

Enoxaparin Bests Heparin for PCI Anticoagulation

BY BRUCE JANCIN

FROM THE ANNUAL CONGRESS OF THE
EUROPEAN SOCIETY OF CARDIOLOGY

STOCKHOLM – Intravenous enoxaparin outperformed conventional unfractionated heparin for anticoagulation in primary percutaneous coronary intervention for ST-elevation MI in the Phase III randomized ATOLL trial.

“This is the first pure, direct head-to-head comparison between two anticoagulants in primary PCI [percutaneous coronary intervention] with no mixing of drugs at any point. Our data demonstrate that enoxaparin, which is easier to use, reduced all serious ischemic events on top of intense antiplatelet therapy. And there was no price to pay on the safety side for the benefit observed on the ischemic side,” Dr. Gilles Montalescot said in presenting the ATOLL data at the meeting.

The ATOLL (Acute STEMI Treated With Primary Angioplasty and Intravenous Enoxaparin or UFH to Lower Ischemic and Bleeding Events at Short- and Long-Term Follow-Up) trial included 910 STEMI patients undergoing primary PCI at 43 sites in 4 countries. None of the patients had received any anticoagulant before randomization. Two-thirds of the participants underwent cardiac catheterization using radial artery access.

During randomization, half of the participants received intravenous enoxaparin at 0.5 mg/kg regardless of whether or not they were on a glycoprotein IIb/IIIa inhibitor.

The other half got intravenous unfractionated heparin (UFH) at either 50-70 IU/kg if they received a glycoprotein IIb/IIIa inhibitor, or 70-100 IU/kg if they did not. UFH dosing was adjusted based on activated clotting

time (ACT) measurements; enoxaparin dosing was not.

The primary study end point – a 30-day composite of death, procedure failure, complications of myocardial infarction, or non-CABG major bleeding – occurred in 33.7% of the UFH group, compared with 28% on enoxaparin. The resultant 17% relative risk reduction favoring the low-molecular-weight heparin fell just shy of statistical significance, probably because the exceptionally high use of radial artery access.

However, hard ischemic secondary end points were markedly reduced with enoxaparin. For example, the prespecified chief secondary end point consisting of the 30-day rate of death, recurrent MI or acute coronary syndrome, or urgent revascularization was reduced by 41% in the enoxaparin arm to 6.7%, compared with 11.3% with UFH, said Dr. Montalescot, professor of medicine and head of the cardiac care unit at Hôpital Pitié-Salpêtrière, Paris.

Similarly, the classic triple ischemic end point comprised of death, reinfarction,

or urgent revascularization was 8.5% in the UFH arm, compared with 5.1% with enoxaparin. The end point of death or complications of MI occurred in 12.4% of the UFH group, compared with 7.8% with enoxaparin, a 37% reduction in risk.

The primary safety end point in ATOLL – in-hospital major bleeding – occurred in 4.5% of patients on UFH and similarly in 4.9% of those on enoxaparin. The combined rate of major bleeding, complications of MI, or death occurred in 15% of the UFH group, compared with 10.2% on enoxaparin, a statistically significant difference.

Many American interventional cardiologists like using UFH because they can monitor ACT and bump up the heparin in the event of a low-flow state after stent de-

ployment. Dr. Montalescot commented that it makes sense to check ACTs in using UFH because the anticoagulation provided by UFH is “totally unpredictable.” But several studies have shown that staying within the ACT targets doesn’t have any impact on ischemic event rates.

“Also, enoxaparin’s anticoagulant capability is very predictable. It has been measured in many studies, and we get 95% of patients within the target range. So it doesn’t make sense, really, to control anticoagulation in the cath lab. We don’t have the ability to adjust anticoagulation with enoxaparin, but you’ll get almost all your patients to target with the IV injection,” he explained.

American observers were duly impressed.

“Enoxaparin probably merits more attention in the acute care setting than it receives,” hotline session cochair Dr. Clyde Yancy said in an interview.

“[It] hasn’t been broadly embraced by the cardiovascular community, but it looks like there are some real clinical advantages. These new data as well as some older data suggest we should pay more attention to enoxaparin than we have,” added Dr. Yancy, immediate past president of the American Heart Association and medical director of the Baylor Heart and Vascular Institute, Dallas.

“Enoxaparin kind of rears its head once again as a superior drug – and this time with no increased bleeding,” commented former American College of Cardiology president Dr. W. Douglas Weaver in an interview.

