Meeting Highlights: Nitric Oxide Donors

James J. Ferguson

Direct nitric oxide (NO) donors are a novel class of pharmacological agents that have vasodilatory properties as well as antiplatelet effects in animal angioplasty models. Two studies of NO donors were presented at the 43rd Annual Scientific Session of the American College of Cardiology: an unstable angina trial and a percutaneous transluminal coronary angioplasty (PTCA) trial.

Dr Thierry Giraud of Paris, France, on behalf of the French Multicentric Group in Unstable Angina, presented the results of a randomized parallel-group study of the efficacy and tolerability of a continuous intravenous infusion of linsidomine (SIN-1, an NO donor) in comparison to isosorbide dinitrate (ISDN). A total of 568 patients with angina at rest and recent ECG changes were randomized at 48 clinical centers in France to receive a 3-day infusion of either intravenous SIN-1 (1 mg/h up to 1.6 mg/h) or ISDN (2.5 mg/h up to 5.5 mg/h). All patients received intravenous heparin, oral aspirin, β-blockers (80%), and/or calcium blockers (40%). End points of the study included recurrent pain, Holter ischemic episodes, and clinical events (death, myocardial infarction, urgent revascularization). There were no significant differences in the frequency of symptomatic episodes, Holter ischemia, or major clinical events (5% total with SIN-1 versus 8% total with ISDN). Dr Giraud concluded that SIN-1 was as effective as (but not more effective than) ISDN for the treatment of severe (class IIIb) unstable angina.

Dr Jean-Marc Lablanche, from the University of Lille in France, on behalf of the ACCORD Study Investigators, presented the results of the Angioplastic Coronaire Corasal et Diltiazem (ACCOD) trial. A total of 723 patients were enrolled in 22 centers in France: 700 patients were randomized to receive either NO donors or diltiazem and underwent PTCA; 629 patients were eligible for 6-month angiographic follow-up, and 520 patients (83% of those eligible) underwent follow-up angiograms. The NO donor–treated group received intravenous SIN-1 (1 mg/h) for at least 3 hours before PTCA, followed by molsidomine (an oral NO donor, 12 mg/d) for 6 months.

There were no significant differences in in-hospital complications between groups. The NO donor–treated group had a slight but significant improvement in immediate post-PTCA minimal lumen diameter (1.94±0.48 versus 1.81±0.43) and 6-month follow-up minimal lumen diameter (1.54±0.68 versus 1.38±0.67) (P=.007). Categorical restenosis (>50% diameter stenosis at follow-up) occurred in 38% of the NO-donor group versus 46.5% in the diltiazem group (P=.052). There did not, however, appear to be any significant difference in overall adverse clinical events (death, myocardial infarction, repeat revascularization). Dr Lablanche concluded that treatment with NO donors is associated with slightly better acute and follow-up angiographic outcome, although there did not appear to be a parallel benefit on clinical events.

This study provides another example of a circumstance in which there appears to be a disparity between clinical and angiographic outcomes and highlights the importance of measuring both in future restenosis studies.

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