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A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

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Association of NSAIDs with atrial fibrillation

Non-steroidal anti-inflammatory drugs (NSAIDs) are one of the most widely used drug groups worldwide. Gastrointestinal toxicity, renal impairment and heart failure associated with these drugs have been a concern for some time. The risk of myocardial infarction associated with NSAIDs has also been highlighted. More recently there has been focus on the association of NSAIDs with atrial fibrillation (AF).

Atrial fibrillation is the most common rhythm disorder in clinical practice, leading to an increased risk of thromboembolic stroke and heart failure. Ageing patients are increasingly more likely to suffer from AF, plus they also may suffer from the conditions prompting NSAID use.

Two case control analyses have examined the risk of AF/flutter associated with traditional non-selective NSAIDs. They both showed an increased rate of AF/flutter, of a similar magnitude, associated with NSAIDs (44% increase in risk of AF/flutter). The most recent of these also showed a higher increase in risk of AF/flutter with COX 2 inhibitors (nearer 70% increase in risk). An inconsistency between the 2 case control studies was that one showed the most increased risk associated with *new* NSAID use whereas the other with *long term* NSAID use.

There is uncertainty as to a plausible biological mechanism for NSAIDs increasing the risk of AF. NSAIDs causing or exacerbating heart failure and hence AF/flutter would seem a reasonable explanation, however the risk was still increased in those without heart failure or cardiovascular disease.

Although the studies addressed many confounders for AF risk amongst the patients analysed, there may be some unaccounted for variable. Perhaps a severe underlying inflammation in new users of NSAIDs might have caused an increase in risk of AF and also prompted the use of NSAIDs. Acute pain, an indication for NSAID use, results in autonomic activation, known to precipitate atrial tachycardias. Hence the association with the drug does not imply a cause and effect relationship. The indication for use of NSAIDs may be the cause of AF.

To date, population based case control studies are the best available evidence. The increased risk when related to the actual risk translates into 4 extra cases per year of AF per 1000 new users on non-selective NSAIDs and 7 extra cases per year per 1000 new users of COX2 inhibitors.

Although a change in current practise is not necessarily warranted, questions are raised about this association. Diclofenac and COX2 inhibitors, previously identified as being associated with cardiovascular death, were associated with the highest risk of AF. Is there a pharmacological role of NSAIDs, in particular COX 2 inhibition, in relation to AF?

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FOR FURTHER INFORMATION – CONTACT THE PHARMACY DEPARTMENT ON 82751763 or email: chris.alderman@rgh.sa.gov.au
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