30 days in medicine

Increased risk of cardiac arrest with commonly used non-steroidal anti-inflammatory drugs

The non-steroidal anti-inflammatory drugs (NSAIDs) diclofenac and ibuprofen are associated with a significantly inreased risk of cardiac arrest, according to a Danish study published in the *European Heart Journal: Cardiovascular Pharmacotherapy*.

Researchers used the Danish Cardiac Arrest Registry to identify all individuals who had a cardiac arrest out of hospital between 2001 and 2010. Of the 28 947 people identified, 3 376 had been treated with an NSAID up to 30 days before their cardiac arrest. Each case was matched with four controls from the Danish Patient Registry.

Ibuprofen and diclofenac were the most commonly used NSAIDs, representing 51% and 22% of total NSAID use, respectively. The study found that use of any NSAID was associated with a 31% increased risk of cardiac arrest. Diclofenac was associated with a 50% increased risk of cardiac arrest (odds ratio (OR) 1.50, 95% confidence interval (CI) 1.23 - 1.82), and ibuprofen was associated with a 31% increased risk (OR 1.31, 95% CI 1.14 - 1.51).

The study found no significant association between cardiac arrest and the COX-2 selective inhibitors celecoxib and rofecoxib, or with the unselective NSAID naproxen. However, these drugs are rarely used in Denmark so relatively few events occurred, leading to low statistical power.

The authors say that the study is a stark reminder that NSAIDs are not harmless and should not be used without advice from a healthcare professional.

Sondergaard K, Weeke P, Wissenberg M, 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. Eur Heart J Cardiovasc Pharmacother 2017;3(2):100-107. http://dx.doi.org/10.1093/ehjcvp/pvw041

Measure blood pressure over 30 minutes to reduce treatment

Automated blood pressure monitoring over 30 minutes reduces not only the number of patients diagnosed with hypertension but also the number diagnosed as needing a change to existing hypertension treatment, according to a primary care study carried out on 201 consecutive patients (mean age 68.6 years) visiting a single primary healthcare centre in The Netherlands over 6 months in 2016.

Researchers measured patients' blood pressure every 5 minutes over 30 minutes using an automated blood pressure monitor. They compared the average readings with previous routine blood pressure measurements. The results, reported in the *Annals of Family Medicine*, showed that mean systolic blood pressure when measured over 30 minutes was 22.8 mmHg (95% confidence interval (CI) 19.8 - 26.1) lower than the mean found on standard measurement. The mean diastolic blood pressure on automated monitoring for 30 minutes was 11.6 mmHg (95% CI 10.2 - 13.1) lower. This backs up previous research showing that up to one-third of patients have white-coat hypertension, which falls to normal levels in other settings.

Based on standard blood pressure measurement, GPs at the health centre said that they would have started or intensified hypertension treatment in 79.1% (73.6 - 84.6%) of patients in the study. With results from automated blood pressure monitoring for 30 minutes, this figure fell to only 24.9% (18.9 - 30.9%).

Bos MJ, Buis S. 2017. Thirty-minute office blood pressure monitoring in primary care. Ann Fam Med 2017;15(2):120-123. http://dx.doi.org/10.1370/afm.2041

Insomnia linked with increased risk of stroke and myocardial infarction

Insomnia is associated with an increased risk of future myocardial infarction (MI) and stroke, according to a meta-analysis of prospective cohort studies published in the *European Journal of Preventive Cardiology*. The study included 15 prospective studies following up 160 876 adults aged >18 years for at least 2 years. The median follow-up ranged from 3 to nearly 30 years, during which time 11 702 adverse events were recorded.

The results showed that non-restorative sleep and difficulty falling asleep and staying asleep were associated with an increased risk of future cardiovascular events, including incidences of or death due to acute MI, coronary heart disease, heart failure, stroke or combined events. Early-morning waking was not associated with an increased risk of adverse events.

The underlying mechanism for the links is not understood, but the authors point out that sleep disorders are common in the general population and that sleep health should be included in a clinical risk assessment.

He Q, Zhang P, Li G, Dai H, Shi J. The association between insomnia symptoms and risk of cardio-cerebral vascular events: A meta-analysis of prospective cohort studies. Eur J Prev Cardiol 2017 (epub 30 March 2017). http://dx.doi.org/10.1177/2047487317702043

Vitamin E, selenium do not prevent dementia

Taking vitamin E or selenium supplements does not prevent dementia in asymptomatic older men, according to a study published in *JAMA Neurology*.

The Prevention of Alzheimer's Disease by Vitamin E and Selenium (PREADViSE) trial was piggybacked onto a larger randomised controlled trial looking at the antioxidant effects of selenium and vitamin E on the incidence of prostate cancer. The parent trial started in 2002, but was stopped in 2009 after a planned futility analysis showed no effects on prostate cancer incidence.

The trial recruited 7 540 men with a mean age of 67.5 years who were randomly assigned to receive vitamin E, selenium, vitamin E and selenium, or placebo. They were given antioxidant supplements for an average of 5.4 years and assessed using a cognitive screen. When the parent trial ended, a subset of 3 786 men received no additional supplements but continued to be observed for up to 6 more years.

Although oxidative stress has been implicated in Alzheimer's disease, the role of antioxidant supplements in disease prevention is not known. This study shows that using vitamin E and selenium supplements do not prevent dementia and should not be used for prevention.

Kryscio RJ, Abner EL, Caban-Holt A, et al. Association of antioxidant supplement use and dementia in the prevention of Alzheimer's disease by vitamin E and selenium trial (PREADVISE). JAMA Neurol 2017 (epub 20 March 2017). http://dx.doi.org/10.1001/jamaneurol.2016.5778

Increased risk of all-cause mortality if overweight at any time

Those who are overweight or obese at any stage of their lives have a greater risk of death from cardiovascular disease, cancer and other causes than those who maintain a normal weight. This is the result of an analysis of three large cohort studies published in the *Annals of Internal Medicine*. The data were from the Nurses' Health Study I

and II and the Health Professionals Follow-up Study, which included 225 072 men and women. Each participant had a maximum body mass index (BMI) recorded over 16 years of weight history and a single baseline BMI recorded after this period. Subjects were then followed up for a mean of 12.3 years, during which time there were 32 571 deaths.

As found in previous research, the overweight category as defined by a single baseline BMI was not associated with an increased risk of death. However, when the maximum BMI was used, it was clearly associated with a significant but modest increase in risk. For those who had been obese at any stage, the risk was even higher. There were no exclusions based on a history of smoking or illness, and the pattern of excess risk with a maximum BMI above normal weight held for all ages, regardless of sex. The highest risk for death was among participants who had substantial decreases in weight, probably caused by illness.

Researchers say that looking at a person's weight history reverses the paradoxical association between overweight and reduced mortality seen in some studies.

Yu E, Ley SH, Manson JE, et al. 2017. Weight history and all-cause and cause-specific mortality in three prospective cohort studies. Ann Intern Med 2017;(epub 4 April 2017). http://dx.doi.org/10.7326/M16-1390

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