Study: Small Increase in Heart Risk From Common Painkillers

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Prolonged use of some widely used painkillers increases the risk of heart attacks by a small but significant amount, a large international study led by Oxford University researchers has found.

Professor Colin Baigent of Oxford's Clinical Trial Service Unit led the research on a class of painkillers called non-steroidal anti-inflammatory drugs (NSAIDs). He said: 'The research shows that, when used in high doses, diclofenac and ibuprofen increase the risk of cardiovascular disease, on average causing about 3 extra heart attacks a year in every 1000 patients treated, one of which would be fatal.

'We would emphasize that the risks are mainly relevant to people with arthritis who need to take high doses over a long period. A short course of lower dose tablets purchased without a prescription, for example for a muscle sprain, is not likely to be hazardous.'

The research is published in The Lancet and was funded by the Medical Research Council (MRC) and the British Heart Foundation (BHF).

The study found that high doses of diclofenac and ibuprofen increased the risk of a major vascular event (heart attack, stroke or dying from cardiovascular disease) by around one third. Most of this additional risk was due to an increased risk of heart attacks.

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Professor Colin Baigent In contrast, high doses of naproxen did not appear to increase the risk of heart attacks. The researchers say this may be because naproxen also has protective effects that balance out any extra risk of heart attacks.

Concerns about the possible heart risks of NSAIDs, many of which have been on the market for several decades, arose after randomized trials showed that a newer class of NSAIDs known as COX-2 inhibitors or coxibs increased the risk of heart attacks.

In England in 2010, there were 17 million prescriptions for NSAIDs, with approximately one third of them diclofenac, one third ibuprofen, and one sixth naproxen. NSAIDs are used for their pain-relieving and anti-inflammatory properties in a wide range of conditions, but the main indications in the trials included in this study were osteoarthritis or rheumatoid arthritis.

Professor Baigent said: 'For many arthritis patients, NSAIDs reduce joint pain and swelling effectively and help them to enjoy a reasonable quality of life. This new research shows how to calculate the likely size of any risks of NSAIDs for an individual patient, which should help doctors and their patients when they consider the treatment options.'

Professor Alan Silman, medical director of Arthritis Research UK, said: 'NSAIDs are a lifeline for many millions of people with arthritis, and when used appropriately can be extremely effective in relieving pain. However, because of their potential side-effects, in particular the increased risk of cardiovascular complications which has been known for a number of years, there is an urgent need to find alternatives that are as effective, but safer. GPs are aware of the risks of NSAIDs, and there has been a marked reduction in the use of diclofenac and a switch to naproxen in recent years.

'For patients with arthritis, not smoking, a healthy diet and having their blood pressure checked regularly are more important factors in reducing the risk of a heart attack. We would advise people with arthritis who are taking NSAIDs not to be unduly concerned by these latest findings and to seek the advice of their GP.'

The study team gathered detailed data, including information on admissions to hospital for cardiovascular or gastrointestinal disease, from all randomized trials that have previously tested NSAIDs.

The researchers brought together the results of 639 randomized trials involving over 350,000 people, and re-analyzed the data in order to predict the magnitude of the adverse effects of NSAIDs in particular types of patients.

The availability of detailed data from so many studies allowed the researchers to predict accurately the size of any increased risk of heart attacks and ulcer bleeding in particular types of patients, including those at increased risk of such adverse effects.

Importantly, the increased risk of heart attacks from individual NSAIDs seemed to be proportional to a patient's underlying risk of such heart attacks, so that the risk is highest in those with a previous history of heart disease or those with cardiac risk factors such as raised blood pressure or cholesterol.

The research also showed that the risks of ulcer bleeding were increased by between two- and four-fold, depending on the NSAID regimen, but the consequences of such bleeding were not usually serious.

Professor David Lomas, Chair of the MRC's Population and Systems Medicine Board, said: 'Large-scale randomized and observational studies such as this one are crucial in identifying adverse drug reactions in patients – even where the risk might be very small.'

Dr. Shannon Amoils, Research Advisor at the BHF said: 'This study supports previous findings showing that taking high doses of some NSAIDs such as diclofenac and ibuprofen for a prolonged period leads to a small increase in the risk of heart attack and stroke.

'Based on this research, we would reiterate the advice that people should take the lowest effective dose of these drugs for the shortest time necessary to control symptoms. Although people who take painkillers infrequently needn't be overly concerned, those who need regularly prescribed painkillers should speak to their doctor about which drug is the most suitable choice for them.