Mycophenolate mofetil treatment for IgA nephropathy: a meta-analysis
Xu G, Tu W, Jiang D, Xu C

CRD summary
This review evaluated treatment with mycophenolate mofetil in patients with IgA nephropathy. There were no differences observed between the intervention and placebo treatment. The authors' conclusions about the paucity evidence and the results of the review are likely to be reliable.

Authors' objectives
To evaluate the benefits and risks of treatment with mycophenolate mofetil (MMF) in patients with immunoglobulin A nephropathy (IgAN).

Searching
PubMed (April 2008) and The Cochrane Library were searched for studies in any language; search terms were reported. Additional studies were identified from references in MEDLINE-cited articles.

Study selection
Randomised controlled trials (RCTs) of adult humans in which MMF was the intervention were eligible for inclusion. Studies in which recovery, deterioration and renal replacement requirements were not reported were excluded. The clinical outcomes of interest were numbers of patients who showed 50% or greater declines in proteinuria, 50% or greater increases in serum creatine and patients who required renal replacement.

The included studies were published between 2002 and 2005. MMF was given at doses ranging from 1.0g/day to 2.0g/day. Patients in most trials received concurrent conventional treatment with blockers of angiotensin-converting enzyme (ACE inhibitors).

Two reviewers selected studies for inclusion.

Assessment of study quality
The reviewers assessed methodological quality using the five-item Jadad scale.

The authors stated neither how the quality assessment was performed nor how many reviewers performed the quality assessment.

Data extraction
Two reviewers independently extracted data to permit the calculation of relative risks (RR) for dichotomous outcomes and weighted mean differences (WMD) for continuous outcomes, both with 95% confidence intervals (CI).

Methods of synthesis
The pooled relative risks, weighted mean differences and 95% CIs for the outcomes were calculated using a Mantel-Haenszel fixed-effect model. The Q statistic test was used to evaluate statistical heterogeneity across the studies. Had statistically significant heterogeneity been observed, a Der Simonian and Laird random-effects model was used. The reviewers explored potential publication bias by visual appraisal of funnel plots and used Begg's test for publication bias.

Results of the review
Four RCTs (n=168) were included in the review. Patient numbers in the included studies ranged from 32 to 60. Treatment with MMF was compared with placebo in three trials and steroids in one trial. A Jadad score for methodological quality of 3 out of 5 was assigned to three studies; the remaining study was judged to be of high quality, with a Jadad score of 5. Follow-up durations ranged between 18 and 36 months.
There were no significant differences observed in the pooled estimates of effect between MMF treatment and placebo or steroid treatment in proteinuria (RR 1.37, 95% CI 0.79 to 2.38, p=0.26). There was statistically significant heterogeneity reported for this outcome (p=0.007). In one trial where MMF was compared to steroids, a statistically significant beneficial effect was observed for steroid treatment compared to MMF (RR 1.47, 95% CI 1.09 to 1.99).

Three trials evaluated MMF treatment compared with placebo. There were no statistically significant benefits of MMF for serum creatinine (RR 1.19, 95% CI 0.62 to 2.25, p=0.60) and requirements for renal replacement therapy (RR 1.10, 95% CI 0.46 to 2.64, p=0.83). There was no statistically significant heterogeneity observed for the analysis of these outcomes.

There were no serious adverse events reported in any of the trials.

For the analysis of publication bias, the funnel plots showed symmetry for both proteinuria and renal function. The Begg's test also showed no significant heterogeneity in the included studies.

Authors' conclusions
The available evidence did not support the routine use of treatment with MMF in patients with IgAN. More research was required with larger study populations that included patients with a more broad spectrum of histopathological changes and longer treatment durations.

CRD commentary
The review addressed a clear question. Inclusion criteria were stipulated. The search was adequate and designed to minimise language bias. There were no attempts to search for unpublished studies, which may have caused relevant studies to be missed. The authors appeared to take steps to minimise errors and bias in most parts of the review process, but no such steps were reported explicitly for quality assessment. The authors found the risk of publication bias was minimal. As acknowledged by the authors, the included studies were all very small and were almost certain to be insufficiently powered to detect differences between treatments. The authors' conclusions about the evidence and the paucity of large well-controlled studies reflect the results of the review and are generally likely to be reliable.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that studies with larger sample sizes with longer durations of follow-up and that included patients with mild and severe disease were required. In addition, the effects of MMF use alone (or with angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers) were also required in patients who did not receive other therapies.

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