

Blood pressure compound may benefit brain tumor patients

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A widely used blood pressure medication may be the key to preventing brain function loss common after radiation treatment, according to a newly published study by researchers at Wake Forest University Baptist Medical Center. The findings offer the hope of an improved quality of life for cancer patients.

Using a rat model, the study drew on a hypothesis from previous studies that a compound similar to the anti-hypertensive drug losartan can prevent the cognition loss that has been closely-associated with radiation therapy for brain tumor treatment.

The findings, recently published in the *International Journal of Radiation Oncology, Biology, Physics*, appear to validate the hypothesis in rats and researchers are optimistic that the same theory could easily be applied in a human clinical trial setting because the drug used has a long-established safety profile in patients who have taken it to treat high blood pressure.

"We need to kill cancer cells but also prevent or reduce treatment-related side effects," said Mike E. Robbins, Ph.D., a professor in the department of radiation oncology at the Brain Tumor Center of Excellence, part of Wake Forest University School of Medicine. "One very interesting feature of this compound is that it has never shown any pro-tumor effects. If anything, it appears to have anti-tumor properties. We're very close to having a compound that will protect the normal brain from cognitive injury as a result of radiation and, at the same time, we may

very well increase the likelihood of one day curing brain cancer patients of their tumors."

Researchers have theorized from previous studies that radiation may lead to the overproduction of angiotensin II (Ang II), a peptide that has been associated with decline of brain function. By blocking the binding of Ang II to the Ang type I receptor in patients receiving radiation, researchers hypothesized that they could prevent or hinder cognitive decline. Anti-hypertensive drugs, such as losartan, have been effective in preventing or minimizing radiation-induced injury in the lungs and kidneys, Robbins said, so testing them in the brain was an obvious next step.

The study involved three groups of 80 rats. Each group was divided in half to either receive radiation or no treatment. Then, each of those halves was divided into two more groups: one that received L-158,809, the compound similar to losartan, in its drinking water, and one group that received plain drinking water. The rats that received the drug received it before, during and for different time intervals - 14, 28 or 54 weeks - post-radiation.

In addition, a small group of rats continued to receive the drug for only five weeks after radiation.

Researchers found that administering L-158,809 before, during and for as little as five weeks after radiation either prevents or lessens the severity of radiation-induced cognitive impairment.

"The extent of cognitive impairment experienced by patients who undergo radiation therapy varies in terms of how it is recognized," Robbins said. "Sometimes the patient realizes that their short-term memory is fading or that they've lost the ability to multi-task. Instead of waking up in the morning and having a clear idea of what needs to get

done that day, patients find themselves having to write things down. They just can't keep thoughts in their brain. Sometimes it's a friend or partner that realizes the impairment, but once it is noticed, it is not going to improve. Cognitive decline resulting from radiation is not stable. It is a chronic, progressive condition."

An estimated 170,000 patients undergo radiation therapy annually to treat primary or metastatic brain tumors. At least 50 percent of adult patients who undergo the treatment and live six months or more post-radiation experience some level of cognitive decline. In children, the effect is even greater, Robbins said. "All will have some form of cognitive impairment if they are long-term survivors and, thankfully, with today's technology, most children will survive long-term."

"This study provides hope that we may be able to take a drug that has been prescribed to millions of individuals with essentially very little morbidity and give it to cancer patients and stop them from experiencing cognitive impairment as a result of brain radiation. These drugs are routinely prescribed for the treatment of hypertension, are well-tolerated and exhibit anti-tumor effects," Robbins said. "They appear to be ideal for future clinical trials because they offer the promise of improving the quality of life for brain tumor patients."

Source: Wake Forest University Baptist Medical Center

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