

Randomized Trial of Homocysteine-Lowering Therapy and Risk for Venous Thromboembolism

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The full report is titled “Homocysteine-Lowering Therapy and Risk for Venous Thromboembolism. A Randomized Trial.” It is in the 5 June 2007 issue of *Annals of Internal Medicine* (volume 146, pages 761-767). The authors are J.G. Ray, C. Kearon, Q. Yi, P. Sheridan, and E. Lonn, for the Heart Outcomes Prevention Evaluation 2 (HOPE-2) Investigators.

What is the problem and what is known about it so far?

The main role of blood clotting is to prevent bleeding by sealing breaks in damaged blood vessels. However, blood clots can form on any damaged area on the surface of blood vessels. As layers of clotted blood are deposited on a tiny blood clot in an artery, the clot can grow big enough to block the flow of blood, which causes damage to the tissues that get their blood supply from that artery. The clot can also break off of the blood vessel and travel through the bloodstream and cause damage by blocking blood flow to an organ. For example, most heart attacks occur when a clot forms on the damaged surface of a small artery that supplies blood to the heart. The lining of veins can also suffer damage that leads to the formation of a clot, typically in the veins of the legs.

Chemicals that damage the surface of arteries or veins can promote the formation of blood clots. Evidence suggests that high levels of homocysteine—a chemical made by the body—can damage the surface of arteries and veins. This evidence shows that people with high blood levels of homocysteine are prone to developing blood clots that cause damage, such as heart attacks or blood clots to the lung. Researchers have found that lowering the homocysteine level does not prevent heart attacks.

Why did the researchers do this particular study?

The researchers wanted to find out whether lowering homocysteine levels would prevent blood clots from forming in veins (deep venous thrombosis) and traveling to the lungs (pulmonary embolism). To answer both questions, they gave vitamins that are known to lower homocysteine levels in the blood.

Who was studied?

5522 adults who were 55 years of age or older and received care at 1 of 145 medical centers in 13 countries were studied. Most participants were from Canada. All participants had a history of cardiovascular disease or risk factors for heart disease, including diabetes.

How was the study done?

The participants were randomly assigned to groups that received either daily placebo (sugar pill) or a supplement containing folic acid and vitamins B₆ and B₁₂ for 5 years. Neither the participants nor the researchers knew who received the vitamin supplements. The participants went to a study clinic every 6 months, where the researchers asked them whether a doctor had diagnosed blood clots in the veins. When a participant said yes, the researchers examined the participant’s medical record to see whether the diagnosis was correct.

What did the researchers find?

As expected, the vitamins lowered homocysteine levels. However, blood clots in the veins occurred at the same rate in both groups, even in persons with the highest levels of homocysteine in their blood.

What are the limitations of the study?

Most of the participants were from the United States and Canada, where the law requires manufacturers to add extra folic acid to flour.

What are the implications of the study?

Lowering homocysteine levels with folic acid and vitamins B₆ and B₁₂ does not reduce the frequency of blood clots in veins.

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