A systematic review on the optimum management of the use of methotrexate in rheumatoid arthritis patients in the perioperative period to minimize perioperative morbidity and maintain disease control

Loza E, Martinez-Lopez JA, Carmona L

CRD summary
This review concluded that continuing with low doses of methotrexate seemed to be a safe option during the perioperative phase for rheumatoid arthritis patients undergoing surgery. Lack of quality assessment, potential clinical differences between included studies and a limited narrative synthesis mean that caution is warranted when interpreting the authors’ conclusions.

Authors' objectives
To examine the use of methotrexate in rheumatoid arthritis patients during the perioperative period.

Searching
MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials (CENTRAL) were searched from 1961 to July 2007 for articles published in any language. Search terms were reported. Conference proceedings from the American College of Rheumatology (2005 to 2006) and the European League Against Rheumatism (2005 to 2007) were scanned. Reference lists of retrieved studies were handsearched.

Study selection
Randomised controlled trials (RCTs) and high quality cohort studies in adult rheumatoid arthritis patients (aged 18 or over) that compared control with methotrexate after any type of surgery were eligible for inclusion. The intervention group was defined as patients taking methotrexate for four weeks prior to surgery and continued on methotrexate. The control group was defined as patients that stopped methotrexate at least one week prior to surgery. Relevant outcomes were surgical complications, rheumatoid arthritis flare-ups, wound morbidity, and infections.

In included studies, methotrexate was given at a mean dose that ranged from 4.3mg/week to 13.1mg/week before surgery (generally more than six weeks before surgery) and not discontinued after surgery in the intervention groups; in control groups methotrexate was given at a mean dose that ranged from 4.9 mg/week to 12.5 mg/week prior to surgery and was discontinued one to two weeks before surgery. The type of surgery was some form of orthopaedic surgery. The mean age of included patients ranged from 49 to 63 years; most patients were women.

Two reviewers independently performed study selection.

Assessment of study quality
There were no specific criteria to assess study quality; studies were graded according to their design using the Oxford Centre for Evidence Based Medicine Level of Evidence.

Data extraction
Data were extracted on surgical complications, rheumatoid arthritis flare-ups, wound morbidity, and infections.

Two reviewers independently performed data extraction, and disagreements were resolved by consensus or discussion with a third reviewer.

Methods of synthesis
A narrative synthesis was presented.

Results of the review
Four studies were included in the review (n=550 patients): two randomised prospective studies, one prospective observational study, and one retrospective observational study.
Three studies showed that methotrexate was not associated with an increased risk of surgical complications, including wound morbidity and infections.

One observational study showed an increase in infections in patients who received methotrexate perioperatively.

There was limited and conflicting information on the rates of rheumatoid arthritis flare-ups with perioperative methotrexate.

**Authors’ conclusions**
Continuing with methotrexate (low doses) seemed to be a safe option during the perioperative phase for rheumatoid arthritis patients undergoing surgery.

**CRD commentary**
Inclusion criteria for the review were clearly defined. Several relevant databases were searched without language restrictions. Publication bias was not assessed and could be ruled out, although there was some attempt to locate unpublished data in the form of conference proceedings. Attempts were made to reduce reviewer error and bias during study selection and data extraction.

Quality assessment was only undertaken using a basic grading of study design, so the specific elements of study quality are uncertain. Studies were narratively synthesised, but there was very little grouping of studies, which it difficult to interpret the results. There were differences in patient characteristics, along with doses and timings of methotrexate between studies, which added to the complexity of interpreting the results.

Overall, lack of included study quality assessment, clinical heterogeneity and limited narrative synthesis mean that caution is warranted when interpreting the authors’ conclusions.

**Implications of the review for practice and research**

**Practice**: The authors did not state any implications for practice.

**Research**: The authors stated that larger studies of more representative patients are needed to confirm the findings of this review. These studies also need to determine the appropriate dose of methotrexate perioperatively, or the timing for stopping and restarting methotrexate if the drug is discontinued.

**Funding**
Unrestricted grant from Abbott (the manufacturers of methotrexate TDX assay).

**Bibliographic details**

**PubMedID**
19917174

**Original Paper URL**
http://www.clinexprheumatol.org/abstract.asp?a=2

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Antirheumatic Agents /administration & dosage /contraindications; Arthritis, Rheumatoid /drug therapy /surgery; Drug Administration Schedule; Female; Humans; Male; Methotrexate /administration & dosage /contraindications; Middle Aged; Orthopedic Procedures; Perioperative Care
Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.