

Does Chemotherapy Work Better in the Afternoon?

Women with lymphoma who received treatment in the afternoon had lower relapse and mortality rates than those treated earlier in the day.

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Women who received chemotherapy for [lymphoma](#) in the afternoon instead of in the morning appeared to respond better and had fewer side effects, according to a study published in [JCI Insight](#). Women treated in the morning had substantially higher rates of disease progression and death than those treated later in the day, but the same pattern was not observed for men.

The timing of treatment to maximize effectiveness and minimize toxicity is gaining interest in oncology and other medical fields, but it is not well understood. (The study authors call this “chronotherapy,” but that term is more often used to describe efforts to reset a person’s biological clock.) The underlying principle is to take advantage of the fact that biological processes vary over the course of the day based on circadian rhythms. Prior research suggests that the timing of chemotherapy for colorectal cancer and immunotherapy for melanoma makes a difference, but the effect may vary by sex.

Dae Wook Kim, PhD, of the Korea Advanced Institute of Science and Technology (KAIST), and colleagues compared treatment outcomes among two groups of patients with diffuse large B cell lymphoma (DLBCL), a type of non-Hodgkin lymphoma, who received chemotherapy at around 8:30 a.m. or around 2:30 p.m. Both groups received rituximab plus cyclophosphamide, doxorubicin, vincristine and prednisone, a regimen known as R-CHOP.

In a cohort of 210 patients, most achieved complete remission at the end of chemotherapy. But among women, both progression-free survival and overall survival were significantly shorter for those treated mostly in the morning compared with those treated in the afternoon. Women treated early in the day were more likely to experience disease progression (33% versus 14%) and had a higher mortality rate (20% versus 3%).

What’s more, women treated in the morning were more likely than those treated later to develop infections (17% versus 2%) and febrile neutropenia due to low white blood cells (21% versus 10%). This led to delayed and reduced drug doses, so morning patients were more likely to receive less than the planned amount of chemotherapy.

However, these associations between treatment timing and outcomes were not observed for men.

The researchers also analyzed data from 14,000 healthy individuals to identify circadian variations in blood lab values. They found that women's white blood cell counts tended to be lower in the morning and higher in the afternoon, indicating that cells were actively produced in the bone marrow earlier in the day. Men, on the other hand, did not show as much variation in blood cell production over the course of the day.

This led the study authors to suggest that women may be more vulnerable to the toxic effects of chemotherapy if they are treated in the morning, while blood cell production is underway.

"In female DLBCL patients, R-CHOP treatment in the afternoon can reduce toxicity while it improves efficacy and survival outcome," they wrote. "The sex-specific chronotherapeutic effects can be explained by the larger daily fluctuation of circulating leukocytes and neutrophils in female than in male patients."

Because not all women or men have the same circadian rhythms, the researchers want to learn how to use chronochemotherapy more precisely.

"Because the time of the internal circadian clock can vary greatly depending on the individual's sleep-wake patterns, we are currently developing a technology to estimate the time of the circadian clock from the patient's sleep pattern," study coauthor Jae Kyoung Kim, PhD, also of KAIST, said in a [press release](#). "We hope that it can be used to develop an individualized anticancer chronotherapy."

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