Relationship Between Infection and Coronary Heart Disease: Results of Two Studies

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One of the hottest topics in vascular biology is the potential role of infection in atherosclerosis, plaque disruption/thrombosis, and restenosis. Although a number of studies have suggested a positive relationship between infection and coronary heart disease (CHD) events, the ultimate proof of the veracity of this relationship is still missing. *Chlamydia pneumoniae* is one of the most frequently cited organisms that has been implicated in this relationship, based on seroepidemiologic data, evidence of presence and/or isolation of *C. pneumoniae* from atherosclerotic plaques, and experimental studies conducted in animal models. Infectious agents have been thought to contribute to atherogenesis and/or plaque rupture/thrombosis by either direct infection of cells within the vessel wall with secondary cellular activation, or through activation of inflammatory gene from infection at remote sites and activation of autoimmune responses through molecular antigenic mimicry with host antigens. Antibiotic therapy to suppress or eradicate bacterial infections such as *C. pneumoniae* is thus a potentially novel approach against vascular disease. The two clinical trials discussed below address both complications related to native atherothrombosis and neointimal hyperplasia related to coronary stenting. Both trials are essentially negative and only post hoc data manipulation showed positive results.

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Dr. Stone and his colleagues from London, England presented data from a randomized, placebo-controlled trial to determine the effects of 1-week course of antichlamydial antibiotic therapy (azithromycin 500 mg/day, plus omeprazole 20 mg/day, plus metronidazole 400 mg b.i.d.), anti–*Helicobacter pylori* therapy (amoxicillin 500 mg b.i.d., plus omeprazole 20 mg/day, plus metronidazole 400 mg b.i.d.), and placebo in 325 patients with acute coronary syndromes.[1] During a 1-year follow-up, there was no significant difference in major adverse cardiac events between the three groups, nor was there a change in markers of inflammation; however, combining the two antibiotic groups, in a post hoc analysis, showed a significant 40% reduction in major adverse clinical events compared to placebo ($P = .034$).

Dr. Neumann and colleagues from

Munich, Germany presented data from a prospective, randomized clinical trial involving 1010 patients undergoing successful coronary stent placement.[2] Patients were randomized to receive placebo or roxithromycin 300 mg/day for 4 weeks. Follow-up angiography showed no difference in restenosis rates (placebo = 29%; roxithromycin = 31%), and at 1 year death and myocardial infarction rates were also comparable (7% in roxithromycin-treated patients compared to 6% in placebo-treated patients). A post hoc analysis showed a significant reduction in restenosis rate by roxithromycin in the subgroup of patients with highest antibody titre (1:512) against *C. pneumoniae*. The odds ratio for target vessel revascularization rate was 0.11 (95% CI: 0.02-0.54) in the high-titre group receiving roxithromycin.

Several large scale clinical trials are currently ongoing in the United States and abroad investigating the effects of anti-chlamydial antibiotic therapy on clinical outcomes in patients with stable CHD or unstable CHD. The results of these large-scale trials are eagerly awaited, especially given that smaller clinical trials of antibiotics, mostly with surrogate endpoints, have been inconclusive or at best tantalizing. Because some of the anti-chlamydial antibiotics may have actions in addition to anti-bacterial effects (such as anti-inflammatory effects, matrix metalloproteinases–inhibiting effects), even if clinical trials show benefit it may be difficult to rule out the role of these ancillary actions in the clinical benefits observed. ■

Antibiotic therapy to suppress or eradicate bacterial infections such as C. pneumoniae *could thus be a potentially novel approach against vascular disease.*

References

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