Exposure to secondhand smoke during chemotherapy makes treatment less effective, study finds

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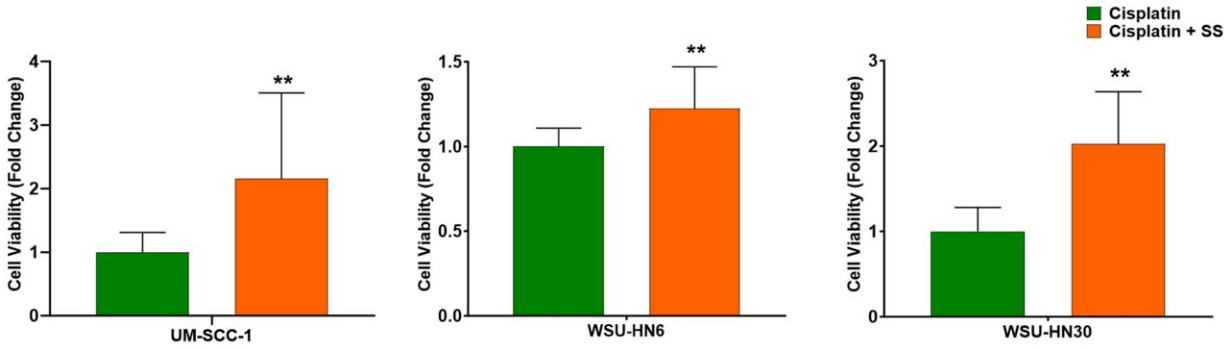

SS smoke extract increases the cell viability of cisplatin-treated head and neck squamous cell carcinoma cells. Cell viability following cisplatin treatment (10 μM) was significantly higher in cells exposed to SS smoke extract than in unexposed cells for all cell lines. Data are shown as mean ± SD. ** p
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People who are diagnosed with head and neck cancer often receive a standard type of chemotherapy as part of their treatment. If they are exposed to secondhand smoke during chemotherapy—even if they have never smoked themselves—the treatment may be far less effective at killing cancer cells. That finding, considered the first of its kind, was revealed in a study recently published by researchers at the University of

Oklahoma Health Sciences.

Tobacco use is a well-established risk factor for cancer and a signal of poor outcomes, especially if a person continues to smoke during treatment. However, researchers have understood much less about the effects of secondhand smoke on cancer treatment.

Lurdes Queimado, M.D., Ph.D., a professor of otolaryngology at the OU College of Medicine, led the investigation into secondhand smoke exposure, which was published in the *International Journal of Molecular Sciences*. Her findings have major implications for cancer patients and the physicians who treat them.

"Head and neck cancer is the sixth most common cancer worldwide and is prevalent in Oklahoma, where we also have a high rate of smoking. This is the first time that researchers have examined the impact of secondhand smoke exposure on cancer patients and the mechanism of why it is happening."

"Our studies will continue, but we think it is important to raise awareness now that people who are exposed to secondhand smoke during treatment will likely have a worse prognosis," said Queimado, who also directs the Tobacco Regulatory Science Lab in the TSET Health Promotion Research Center, a program of OU Health Stephenson Cancer Center.

In her laboratory, Queimado and her team exposed head and neck cancer cells to secondhand smoke for 48 hours (a control group of cancer cells was not exposed to secondhand smoke). Simultaneously, the cells were treated with cisplatin, a chemotherapy drug commonly used to treat head and neck cancer. The findings were significant: Twice as much chemotherapy was needed to kill the cells than would have been necessary without exposure to secondhand smoke. In addition, the cancer cells that survived chemotherapy treatment were much more

likely to replicate indefinitely.

"This was concerning to discover because not only was the effectiveness of the chemotherapy cut in half, but the cells that survived were able to divide and create huge colonies of cancer cells," Queimado said. "If the chemotherapy can't kill all the cancer, it will come back. And it will come back sooner because the cells are dividing so quickly. In addition, we cannot simply double the amount of chemotherapy we give to patients because it would be too toxic."

Queimado and her team took the research a step further to understand how secondhand smoke decreases the effectiveness of chemotherapy. They found that secondhand smoke alters the expression of several proteins involved in drug resistance, effectively restricting chemotherapy's ability to do its job.

"Cisplatin kills cancer cells by binding to their DNA and keeping the cells from dividing," she said. "But if cisplatin can't get into the cell, it's not going to kill it. Essentially, there are doors to the cancer cells that control how cisplatin gets in and out. In the presence of secondhand smoke, there were fewer doors for cisplatin to enter, and there were many more doors for cisplatin to exit. So not only is less cisplatin getting into the cell, but more of it is leaving the cell before it has a chance to kill it."

Greg Krempl, M.D., professor and chair of the Department of Otolaryngology—Head and Neck Surgery in the OU College of Medicine, said Queimado's study broadens the importance of smoking cessation during cancer treatment.

"For patients with tobacco-related cancers, smoking cessation has been shown to improve survival, so it is a part of comprehensive cancer treatment plans. This study provides novel data that would suggest

including family members in the smoking cessation plan to reduce secondhand smoke exposure during chemotherapy for head and neck cancer may improve outcomes," Krempl said.

According to tobacco use data, more than 20% of nonsmoking U.S. adults are exposed to secondhand smoke. Exposure is highest among Black people, those living in poverty, and children ages 3 to 11. Each year, secondhand smoke exposure causes more than 41,000 deaths among nonsmoking adults and 900 deaths in infants.

This new study points to the ongoing public health ramifications of both active smoking and exposure to secondhand smoke, said Balaji Sadhasivam, Ph.D., an assistant professor of occupational and environmental health at the OU Hudson College of Public Health. Sadhasivam was the lead author of the research publication.

"Even though this study was conducted in the laboratory, it closely mimics human exposure to secondhand smoke," Sadhasivam said. "If cancer patients live with someone who smokes, it is important for them to avoid being exposed to smoke while they are being treated. We want to do everything we can to help people have better outcomes from their treatment."

Cisplatin is the preferred type of chemotherapy for treating head and neck cancer, Queimado said, but physicians may want to consider another drug if they know their patients will be exposed to secondhand smoke during treatment. However, secondhand smoke exposure may affect other drugs, including non-cancer treatments.

"The proteins affected by secondhand smoke are not specific for cisplatin; they are involved in resistance to other drugs. We have not studied that yet, but it is likely that secondhand smoke decreases the effectiveness of several types of drugs."

More information: Balaji Sadhasivam et al, Exposure to Secondhand Smoke Extract Increases Cisplatin Resistance in Head and Neck Cancer Cells, *International Journal of Molecular Sciences* (2024). DOI: 10.3390/ijms25021032