for treatment of orthostatic intolerance in returning astronauts, says Meck. Unlike some other drugs that have been considered for this purpose, midodrine can be taken by mouth. It acts quickly, so astronauts can take it on landing or shortly before. Its effects wear off in a few hours and it has minimal side effects.

Meck cautions, however, that testing in a larger number of subjects is needed before midodrine can be recommended for routine use in returning astronauts.

References

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