



Published in final edited form as:

Clin Infect Dis. 2010 January 1; 50(1): 121–122. doi:10.1086/649005.

High serum cholesterol levels are associated with herpes zoster infection after heart transplantation

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Sun and Singh reported that statins might improve morbidity and mortality attributable to sepsis or infection in organ transplant recipients (1). Statins have antiviral effects against HIV-1(2), BK virus, cytomegalovirus, Epstein-Barr virus and hepatitis C (1). Cholesterol is required for varicella zoster virus (VZV) cell entry (3,4). The relationship between cholesterol serum levels and risk of VZV post-transplant infection, if any, is unknown. We performed a case-control analysis to test the hypothesis that serum cholesterol is associated with an increased risk of zoster in heart transplant patients.

We studied patients who underwent heart transplantation at Mayo Clinic from January 1994 through June 2006, from one-month pre- through 12-months post-transplantation. Details of this cohort have been previously reported (5,6). Cases were patients diagnosed with post-transplantation zoster. For each case, three individually matched controls with no history of zoster, matched by age, gender, and transplantation year, were randomly selected. The degree of likeness between cases and controls was assessed using conditional logistic regression. Initial analysis compared mean serum cholesterol level within the first post-transplantation year in cases and controls. A second analysis compared serum cholesterol level within the month before the zoster episode in cases with the mean serum cholesterol level within the first post-transplantation year in cases.

Twelve patients developed zoster at a median of 170 days after transplantation. One patient had disseminated zoster, and another eye involvement. Cases and controls had a median age of 59 years; 91 and 94%, respectively, were male. There were no differences between cases and controls in the following variables (univariate conditional logistic regression, Wald χ^2 test): Use of antiviral prophylaxis (p,0.38) or statins (p,0.21) during the first post-transplantation year, reason for transplantation (p,0.96), diabetes (p,0.99), dyslipidemia (p,0.48), or BMI (p,

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Disclosures: The authors report no conflicts of interest

0.58). There was no difference in mean serum cholesterol level in the first post-transplantation year between cases (mean 208.83 ± 49.3 mg/dl) and controls (mean 204.13 ± 31.63 mg/dl). However, mean cholesterol levels of cases within one month before the zoster episode were significantly higher (mean 241.08 ± 56.05 mg/dl) than those of the same patients within the first post-transplant year ($p,0.007$), or those in control patients within the first post-transplant year ($p,0.0251$).

Cholesterol may play a role in the reactivation and spread of VZV in vivo. While no epidemiological studies have examined the relationship between serum cholesterol and zoster, a relationship between statins and infection risk has been reported (1). Statins have immunomodulatory (7), and direct antimicrobial effects (2). Depletion of cholesterol in membranes of inflammatory cells or reduced isoprenylation of signaling proteins are other possible mechanisms. HSV DNA in the brain, coupled with apolipoprotein E allele e4, has been suggested to confer an increased risk for Alzheimer's disease. Cholesterol-lowering statins have recently been linked with a reduced risk of Alzheimer's disease, possibly by reducing the neuronal spread of HSV-1 (8). It is biologically plausible that serum cholesterol levels are causally linked to the occurrence of zoster infections after heart transplantation.

Acknowledgments

Diederik van de Beek is supported by Meerwaldt Foundation and the Netherlands Organization for Health Research and Development (ZonMw); NWO-Rubicon grant 2006 (019.2006.1.310.001). This publication was made possible by Grant Number 1 UL1 RR024150 from the National Center for Research Resources (NCRR), a component of the National Institutes of Health, and the NIH Roadmap for Medical Research. Its contents are solely the responsibility of the authors and do not necessarily represent the official view of the NCRR or NIH. Information on NCRR is available at <http://www.ncrr.nih.gov/>. Information on Reengineering the Clinical Research Enterprise can be obtained from <http://nihroadmap.nih.gov>.

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