New evidence that females might benefit most from a low-salt diet

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Drs. Eric Belin de Chantemele and Jessica Faulkner. Credit: Phil Jones, Senior Photographer, Augusta University

A low-salt diet may be more beneficial in lowering blood pressure in females than males, report scientists who found that while actual salt retention isn't higher in females, there is still an effect that drives

pressure up.

Females also might benefit most from drugs that directly block aldosterone, a hormone and blood vessel constrictor that is naturally higher in females and is further elevated by a high-salt diet, they report in the journal *Hypertension*.

After just seven days on a high-salt diet, the ability of female mice to relax blood vessels decreased while their blood pressure increased, says Dr. Eric Belin de Chantemele, physiologist in the Vascular Biology Center at the Medical College of Georgia at Augusta University.

"When we gave mice a high-salt diet for a week, we saw an increase in blood pressure of about 10 mmHg—which is significant clinically—only in the females," says Dr. Jessica L. Faulkner, MCG postdoctoral fellow and the study's first author.

Treatment with the aldosterone antagonist eplerenone restored a healthier blood pressure and the ability of the lining of the blood vessels to relax, says Belin de Chantemele, the study's corresponding author.

Blood pressures in males and females were similar at the start of the studies and aldosterone levels were higher in the females, a typical difference between the sexes, which Faulkner and Belin de Chantemele had previously found.

"We thought that if the female mice have more aldosterone than the males, they should be more salt- sensitive," says Belin de Chantemele. "That is what really pushed us to do this study."

Eating too much salt is a daily occurrence for most of us and one of aldosterone's functions is increasing sodium and fluid retention by the kidneys, the scientists say. There is supposed to be sort of seesaw effect

so that when we eat too much salt, aldosterone levels go down so we don't retain too much salt, which drives up fluid retention and blood pressure.

The MCG scientists found that in males, the aldosterone-salt interaction action works: increased salt intake suppresses aldosterone, which helps protect males from this path to hypertension.

However, females taking in a lot of salt don't suppress aldosterone as much, so aldosterone levels and blood pressure both are higher, Faulkner says.

In this scenario, rather than holding onto more fluid and salt, aldosterone appears to cause problems by impairing the ability of blood vessels to relax. In fact, the scientists found no evidence that the kidneys, which should eliminate excessive sodium, were the problem. Both sexes excreted more sodium when they consumed more, and the females actually excreted the most.

"In the salt-sensitivity field there are two main concepts," says Belin de Chantemele. "One is it's mediated by the kidney retaining more salt. Another one suggests that it's an improper relaxation of the blood vessels in people who are salt-sensitive. Our data supports that second concept."

When they used the drug, eplerenone—a diuretic that blocks the receptor for aldosterone and is already used to treat high blood pressure and more commonly heart failure—it restored blood pressure and endothelial function in the females.

It decreased both day- and nighttime measures of the systolic blood pressure (top number which indicates pressure when the heart is contracting), diastolic pressure (bottom number, which indicates pressure when the heart is relaxed) and mean arterial pressure (an

average between the two which gives an overall idea of blood flow).

In males, the drug didn't affect any of those pressures or alter the function of the endothelial cells that line blood vessels and aid their contraction and relaxation.

The findings provide more evidence that the aldosterone system is a particularly good target for females in the face of pathological problems like obesity and salt-sensitive hypertension, they write.

The females actually experienced lower activity than males of the renin-angiotensin system, a kidney-based system for regulating blood pressure and fluid levels often targeted by common hypertension medications like ACE inhibitors.

Clinical studies have indicated that females are generally more salt-sensitive, but those findings have not held up in animal studies—which mostly have been done in male rodents—until now.

The INTERSALT study, for example, of more than 10,000 males and females worldwide from 1984-97 surmised that high salt intake is an important and preventable factor in increasing blood pressure trends and that females are more at risk than males for salt-sensitive increases in their blood pressure.

The MCG investigators' previous work has indicated that female mice are particularly susceptible to mineralocorticoid receptor activation and aldosterone-mediated hypertension mechanisms. Mineralocorticoids are steroid hormones produced by the adrenal gland that affect salt and water balance in the body. Aldosterone is the primary mineralocorticoid and works directly in the kidneys to get the kidneys to hold onto sodium and water.

The American Heart Association says a normal blood pressure in less than 120/80.

Provided by Medical College of Georgia at Augusta University