Researchers find possible cardiovascular risk with NSAID use

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A new study from Rhode Island Hospital researchers suggests that controlling cholesterol may be important for heart health in patients who are taking non-steroidal anti-inflammatory drugs (NSAIDs) such as naproxen. The findings are based on a study on the safety of NSAID medications in clinically relevant animal models when high cholesterol is a factor. The study is published in the current issue of the journal *Surgery*.

NSAIDs are among the most widely-used drugs today for the treatment of post-operative pain, inflammatory conditions and fever. Despite that, the factors that affect their cardiovascular safety are not well understood and some studies suggest that there may be an increased incidence of cardiovascular complications such as heart attack or death.

This study, led by principal investigator Frank Sellke, M.D., chief of cardiothoracic surgery and research at Rhode Island Hospital, developed an animal model of hypercholesterolemia in swine to investigate the formation of collateral vessels and other effects in the heart, and the safety of NSAID and other medications.

Through their study, Sellke says, "We found that a high-cholesterol diet reduced blood flow to the heart muscle in our animal models with chronic heart disease when given daily naproxen. We also found reduced levels of prostacyclin, a compound that dilates blood vessels and prevents blood clots. These findings suggest that there may be a stronger risk of negative effects on the heart in patients who have high

cholesterol levels and are taking NSAIDs as a form of pain or inflammation relief."

The researchers compared two groups within the animal model, one with a normal diet, and one group that received a diet high in cholesterol, and both groups received daily naproxen. The animals also underwent surgery to simulate coronary artery disease, which affects many human patients who take NSAIDs. Several differences were found between the two groups.

Compared to animals with normal cholesterol, the high-cholesterol animals treated with naproxen had lower blood flow to the heart, decreased levels of prostacyclin, and decreased levels of several proteins that promote cardiac cell survival. In addition, previous studies by the group showed that while naproxen helped increased blood flow in the hearts of animals with normal cholesterol, this effect was not seen in animals with high cholesterol.

Sellke says, "These results show that high blood cholesterol levels change the way naproxen affects the heart, and alters blood flow to the heart. This 'myocardial perfusion' may be one predictor of angina frequency and quality of life in patients with chronic ischemia. Thus, these findings may have important implications for cardiac patients taking NSAIDs."

First author Louis Chu, M.D., who worked with Sellke on the study, adds, "Our study indicates that physicians should be aware that cholesterol control may be especially important if patients are taking NSAID medications such as naproxen."

Sellke adds, "While the results of these animal experiments are interesting and may provide information regarding the effect of a high fat diet on the response to naproxen and other similar medications, one cannot make definitive statements on the effect of these medications on

patients without first doing clinical studies."

Provided by Lifespan

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