Cytomegalovirus prophylaxis with antiviral agents in solid organ transplantation: a meta-analysis

Couchoud C, Cucherat M, Haugh M, Pouteil-Noble C

Authors' objectives
To assess the efficacy of antiviral agents to prevent cytomegalovirus (CMV) infection and symptomatic disease in solid organ transplant recipients, and to decrease the incidence of acute rejection, graft loss and death.

Searching
MEDLINE was searched from January 1982 to September 1996, EMBASE from January 1988 to September 1996, and Pascal from January 1990 to December 1995. In addition, the reference lists of the articles and some congress proceedings were searched manually. Studies published in any language were considered.

Study selection
Study designs of evaluations included in the review
Prospective, randomised controlled trials (RCTs) with participants randomised to receive treatment (before CMV infection), no treatment or placebo.

Specific interventions included in the review
The specific interventions were the antiviral agents acyclovir and/or ganciclovir, no treatment or placebo.

Participants included in the review
The participants were adults or paediatric solid organ transplant recipients.

Outcomes assessed in the review
The primary outcome was the incidence of symptomatic CMV disease. The secondary outcomes were CMV infection, death, graft loss and acute rejection.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The authors do not state that they assessed quality.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction. However, the authors were asked (by letter) to verify the data extracted and to provide any missing data.

Methods of synthesis
How were the studies combined?
The studies were combined using the fixed-effect methods of either an additive model (rate difference) or a multiplicative model (log relative risk, log RR), and the 95% confidence intervals (CIs) were calculated. Subgroup analyses were conducted to assess the effects of the type of organ (kidney or liver), the CMV serology matching of the donor and the recipient, and the type of antiviral agent (acyclovir or ganciclovir).

How were differences between studies investigated?
The chi-squared test for homogeneity was calculated using the Cochran-Q test, with significance set at a p-value of less
than 0.1.

**Results of the review**
Thirteen RCTs with 1,138 participants (585 in the treatment group and 553 in the control group) were included.

No heterogeneity was detected for any of the analyses.

Prophylactic treatment was found to be associated with a statistically-significant decrease in CMV disease (RR 0.50, 95% CI: 0.40, 0.62, p<0.001), compared with placebo or no treatment.

Prophylactic treatment also decreased the rate of CMV infection (RR 0.74, 95% CI: 0.62, 0.88, p<0.001).

The analysis failed to show a statistically-significant decrease in graft loss, death or the acute rejection rate.

The subgroup analysis based on the type of antiviral agent (acyclovir or ganciclovir) showed a statistically-significant decrease in CMV disease: the RRs were 0.48 (95% CI: 0.27, 0.84) and 0.48 (95% CI: 0.37, 0.63) for acyclovir and ganciclovir, respectively.

Ganciclovir was associated with a statistically-significant decrease in CMV infection (RR 0.67, 95% CI: 0.52, 0.87), whereas acyclovir was not (RR 0.80, 95% CI: 0.60, 1.05).

**Authors' conclusions**
The use of antiviral agents for the prevention of CMV disease and infection in solid organ transplantation was supported by this meta-analysis.

**CRD commentary**
The authors clearly stated their research question and the inclusion and exclusion criteria. A good review of the literature was conducted. The data were combined appropriately and the studies were tested for homogeneity, including subgroup analyses for the different groups included in the review. There was also a detailed report and discussion of the data extracted from the studies.

The drawbacks in the review concerned the processes of selecting the articles and extracting the data, and the lack of a quality scoring for the included studies. These processes were not transparent and could have introduced bias at any of those stages of the review.

The authors' conclusions follow from the reported results but should be viewed with caution because of the observed limitations.

**Implications of the review for practice and research**
The authors state that further clinical trials are required to estimate the cost of using antiviral agents for prophylaxis of CMV disease and CMV infection, compared with a pre-emptive approach. The authors also state that the observed 20% decrease in the RR for graft loss and death should be assessed in larger trials, since this would be of major importance in clinical practice if confirmed.

**Bibliographic details**

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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.