

Study: First-pass metabolism of alcohol occurs in women's stomachs

March 22 2022, by Sharita Forrest



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While scientists have broadly agreed that a fraction of the alcohol people consume is broken down before it reaches the bloodstream in a process called first-pass metabolism (FPM), they have been uncertain whether

this process occurs in the stomach or the liver.

Published online in the journal *JAMA Network Open*, a new study of alcohol metabolism in women who underwent sleeve gastrectomy and peers who had not had weight loss surgery indicates that this process occurs in the stomach.

In addition to clarifying where FPM occurs, the findings also explain why some patients' sensitivity to alcohol increases dramatically after [bariatric surgery](#), significantly heightening their risks of alcohol-related disorders.

A team of researchers led by [food science](#) and human nutrition professor M. Yanina Pepino at the University of Illinois Urbana-Champaign compared alcohol metabolism in 12 sleeve gastrectomy patients with that of nine women of similar ages, body mass indices and drinking habits who had not undergone weight loss surgery.

Once absorbed, most of the alcohol a person ingests is broken down in the liver by an enzymatic process that is saturable.

The challenge in identifying the site of FPM was that the stomach could play dual roles, both serving as the site where alcohol was broken down before being released to the liver and affecting a saturable FPM in the liver by modulating the speed at which the dose of alcohol was being delivered, if the liver were the site where FPM was occurring instead, Pepino said.

That is, the slower the stomach emptied, the more efficient the liver would be in metabolizing alcohol during FPM, she said. If, however, FPM occurred in the stomach, the slower the gastric emptying, the more time the stomach would have to break down the alcohol.

Previous findings from this research team and other laboratories showed that sleeve gastrectomy and [gastric bypass surgery](#) decreased the FPM of alcohol by accelerating gastric emptying, causing more rapid and higher peak blood alcohol concentrations than those patients experienced when they drank the same amount of alcohol prior to their surgeries.

In the current study, the researchers took advantage of [sleeve gastrectomy](#) to determine the site of FPM. Sleeve gastrectomy removes 80% of the patient's stomach but preserves the pylorus, the valve that controls the passage of stomach contents to the intestine.

"The data help clarify where alcohol FPM occurs and provide a plausible mechanism for the observed increase in alcohol-related diseases among many patients who have undergone bariatric surgery," Pepino said.

Co-authors of the paper included Dr. Blair Rowitz, the associate dean for clinical affairs of the Carle Illinois College of Medicine; Vijay A. Ramchandani, the senior principal investigator of human psychopharmacology with the National Institute on Alcohol Abuse and Alcoholism; and Dr. Martin H. Plawecki, a professor of psychiatry at the Indiana University School of Medicine.

A week apart, the women in the study participated in two experiments that assessed their metabolism of alcohol—an oral challenge in which they drank alcohol, and an alcohol clamp session in which it was administered through an IV catheter so their blood alcohol concentrations could be precisely controlled by removing the variable process of absorption.

For the oral challenge, after fasting overnight the participants drank 0.5 grams of alcohol per kilogram of their fat-free body mass over a 10-minute period. Through an IV catheter inserted in a hand vein, the scientists obtained blood samples at regular intervals to measure

participants' blood alcohol concentration and the time it took for each person to reach peak concentration.

In the alcohol clamp session, participants were administered 6% alcohol in a saline solution through an IV catheter. Using a computer-assisted alcohol infusion system developed by Indiana University's Neural Systems Laboratory, participants reached a target breath alcohol concentration of 60 mg/dl within 15 minutes.

That level was maintained for the next 135 minutes, allowing the researchers to estimate how quickly each person was eliminating the alcohol from their bloodstream, Pepino said.

The alcohol clamp session helped ensure that the differences found between the two groups of women during the ingested alcohol session were not due to variations in their livers' alcohol elimination rates.

"Despite the overnight fast, which minimizes alcohol FPM, the amount of the ingested alcohol dose that reached their bloodstreams—that is, the alcohol bioavailability—increased by 34% in the gastrectomy patients compared with their peers in the [control group](#)," said lead author Neda Seyedsadjadi, a postdoctoral researcher at the U. of I.

"This increased bioavailability was not explained by a decrease in their alcohol elimination rate or gastric emptying rate—differences between the groups remained when subsets of the participants were matched on the time it took to reach peak blood alcohol concentrations."

A limitation of the current study was that the participants were all women, who represent the majority of patients undergoing these surgeries. The researchers said future research should include men to determine if sex differences exist in the site of [alcohol](#) FPM.

Additional co-authors of the current paper were postdoctoral research associate Maria Belen Acevedo and doctoral student Raul Alfaro Leiva, both of the U. of I.

More information: Neda Seyedsadjadi et al, Site of Alcohol First-Pass Metabolism Among Women, *JAMA Network Open* (2022). [DOI: 10.1001/jamanetworkopen.2022.3711](https://doi.org/10.1001/jamanetworkopen.2022.3711)

Provided by University of Illinois at Urbana-Champaign

Citation: Study: First-pass metabolism of alcohol occurs in women's stomachs (2022, March 22) retrieved 26 April 2024 from <https://medicalxpress.com/news/2022-03-first-pass-metabolism-alcohol-women-stomachs.html>

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