Cytomegalovirus And Drugs Used To Prevent And Treat This Infection As Risk Factors For Longer Term Deterioration Of Kidney Function After Solid Organ And Human Stem Cell Transplantation

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BACKGROUND

- Deterioration of kidney function is a serious complication following transplantation
- Factors associated with longer-term deteriorating kidney function after transplantation are poorly understood

Hypothesis

- The occurrence of post-transplant Cytomegalovirus (CMV) infection may increase deterioration; directly by causing nephritis or secondarily by the use of nephrotoxic antiviral drugs

Objectives

- To assess effects of CMV infection, CMV viral load and drugs used as prophylaxis or treatment on evolution of eGFR in the first year following a transplantation

METHODS

Patients and study design

- Inclusion: Consecutive transplanted patients (2004 to 2008), monitored for CMV infection, above 18 years at the time of their transplantation

Statistical methods

- Factors affecting eGFR levels from month 1 to 12 following the transplantation were evaluated by regression coefficients using unadjusted and adjusted multivariable mixed effects models. Models included both fixed time and time-dependent covariates

RESULTS

- There were 303 individuals who satisfied the entry criteria
- Overall eGFR decreased from a median (IQR) of 68 (48.96) at month 1 to 55 (40.08) at month 12 (Table 2)
- After adjustment, eGFR decreased by -0.23 [95% CI: -0.26 to -0.19, p<0.0001], -0.68 [95% CI: -0.78 to -0.59, p<0.0001], and -0.05 [95% CI: -0.11 to 0.01, p=0.10] for each 5 days of follow up in kidney transplant, non kidney solid organ transplant, and HSCT recipients, respectively

- Valganciclovir used as CMV chemoprophylaxis was associated with a negative eGFR slope (-0.4 [-0.5 to -0.3] ml/min/1.73m2 for each week longer usage, p<0.0001) (Table 2)
- Use of foscarnet to treat CMV infection was associated with a negative eGFR slope (-1.3 [-2.2 to -0.4] ml/min/1.73m2 for each week longer usage, p<0.0001) (Table 2)

CONCLUSION

- The eGFR decreased substantially in the first year among individuals undergoing kidney transplantation and, in particular, non kidney solid organ transplantation
- The eGFR remained stable in human stem cell transplant recipients
- Larger area under the curve CMV viraemia was associated with larger decrease in eGFR
- Drugs used to prevent and treat CMV infection may contribute to the decrease in eGFR following transplantation
- Strategies for reducing use of chemoprophylaxis in patients at low risk of CMV infection may reduce the loss of kidney function
- Further, earlier diagnosis and treatment of emerging CMV infection may assist in reducing the loss of kidney function following transplantation

*Andrew S. Lenvo; Lesley A. Stevent; Christopher H. Schrön; et al. A New Equation to Estimate Glomerular Filtration Rate. Ann Intern Med. 2009 May 5179515.6246.142

**Table 1: Characteristics of 303 patients 1 month after transplantation according to the type of transplantation**

<table>
<thead>
<tr>
<th>Type of Transplantation</th>
<th>eGFR (ml/min/1.73m2)</th>
<th>IQR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney transplant</td>
<td>68 (48.96)</td>
<td>55</td>
<td>0.0001</td>
</tr>
<tr>
<td>Non-kidney solid organ</td>
<td>68 (48.96)</td>
<td>55</td>
<td>0.0001</td>
</tr>
<tr>
<td>HSCT</td>
<td>68 (48.96)</td>
<td>55</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

**Table 2: Effects of area-under-the-curve (AUC) CMV viral load on change in eGFR from month 1 to 12 after transplantation**

<table>
<thead>
<tr>
<th>CMV AUC tertile</th>
<th>eGFR change (ml/min/1.73m2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lowest</td>
<td>0.25 (-0.29 to -0.22)</td>
</tr>
<tr>
<td>Mid</td>
<td>1.3 (-2.2 to -0.4)</td>
</tr>
<tr>
<td>Highest</td>
<td>4.0 (-0.5 to -0.3)</td>
</tr>
</tbody>
</table>

**Figure 1: Comparison of eGFR at month 1 and 12 following a transplantation**

**Figure 2: Regression coefficients for time from transplantation, CMV infection, CMV viral load area under the curve, use of valganciclovir, ganciclovir, foscovir, methylprednisolone, ciclosporin, tacrolimus, sirolimus, mycophenolic acid and mycophenolate mofetil.**