

## NSAIDに加えてミソプロストールを服用することにより心血 管系リスクが低下する(Abstract 17-A-9724)

ミソプロストールを非ステロイド性抗炎症薬と併用することでNSAID単独服用に比べ安全な 可能性がある

Combining misoprostol with non-steroidal anti-inflammatory drugs could be safer than NSAIDs alone

胃潰瘍に対して、ミソプロストールを非ステロイド性抗炎症薬(NSAID)とともに服用した人は、 NSAID単独服用した人に比べ、重篤な心血管イベント、脳卒中および腎不全のリスクが有意に 低かった、とAmerican College of Cardiology's 66th Annual Scientific Sessionで発表された。 NSAIDをミソプロストールとともに服用している人は、心筋梗塞、心停止、または心室細動の発現 リスクが44%低かった。両薬剤服用者は、NSAID単独服用者に比べ、脳卒中または一過性脳 虚血発作のリスクが25%低く、急性腎不全のリスクが34%低かった。

## Full Text

People who took the drug misoprostol for stomach ulcers along with non-steroidal anti-inflammatory (NSAID) drugs had a significantly lower risk of serious cardiovascular events, stroke and kidney failure than those who took NSAIDs alone, according to a study presented at the American College of Cardiology's 66th Annual Scientific Session

NSAIDs, a large category of drugs that includes ibuprofen, celecoxib and dozens of others, are commonly used to treat pain, inflammation and fever and are available by prescription and over the counter. They are one of the most commonly used medications worldwide. They have been linked with rare but life-threatening side effects including myocardial infarction, cardiac arrest, stroke and acute kidney failure, collectively referred to as cardio-renal complications. Because stomach ulcers are a common side effect of many NSAIDs, misoprostol and NSAIDs are sometimes prescribed together in people at high risk for ulcers

"Right now, clinicians have no direct treatment options to reduce the risk for these NSAID-induced cardio-renal complications, other than to advise against NSAID use, reduce the duration of use or recommend alternative pain management agents, so we set out to discover a treatment to reduce the risk of these effects," said Mark Munger, PharmD, professor of pharmacotherapy at the University of Utah College of Pharmacy and the study's lead author. "Our data, from a large and well-characterized health care system, support a potentially safer NSAID alternative when NSAIDs are combined with misoprostol.

The researchers analyzed the health records of more than 1.6 million people in the U.S. Veterans Affairs health system who took prescription doses of NSAIDs and/or misoprostol between 2005 and 2013. Eleven different NSAID drugs were represented in the sample. After accounting for dozens of baseline characteristics and health conditions, they identified 1,875 people who took NSAIDs alone who were "matched," in terms of baseline health status, with 1,875 people who took NSAIDs plus misoprostol. They then compared health outcomes in the two groups based on their health records over a five-year period.

People taking NSAIDs and misoprostol together had a 44 percent lower risk of having a myocardial infarction, suffering cardiac arrest, or having ventricular fibrillation. Those taking both drugs also had a 25 percent lower risk of strokes or transient ischemic attacks (TIA, "ministroke") and a 34 percent lower risk of acute kidney failure compared to people taking NSAIDs alone.

The study results suggest that combining NSAIDs with misoprostol, either by prescribing them together or by developing a combination pill, could help reduce the risk of cardio-renal NSAID-induced side effects.

Drug labels currently warn of cardio-renal complications for any NSAID dose, whether prescription or over the counter. Studies have shown the highest risk of these complications is seen in people who have recently started NSAID treatment, in those prescribed higher doses and in those who take them for long periods of

NSAIDs reduce the levels prostaglandins circulating in the body. This helps to reduce inflammation and thus relieve pain, but it also can have harmful effects in other parts of the body. Misoprostol is thought to counter these harmful effects by potentially replacing some of the reduced prostaglandins. Previous studies have shown misoprostol can lower blood pressure and improve measures of kidney function

"Hopefully we can reduce the incidence of NSAID-induced cardio-renal adverse effects, which could be especially important in an era in which pain management is in flux," Munger said. He noted that sharp increases in opioid abuse and addiction have fueled a growing emphasis on non-opioid pain management options, such as NSAIDs

An unrelated recent study suggested some NSAIDs increase the risk of heart failure. Heart failure was not included among the outcomes tracked in this study.

A key limitation of the study is that it was a retrospective analysis based on health records, rather than a prospective or randomized trial

The study was funded by the Salt Lake City Veterans Affairs Health Services Research and Development (HSR&D) Informatics, Decision-Enhancement and Analytic Sciences (IDEAS) Center with grant support from Veterans Affairs Informatics and Computing Infrastructure (VINCI) and the University of Utah Clinical Cardiovascular Research Fund

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