

Why Certain Cancer Treatments Cause High Blood Pressure

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(PhysOrg.com) -- Drugs that block the formation of new blood vessels that feed tumor growth are helping some cancer patients enjoy longer lives.

But they come with a price: Studies show that up to a third of all patients who take the anti-angiogenesis drugs develop high <u>blood pressure</u>. Scientists at Duke University Medical Center may have figured out why.

"Anti-angiogenesis drugs like Avastin, Sutent, or Nexavar inhibit an important substance called vascular endothelial growth factor (VEGF) that stimulates the creation of new vessels that support malignant growth," says Thomas Coffman, MD, a professor of medicine, cell biology and immunology at Duke and the senior author of the study appearing online in the journal Hypertension.

"Our studies in mice show that blocking VEGF causes hypertension because it disrupts an important biological system -- the <u>nitric oxide</u> pathway that regulates blood vessel health."

Scientists discovered the connection through experiments in mice. Carie Facemire, PhD, a researcher in Coffman's lab, used an antibody to block a key VEGF receptor called VEGFR2 in the animals.

She found that after about a week, all of the mice that received the antibody experienced a "rapid and sustained" increase in blood pressure. Animals that got a <u>placebo</u> maintained normal blood pressure.



Researchers found that dose mattered. A modest amount of the VEGFR2 antibody didn't do anything to cause a jump in blood pressure, but a high dose equivalent to a therapeutic amount a <u>cancer</u> patient would receive, did cause blood pressure to rise.

"The higher doses of anti-angiogenesis drugs that patients need to keep their cancers from growing translate into a significant increase in risk for hypertension and, by extension, for cardiovascular complications," says Coffman.

To further determine what role nitric oxide dysregulation plays in promoting hypertension, Coffman gave the mice in the placebo group a compound to block nitric oxide production. Sure enough, those mice developed high blood pressure, too, just like the group that got the VEGFR2 antibody.

Coffman says as cancer patients live longer, side effects like hypertension, which might once have seemed less important, take on new meaning. "Long-term hypertension can have serious consequences," he says.

Herbert Hurwitz, MD, a medical oncologist at Duke and one of the first to document how Avastin and other anti-angiogenesis drugs provide benefit to cancer patients, says for most patients, anti-angiogenesis drugs are helpful and any resulting hypertension is usually manageable with traditional blood pressure medications.

"However, these new findings are important since they point to specific ways to better protect against the risks of long-term hypertension. They also suggest ways to protect patients against other serious but uncommon side effects, like stroke or heart attack."

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Center for <u>Hypertension</u> and Atherosclerosis, and the Research Service of the Department of Veteran's Affairs.

Carie Facemire is the lead author on the study. Additional Duke researchers who contributed to it include Andrew Nixon, Robert Griffiths and Herbert Hurwitz.

Provided by Duke University (<u>news</u> : <u>web</u>)

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