Systemic treatments for inflammatory disease may protect against cardiovascular risks such as stroke

Some medicines used to treat inflammatory diseases such as rheumatoid arthritis, psoriasis or psoriatic arthritis might help to protect patients against cardiovascular problems such as heart attacks or stroke.

INTRODUCTION
Rheumatoid arthritis, psoriasis and psoriatic arthritis are chronic inflammatory conditions. Rheumatoid arthritis and psoriatic arthritis affect the joints, and psoriasis affects the skin. All three diseases can cause pain and disability. It is known that patients with rheumatoid arthritis, psoriasis or psoriatic arthritis are more likely to have cardiovascular problems such as heart attacks, heart failure or stroke. This is because these diseases have an inflammatory effect on other systems in the body, as well as the joints and the skin.

WHAT DID THE AUTHORS HOPE TO FIND?
The authors wanted to see whether there was a link between the medicines that some patients take for rheumatoid arthritis, psoriasis or psoriatic arthritis and the likelihood of having cardiovascular problems. They looked at four different types of systemic medicines used in these diseases. A systemic medicine is one that may have an effect anywhere in the body, as well as in the place where the disease is active – for example, in the joints.

HOW WAS THE REVIEW CONDUCTED?
A systematic review aims to identify all the published evidence on a particular topic and draw it together into one summary. This paper was also a meta-analysis, which means that statistical analyses have been performed on the results in order to be sure that the conclusions being drawn are meaningful.

The authors searched for trials and studies that reported cardiovascular problems in patients taking a group of medicines called TNF inhibitors, as well as those taking methotrexate, corticosteroids or non-steroidal anti-inflammatory drugs (also known as NSAIDs). The search gave a long list of 2630 articles. Of these 34 had the correct type of information and were included in the review.

WHAT DO THE RESULTS SAY?
The review found that in patients with rheumatoid arthritis TNF inhibitor medicines or methotrexate reduce the chance of suffering from cardiovascular problems by around one-third. For patients taking TNF inhibitors there were reductions in the numbers of heart attacks and strokes that would normally be expected, although no difference was seen for heart failure. Methotrexate was not associated with a significant reduction in the risk of having a stroke, but there was a trend towards fewer instances of heart failure. The review also found that corticosteroids and non-steroidal anti-inflammatory drugs increased the chance of having a cardiovascular problem, especially a stroke.

In patients with psoriasis or psoriatic arthritis the evidence was more limited as only six studies in these patients were included, so it was harder to draw conclusions. But the findings suggest that some of the medicines used to treat the symptoms of psoriasis/psoriatic arthritis might also reduce the chance of patients experiencing cardiovascular problems.

ARE THESE FINDINGS NEW?
Yes – this is the first time anyone has performed a systematic review and meta-analysis to look at the association between certain medicines and cardiovascular risks in patients with rheumatoid arthritis, psoriasis or psoriatic arthritis. But there have been two previous systematic reviews\(^1\)\(^2\) and two separate meta-analyses\(^3\)\(^4\) that asked similar questions. These four reviews also found that TNF inhibitors and methotrexate may reduce the number of cardiovascular problems in patients with rheumatoid arthritis, but they did not look at corticosteroids or non-steroidal anti-inflammatory drugs, or at the effects in patients with psoriasis or psoriatic arthritis.

HOW RELIABLE ARE THE FINDINGS?
There were some limitations in the review. The search included only articles written in English, and only one reviewer screened all the initial search results, so it is possible that some articles were excluded that would not have been by other people. The review also included only observational studies, not randomised clinical trials. These different types of studies have different rules for which patients are included and how they are treated and followed up. In general, randomised clinical trials are very strict because they are testing a certain question or medicine in a very precise way. A randomised clinical trial assigns patients by chance to separate groups.
Using chance in this way means that the groups will be similar and will allow the variable or treatment under investigation to be compared objectively. Observational studies follow a set of normal patients and draw conclusions from them, but these patients have not been assigned to their treatments by chance, and not all groups will be similar. This means that the authors of this review can suggest that there might be an association between the medicines and the cardiovascular problems recorded, but because the studies were not randomised clinical trials they cannot say for sure that the medicines have caused the effect. Also, there are differences in some of the definitions and variables between some of the studies, which could mean that it is difficult to exactly compare the results.

There were only six studies included for psoriasis and psoriatic arthritis, which means the results for these diseases are less reliable than the ones for rheumatoid arthritis because the sample is smaller. This can affect how reliable we can say the statistics are for this group.

Some of the studies included looked at the effects of a medicine called rofecoxib – a non-steroidal anti-inflammatory drug which is no longer available for safety reasons. This may have affected the results for this group of medicines. But overall the authors are confident that this is a reliable review of the current knowledge that is available.

**WHAT DOES THIS MEAN FOR ME?**

The authors say that using medicines that target inflammation in rheumatoid arthritis, psoriasis and psoriatic arthritis might also have a positive effect on the cardiovascular problems commonly found in these patients. In particular, TNF inhibitors and methotrexate may offer protection against heart attacks, heart failure and stroke in addition to their disease-modifying effects on the joint disease. Patients who are taking corticosteroids or non-steroidal anti-inflammatory drugs for their rheumatoid arthritis should be monitored closely by their doctor for signs of cardiovascular problems. The results of this study might mean that doctors will weigh the risks of prescribing corticosteroids or non-steroidal anti-inflammatory drugs in patients with rheumatoid arthritis against the benefit in terms of less joint inflammation, less pain and better function. Some doctors may consider prescribing TNF inhibitors or methotrexate instead of corticosteroids or non-steroidal anti-inflammatory drugs, although TNF inhibitors are usually only recommended in people who have already tried other treatments, or who aren’t able to take other treatments. More studies will be needed to confirm these findings and for recommendations to be made to doctors.

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Date summary prepared: February 2015

Summary based on research article published on: 5th January 2015


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**REFERENCES**