Eptifibatide使用のタイミングに関する疑問への回答がスタディにより得られた

EARLY-ACS：高リスク患者に対するPCI中の早期eptifibatide使用の有意な有益性は認めない

EARLY-ACS: Insignificant advantage to early Eptifibatide use during PCI in high-risk patients

心筋梗塞の高リスク患者に対する抗凝固薬使用の最良のタイミングに関する10年間に渡る論争が解決した：結論は「どのタイミングで投与しても構わない」である。EARLY ACSスタディ（非ST上昇急性冠症候群に対する早期の糖蛋白IIb/IIIa阻害）の結果が2009年第58回American College of Cardiology学会レイトブレイキングクリニカルトライアルのセッションで発表され、同時にNew England Journal of Medicineに掲載された。EARLY ACSは、標準的な抗血栓療法に加え、早期eptifibatide投与とPCI中のeptifibatide臨時投与を比較した、無作為化二重盲検コントロールスタディであった。計9,492人の患者が組み入れられ、全員が試験薬開始から12～96時間後に侵襲的治療を施行された。有効性の一次エンドポイントは、あらゆる原因による死亡、心筋梗塞、緊急血行再建術を必要とする虚血の再発、または96時間以内のベイルアウトステント施行の総合であった。二次エンドポイントは30日以内の死亡または心筋梗塞であった。その結果、早期のeptifibatide使用は一次エンドポイントも二次エンドポイントも有意に低下させないことが示された。しかし、早期にeptifibatideを使用することにより生命を脅かさない出血は増加することが明らかにされた。

Full Text

In patients with high risk of myocardial infarction, early utilization of eptifibatide is not superior to delayed, provisional use of eptifibatide during percutaneous coronary intervention (PCI), according to research presented at the American College of Cardiology's 58th annual scientific session.

The EARLY ACS study (Early Glycoprotien IIb/IIIa Inhibition in Non-ST-Segment Elevation Acute Coronary Syndromes) aimed to clarify the best strategy for eptifibatide use, an antiplatelet drug therapy successfully implemented in clinical practice for 10 years. Two common strategies of eptifibatide utilization were examined in patients with high-risk of myocardial infarction: early intravenous injection upon immediate arrival at the hospital, and delayed, provisional injection during PCI.

"The drivers for our study are the gaps that exist in the practice guidelines for when and how best to use eptifibatide, an already tested and proven treatment, in the context of other modern therapies that have evolved since the drug was first introduced," said L. Kristin Newby, M.D., MHS, associate professor of medicine at Duke University Medical Center, Durham, N.C.

"Guidelines in North America and Europe vary in their recommendations regarding early use vs. delayed provisional treatment with eptifibatide and drugs like it. Individual hospitals and individual clinicians in all regions apply these recommendations differently."

EARLY ACS was a randomized, double-blind, controlled study of early eptifibatide vs. provisional eptifibatide during PCI with standard background antithrombin therapy. A total of 9492 patients were enrolled, all of whom were scheduled to undergo an invasive strategy 12 to 96 hours after starting the study drug.

The primary efficacy endpoint for EARLY ACS was composite all-cause death, myocardial infarction, recurrent ischemia requiring urgent revascularization or thrombotic bailout during the first 96 hours. The secondary endpoint was death or myocardial infarction through 30 days. Safety endpoints included bleeding, transfusions, stroke and serious adverse events. At its final enrollment, EARLY ACS had a 98 percent power to detect a 22.5 percent reduction in the 96-hour primary composite with early eptifibatide vs. delayed, provisional eptifibatide and 81 percent power for a 15 percent reduction in 30-day death or myocardial infarction.

"We set out to determine what is the better strategy when it comes to the treatment of these high- risk patients," said Robert P. Giugliano, M.D. assistant professor of medicine at the Brigham and Women's Hospital, Harvard, M.A. "Many hospitals in the United States routinely start a course of injectable eptifibatide early when a patient arrives at the hospital. However, there are other physicians who prefer to employ a 'wait and see' approach with the drug until after catheterization. Prior to this study, it was not clear which strategy was better. And, according to current practice guidelines, either strategy would be supported."

They found that early use of eptifibatide was not associated with any significant reduction in either the primary or the secondary endpoints. They did find, however, that earlier use of eptifibatide was associated with more non-life-threatening bleeding.

"Our study, although not the final word regarding eptifibatide, has helped shed a light on how to best use eptifibatide among high-risk patients," Newby said. "In general, physicians can feel comfortable with a strategy of delayed, provisional administration after a decision to proceed to PCI is made." As far as patients are concerned, the primary results from EARLY ACS are the key message - an early routine strategy of eptifibatide is not superior to a delayed provisional strategy."

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Co-authors include Robert Harrington, Robert Califf, Kerry Lee, Jennifer White and Lisa Berdan from Duke, Christoph Bode, from the University of Freiberg; Paul Armstrong, from the University of Alberta; Gilles Montalescot, of Centre Hospitalier Universitaire Pitie-Salpetriere; Frans Van de Werf, Universitair Ziekenhuis Gasthuisberg; Eugene Braunwald, Brigham and Women's Hospital; Steven Hildemann, Essex-Pharma GmbH; and John Strony and Enrico Veltri, Schering-Plough Corporation.