

## New hypothesis explains why drugs increase risk of heart attacks and strokes

February 23 2011

New research shows that medications which have raised safety concerns over heart attack and stroke risks may not have gotten approval from the Food and Drug Administration (FDA) if the cardiovascular effects of fluid retention had been better understood. Fluid retention may explain the increased risk of heart attacks and strokes of medications such as Vioxx, Bextra, and Avandia.

The research published in *Clinical Hemorheology and Microcirculation* (IOS Press, ISSN 1386-0291), calculates the effects of fluid retention upon the velocity of blood flow and the turbulence of flowing blood. These calculations demonstrate that fluid retention increases the risk of heart attacks and strokes. Since numerous medications cause fluid retention, the paper's findings have implications to ensure drugs on the market are safe. The pain medications Vioxx and Bextra, and the anti-diabetic medication Avandia, cause fluid retention. Vioxx and Bextra, known as cyclo-oxygenase-2 (COX-2) inhibitors, were withdrawn from the market because of safety concerns over heart attacks and strokes, and Avandia has been suspected in some reports of increasing the risk of heart attacks.

The paper's author, Robert P. Blankfield, MD, MS, clinical professor of family medicine at Case Western Reserve University School of Medicine, and a member of the Department of Family Medicine at University Hospitals Case Medical Center, used several basic cardiovascular and hydraulic equations to demonstrate that fluid retention is detrimental for the cardiovascular system.



Fluid retention increases the likelihood that blood will flow in a turbulent manner. Turbulent blood flow accelerates atherosclerosis (hardening of the arteries), thereby increasing the risk of heart attacks and strokes. Many medications cause fluid retention, which raises blood pressure in some, but not all, individuals. Physicians worry about fluid retention if it does raise blood pressure, but are unconcerned when blood pressure is unaffected.

"This paper demonstrates that fluid retention is unhealthy because it increases the likelihood that blood will flow in a turbulent manner regardless of whether or not blood pressure is raised. Therefore, drugs that cause the body to retain fluid are dangerous for the cardiovascular system," says Dr. Blankfield.

"If the FDA had been aware of the increased cardiovascular risk that arises from drugs that cause fluid retention, Vioxx, Bextra, and Avandia might never have been approved. These findings might spur the FDA to alter some of its current policies," he continues. "The calculations in this paper might also help pharmaceutical manufacturers screen drugs for their cardiovascular risk at an early stage in the drug development process."

The cardiovascular safety problems with Avandia have prompted the FDA to require verification of cardiovascular safety for new antidiabetic medications. It is Dr. Blankfield's opinion that this response by the FDA does not go far enough. "Based upon the calculations in the manuscript, the FDA ought to require verification of cardiovascular safety for all medications, old as well as new, that cause fluid retention," says Dr. Blankfield. Several older anti-diabetic medications cause fluid retention, including insulin and sulfonylureas (glyburide, glipizide, glimerperide). The paper suggests it would make more sense to scrutinize these older anti-diabetic medications, such as saxagliptin,



that do not cause fluid retention.

Additional medications currently on the market that cause fluid retention include the COX-2 inhibitor Celebrex, non-selective non-steroidal anti-inflammatory drugs (ibuprofen, known as Advil, Motrin) and some anti-seizure medications (Neurontin, Lyrica, Tegretol).

Fluid retention increases blood pressure in some individuals, increases stroke volume (the amount of blood that is ejected by the heart with each contraction) in others, and causes edema (swelling). Some blood pressure lowering medications also increase stroke volume and cause edema but prevent heart attacks and strokes when used to treat hypertension. According to Dr. Blankfield, it would make sense for <u>drug</u> companies to be cautious about bringing drugs to market that cause fluid retention but do not lower blood pressure.

He adds that it may be possible to reduce or neutralize the increased cardiovascular risk that occurs as a result of fluid retention simply by using a diuretic. Therefore, patients may be able to safely use medications such as Vioxx, Bextra, and Avandia if they simultaneously use a water pill.

The mathematical analysis performed by Dr. Blankfield has implications for public health and safety that extend beyond medications. Because sodium chloride (table salt) causes fluid retention, it likely increases the risk of heart attacks and strokes. Since it is a food additive, it would be appropriate for the FDA to address the danger of consuming sodium chloride. It would be possible to categorize processed foods based upon whether they have a low or high salt content. The FDA could mandate that processed foods with a high salt content be labeled with a simple warning: Based upon the amount of sodium chloride (salt) in this food, eating this product increases the risk of heart attacks and strokes.



In summary, if Dr. Blankfield's mathematical analysis accurately reflects the workings of the cardiovascular system, pharmaceutical manufacturers may be able to identify the cardiovascular risk of drugs by utilizing basic principles of hemodynamics and hydraulics; the FDA may be able to assure the cardiovascular safety of all drugs by mandating that pharmaceutical manufacturers obtain detailed data on those drugs that cause fluid retention but do not lower blood pressure; and for drugs that have beneficial effects but also cause fluid retention, it may be possible for patients to safely use these drugs if they simultaneously use a water pill.

**More information:** The article Calculated effect of fluid retention upon velocity of blood flow and turbulence: Implications for atherosclerosis by Robert P. Blankfield (DOI 10.3233/CH-2010-1369, pages 79-89) is published in Clinical Hemorheology and Microcirculation (ISSN 1386-0291, Impact Factor 1.78 (JCR '09)), volume 47, number 2 (2011), and can be viewed through this link iospress.metapress.com/content ... 8dd4737d9b59bcb&pi=0, free of charge.

## Provided by IOS Press

Citation: New hypothesis explains why drugs increase risk of heart attacks and strokes (2011, February 23) retrieved 28 April 2024 from <u>https://medicalxpress.com/news/2011-02-hypothesis-drugs-heart.html</u>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.