“To be superior with MI as an end point, that’s pretty striking. I’m surprised. It’s fascinating. I can’t wait to see all the data. This could be practice changing. Enoxaparin is easier to use. People have been unwilling to use it in the cath lab because you just can’t measure the extent of anticoagulation. But as Professor Montalescot says, why do you need to measure it if you know that it’s perfect? I thought the data were quite impressive,” said Dr. Weaver of the Henry Ford Health System, Detroit. ■

Disclosures: Dr. Weaver serves on several data safety and monitoring boards, and has received research support from several drug and device makers, including the Medicines Co., Johnson & Johnson, Boehringer Ingelheim, and Schering Plough. Dr. Yancy has no relevant disclosures.

VITALS

Major Finding: The prespecified chief secondary end point consisting of the 30-day rate of death, recurrent MI or acute coronary syndrome, or urgent revascularization was reduced by 41% in the enoxaparin arm to 6.7%, compared with 11.3% with UFH.

Data Source: Prospective, active-control arm Phase III trial involving 910 STEMI patients undergoing primary PCI at 43 sites in 4 countries randomized to enoxaparin (0.5 mg/kg) or 50-70 IU/kg UFH (with a glycoprotein IIb/IIIa inhibitor) or 70-100 IU/kg without.

Disclosures: The study was sponsored by Assistance Publique-Hôpitaux de Paris with the help of a research grant from Sanofi-Aventis. Dr. Montalescot disclosed that he has received consulting and/or lecture fees from Sanofi-Aventis as well as more than a dozen others.

Routine Use of Intra-Aortic Balloon Pump Disappoints

BY MARY ANN MOON

FROM JAMA

Prophylactic counterpulsation with an intra-aortic balloon pump did not prevent major adverse cardiovascular events from developing in high-risk PCI patients, according to a randomized study of 294 patients in the United Kingdom.

In what they described as the first randomized controlled trial to assess the efficacy and safety of the prophylactic use of an IABP in patients at high risk due to severe left ventricular impairment and extensive coronary disease, investigators found no difference in cardiovascular events between patients randomly assigned to planned IABP counterpulsation and those assigned to no planned IABP counterpulsation before PCI.

In addition, “elective IABP use

was associated with significantly fewer procedural complications but more minor bleeding and more access-site complications than when PCI was performed without planned IABP insertion,” said Dr. Divaka Perera of King’s College, London, and his associates.

They performed the prospective, open-label trial at 17 interventional cardiology centers in the United Kingdom in 2005-2009. The study involved 294 patients with multivessel disease, impaired left ventricular function, and a large amount of myocardium subtended by stenosed vessels who were scheduled for PCI of either native coronary arteries or bypass grafts.

A total of 147 patients underwent IABP insertion before PCI

and 147 had no IABP insertion unless the need for counterpulsation developed during PCI. All the subjects were followed

Major adverse cardiac or cardiovascular events within 28 days occurred in 15% of patients treated with a prophylactic intra-aortic balloon pump and in 16% of controls.

until hospital discharge or for 28 days following the procedure.

Of the 147 patients in the control group who did not receive prophylactic IABP, 18 (12%) required rescue IABP counterpulsation during PCI, usually because they developed prolonged hypotension during the procedure (13 cases).

The primary end point of ma-

major adverse cardiac or cardiovascular events (MACCE) within 28 days occurred in 15% of the patients who had prophylactic placement of an IABP and 16% of those who did not, a non-significant difference. There was a 2.8% absolute decrease in mortality at 6 months with prophylactic IABP counterpulsation, but that difference also was non-significant, according to the researchers (JAMA 2010; 304:867-74).

The MACCE rates also did not differ significantly in important subgroups of patients, including those who had impaired kidney function, diabetes, or extremely high risk of PCI-related complications.

Major procedural complications occurred less often in the

group with prophylactic IABP (1.3%) than in the control group (10.7%), but bleeding events and access-site complications were more frequent with prophylactic IABP (19.2% vs. 11.3% and 3.3% vs. 0%, respectively).

“These results do not support a strategy of prophylactic placement of an intra-aortic balloon catheter during PCI in all patients with severe left ventricular dysfunction” and a high risk of PCI-related complications, Dr. Perera and his associates said. ■

Disclosures: The study was sponsored by the British Cardiovascular Intervention Society, funded by Maquet Cardiovascular, Cordis, and Johnson & Johnson, and was supported in part by Lilly. Dr. Perera and an associate received financial support from the U.K. Department of Health.