

'Harmless' painkillers associated with increased risk of cardiac arrest

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Pills. Credit: Public Domain

Painkillers considered harmless by the general public are associated with increased risk of cardiac arrest, according to research published today in the March issue of *European Heart Journal - Cardiovascular Pharmacotherapy*.

Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most commonly used drugs worldwide and some, including [ibuprofen](#), are available over the counter.

"Allowing these drugs to be purchased without a prescription, and without any advice or restrictions, sends a message to the public that they must be safe," said author Professor Gunnar H. Gislason, professor of cardiology at Copenhagen University Hospital Gentofte, Denmark. "Previous studies have shown that NSAIDs are related to increased cardiovascular risk which is a concern because they are widely used."

The current study investigated the link between NSAID use and cardiac arrest. All patients who had an out-of-hospital cardiac arrest in Denmark between 2001 and 2010 were identified from the nationwide Danish Cardiac Arrest Registry. Data was collected on all redeemed prescriptions for NSAIDs from Danish pharmacies since 1995. These included the non-selective NSAIDs (diclofenac, naproxen, ibuprofen), and COX-2 selective inhibitors (rofecoxib, celecoxib).

A case-time-control design was used to examine the association between NSAID use and cardiac arrest. Each patient served as both case and control in two different time periods, eliminating the confounding effect of chronic comorbidities. Use of NSAIDs during the 30 days before

cardiac arrest (case period) was compared to used of NSAIDs during a preceding 30 day period without cardiac arrest (control period).

Information was not obtained on over-the-counter drugs. Ibuprofen is the only over-the-counter NSAID in Denmark and is limited to small packages of 200 mg dosages. As patients were their own control, any underestimation of ibuprofen use should be equally distributed between the case and control periods.

A total of 28 947 patients had an out-of-hospital cardiac arrest in Denmark during the ten year period. Of these, 3 376 were treated with an NSAID up to 30 days before the event. Ibuprofen and diclofenac were the most commonly used NSAIDs, making up 51% and 22% of total NSAID use, respectively.

Use of any NSAID was associated with a 31% [increased risk](#) of cardiac arrest. Diclofenac and ibuprofen were associated with a 50% and 31% increased risk, respectively. Naproxen, celecoxib and rofecoxib were not associated with the occurrence of cardiac arrest, probably due to a low number of events.

"The findings are a stark reminder that NSAIDs are not harmless," said Professor Gislason. "Diclofenac and ibuprofen, both commonly used drugs, were associated with significantly increased risk of cardiac arrest. NSAIDs should be used with caution and for a valid indication. They should probably be avoided in patients with cardiovascular disease or many [cardiovascular risk](#) factors."

NSAIDs exert numerous effects on the cardiovascular system which could explain the link with [cardiac arrest](#). These include influencing platelet aggregation and causing blood clots, causing the arteries to constrict, increasing fluid retention, and raising blood pressure.

Professor Gislason said: "I don't think these drugs should be sold in supermarkets or petrol stations where there is no professional advice on how to use them. Over-the-counter NSAIDs should only be available at pharmacies, in limited quantities, and in low doses."

"Do not take more than 1200 mg of ibuprofen per day," he continued. "Naproxen is probably the safest NSAID and we can take up to 500 mg a day. Diclofenac is the riskiest NSAID and should be avoided by patients with [cardiovascular disease](#) and the general population. Safer drugs are available that have similar painkilling effects so there is no reason to use diclofenac."

Professor Gislason concluded: "The current message being sent to the public about NSAIDs is wrong. If you can buy these drugs in a convenience store then you probably think 'they must be safe for me'. Our study adds to the evidence about the adverse cardiovascular effects of NSAIDs and confirms that they should be taken seriously, and used only after consulting a healthcare professional."

More information: Kathrine B. Sondergaard et al, Non-steroidal anti-inflammatory drug use is associated with increased risk of out-of-hospital cardiac arrest: a nationwide case–time–control study, *European Heart Journal - Cardiovascular Pharmacotherapy* (2016). [DOI: 10.1093/ehjcvp/pvw041](#)

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