Abstracts

Anti-inflammatories, arthritis and gastric outcomes

This recent paper in the *Lancet* caught my eye, mainly because my mother-in-law is riddled with arthritis and has been on anti-inflammatories of various kinds for many years. She started on the now notorious Vioxx, was taken off it, continued on cyclo-oxygenase (COX)-2 selective inhibitors and was finally taken off those when she was found to have oesophageal erosion. She is actually now feeling a lot better without the drugs, but had a hard time for the first few months without them.

This paper in the *Lancet* suggests that the COX-2 inhibitors do indeed reduce the incidence of gastrointestinal events, of the uncomplicated kind, but not the incidence of more serious, complicated events. As the authors of this study point out, traditional non-steroidal anti-inflammatory drugs (NSAIDs) significantly increase the risk of upper gastrointestinal events such as bleeding ulcers by 2 - 5 times compared with no NSAID therapy. Strategies used to decrease the risk of NSAID-associated upper gastrointestinal clinical events include medical co-therapy with misoprostol or proton pump inhibitors (PPIs), or the use of COX-2 selective inhibitors. The incidences of upper gastrointestinal clinical events have been shown to be significantly less with COX-2 selective inhibitors than traditional NSAIDs in randomised gastrointestinal outcomes trials of 12 weeks - 12 months' duration. However, none of these trials simulated real-world practice because gastrointestinal protective therapies, e.g. PPIs, were not allowed. Thus, the effect of COX-2 selective inhibitors versus traditional NSAIDs in patients taking PPIs is unknown.

Upper gastrointestinal symptoms such as dyspepsia are the most common side-effects that occur with NSAID use. Dyspepsia is reported weekly in up to about 30% of patients taking NSAIDs regularly, and in up to 15% daily. Furthermore, dyspepsia is the most common reason for discontinuation of NSAID therapy. Among patients without ulcers, PPIs have shown significant benefit in relief or prevention of NSAID-associated upper gastrointestinal symptoms. COX-2 selective inhibitors have also been reported to induce less dyspepsia than traditional NSAIDs. However, the relative benefit of traditional NSAIDs versus COX-2 selective inhibitors on upper gastrointestinal symptoms in PPI users has not been studied in a clinical trial.

In this trial the authors set out to compare the upper gastrointestinal safety of COX-2 selective inhibitors versus traditional NSAIDs in a way that simulated standard clinical practice. Their aim was to assess the effects of these drugs on gastrointestinal outcomes in a population that included patients taking gastrointestinal protective therapy.

The MEDAL (Multinational Etoricoxib and Diclofenac Arthritis Long-term) programme provides a randomised comparison of the COX-2 selective inhibitor etoricoxib and the traditional NSAID diclofenac in 34 701 osteoarthritis and rheumatoid arthritis patients followed up for a mean duration of 18 months.

They found that there were significantly fewer upper gastrointestinal clinical events with the COX-2 selective inhibitor etoricoxib than with the traditional NSAID diclofenac due to a decrease in uncomplicated events, but not in the more serious complicated events. The reduction in uncomplicated events with etoricoxib is maintained in patients treated with PPIs and is also seen with regular low-dose aspirin use.

Lain L, *et al. Lancet* 2007; 369: 465-473.

Preventing type 2 diabetes

Type 2 diabetes is distressingly common in Westernised societies and is predicted to rise to alarming levels. We know that people with impaired glucose tolerance have a high risk of progressing to type 2 diabetes and as a result there have been many trials of interventions to prevent the onset of the disease, including pharmacological, lifestyle and herbal remedies. The authors of this paper in the *British Medical Journal* used an analysis of such trials to look at the effectiveness of pharmacological and lifestyle interventions to prevent or delay the onset of type 2 diabetes.

They searched Medline (1966 - July 2006) and Embase (1980 - July 2006) with search strategies developed by combining phase 1 and 2 of the Cochrane Collaboration's randomised controlled trials filter, search terms covering both type 2 diabetes and prevention, and clinical terms for impaired glucose tolerance. They also searched the Cochrane central register of controlled trials and the *Cochrane Library of Systematic Reviews* (issue 2, 2006), sought expert opinion on relevant trials, and checked references of any articles that met the inclusion criteria and published reviews that considered prevention of type 2 diabetes.

They found that lifestyle and pharmacological interventions reduce the rate of progression to type 2 diabetes in people with impaired glucose tolerance. Lifestyle interventions seem to be at least as effective as drug treatment.

Gillies CL, *et al. BMJ* 2007; 334: 299.

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