CMV-hyperimmune globulin for preventing cytomegalovirus infection and disease in solid organ transplant recipients: a meta-analysis

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CRD summary
This review, which assessed the effectiveness of cytomegalovirus hyperimmune globulin in preventing cytomegalovirus disease in organ transplant recipients, concluded that cytomegalovirus hyperimmune globulin improved total survival, reduced cytomegalovirus disease, and reduced cytomegalovirus-associated deaths. A lack of reporting of certain data means that the authors' conclusions should be interpreted with some caution.

Authors' objectives
To assess the effectiveness of cytomegalovirus hyperimmune globulin in preventing cytomegalovirus disease in solid organ transplant recipients.

Searching
MEDLINE and EMBASE were searched to June 2006. Search terms were reported. It also appears that the Cochrane databases were searched.

Study selection
Randomised controlled trials (RCTs) of prophylactic cytomegalovirus hyperimmune globulin treatment in solid organ transplant recipients were eligible for inclusion. Eligible trials had to report any of the following outcomes: death, cytomegalovirus-related death, cytomegalovirus infection, cytomegalovirus disease, and episodes of acute rejection. Trials including bone marrow transplant recipients were excluded.

Participants in included trials received transplants of either a lung, liver, heart or kidney, and received cytomegalovirus hyperimmune globulin at doses ranging from 100-500mg/kg (sometimes with acyclovir) for between 10 weeks and 6 months after transplantation; doses often varied with time. Over half the trials included only kidney transplant recipients. Control groups received a placebo, no cytomegalovirus hyperimmune globulin treatment, or acyclovir. Cytomegalovirus disease, cytomegalovirus infection, and cytomegalovirus-associated death were the most commonly reported outcomes. Median follow-up time was 12 months (range from three to 22 months).

The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Trial quality was rated by assessing method of randomisation, allocation concealment, blinding of outcome assessors, and dropouts.

It was unclear exactly how many reviewers performed the quality assessment, but disagreements were resolved by consensus.

Data extraction
Relative risks with 95% confidence intervals (CI) were calculated for each trial. For trials with no events in a group, 0.5 was added to each cell of the 2x2 table. Analyses were done using intention-to-treat data.

It was unclear exactly how many reviewers extracted data, but disagreements were resolved by consensus.

Methods of synthesis
Meta-analyses of pooled relative risks (RR) were performed using a fixed-effect model (or a random-effects model if heterogeneity was observed using the Q statistic). Sensitivity analyses were performed which assessed the influence of
individual trials by excluding each in turn. Subgroup analysis was carried out using just data for kidney transplant patients. Publication bias was assessed using a funnel plot.

**Results of the review**

Eleven RCTs (n=698 participants) were included in the review. Sample sizes ranged from 21 to 162 participants. Results of the trial quality assessment were not provided. A funnel plot showed no evidence of publication bias.

Use of cytomegalovirus hyperimmune globulin was beneficial for total survival (RR 0.67, 95% CI 0.47 to 0.95; five RCTs) and for preventing cytomegalovirus-associated death (RR 0.45, 95% CI 0.24 to 0.84; nine RCTs), although the subgroup analysis results for kidney transplant recipients were not statistically significant.

Cytomegalovirus hyperimmune globulin treatment significantly reduced cytomegalovirus disease in both the whole group (RR 0.69, 95% CI 0.57 to 0.85) and the kidney subgroup (RR 0.70, 95% CI 0.56 to 0.87), but had no significant effect on cytomegalovirus infections nor clinically relevant rejections.

**Authors’ conclusions**

Prophylactic administration of cytomegalovirus hyperimmune globulin after solid organ transplantation was associated with improved total survival, reduced cytomegalovirus disease and reduced cytomegalovirus-associated deaths.

**CRD commentary**

The review addressed a clear question and was supported by appropriate inclusion criteria. A fairly basic search (two databases) was undertaken to find relevant studies. It did not appear that the authors searched for unpublished work, so some relevant studies may have been missed (although a funnel plot suggested that publication bias may not have been a major issue). It appears that language bias may also have not be an issue, since the authors stated that two of the included trials were not published in English. Suitable methods appeared to have been employed to minimise the risks of reviewer error and bias for the processes of data extraction and assessing trial quality, but the authors did not report on the methods used to select trials for inclusion. Although the authors stated that they performed a quality assessment of the included trials, no results were presented, making interpretation of the review’s results quite difficult. Although appropriate methods were used to pool results and assess heterogeneity, the heterogeneity results were not reported. Results for the sensitivity analyses were also not reported. The lack of reporting of certain data in this review, especially with respect to trial quality, means that the authors’ conclusions should be interpreted with some caution.

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

The authors did not state any implications for practice or further research.

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