How much eculizumab should be replaced after antibody removal for treatment of antibody-mediated rejection?

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Introduction

Antibodies directed against either ABO blood group or HLA antigens can damage endothelial cells in the renal allograft by activation of the complement cascade. Eculizumab inhibits complement protein C5 preventing formation of the membrane attack complex and protects the graft from the deleterious effect of circulating antibody. Eculizumab is being increasingly used in the treatment of antibody-mediated rejection (AMR) in combination with antibody removal. A supplementary dose of eculizumab is recommended after each plasma exchange procedure to ensure a therapeutic concentration. There are no studies evaluating the need for eculizumab replacement after double filtration plasmapheresis (DFPP) and immunoadsorption (IA).

Methods

We have measured levels of eculizumab before and after DFPP and Therasorb IA in a patient treated for antibody-mediated rejection. Drug levels over time were calculated using the formula $C_1 = C_0 \cdot e^{(-\log/T \cdot t)}$, where C_1 = concentration after time t , C_0 = initial concentration, T = half-life.

Results

Eculizumab concentration decreased from 265.3 ug/mL to 114.8 ug/mL after DFPP and from 168.7 ug/mL to 109.9 ug/mL after Therasorb IA (43.7% and 65.1% of the concentration prior to antibody removal procedure, respectively).

Taking into consideration the half-life of eculizumab (on average 261 – 271 hours), in both cases a concentration higher than 50 ug/mL (recommended concentration in the treatment of aHUS) would persist for 12 days (313 – 325 and 297 – 308 hours respectively).

Results cont.

A supplementary dose of 600 mg was given in both cases with peak levels after 1 hour of infusion of 347.9 ug/mL and 257.2 ug/mL respectively. A concentration higher than 50 ug/mL would last for at least 26 days (730 – 758 and 617 – 649 hours respectively).

Figure 1. Comparison of percent decrease in eculizumab concentrations after different types of antibody removal sessions. Between DFPP and IA the difference is 21%. Eculizumab concentration is given in ug/mL.

Discussion

Even though Eculizumab concentration decreases during DFPP and Therasorb IA, a supplementary dose is probably not necessary after a single antibody removal procedure. It should be consider if two or more antibody removal sessions are required.

References

Eculizumab Parker CJ, Kar S, Kirkpatrick P. *Nat Rev Drug Discov.* 2007 Jul;6(7):515-6.

The use of eculizumab in renal transplantation. Barnett AN et al. *Clin Transplant.* 2013 May-Jun;27(3):E216-29.