TicagrelorはプライマリPCIにおける心イベントを軽減する

PLATO STEMI：可逆的な新規経口抗血小板薬はSTEMI後のプライマリPCIを受けた患者において心イベントを抑制する

PLATO STEMI: New reversible oral anti-platelet drug reduces cardiac events in primary PCI patients following STEMI

可逆的経口抗血小板薬ticagrelorによりクロピドグレルによる標準的な治療と比較し、ST上昇心筋梗塞（STEMI）患者における心イベントが少なかったと、2009年American Heart Association学会レイトブレイキング臨床試験のセッションで発表された。血小板抑制と患者の予後（PLATelet Inhibition and Patient Outcomes：PLATO）トライアルは、ステントを用いたプライマリ冠動脈形成術（PCI）を予定されたSTEMI患者8,430人を、アスピリンに加え治験薬ticagrelorまたはクロピドグレルを内服する群に無作為に割り付けた。この無作為化二重盲検試験において、被験者は2006～2008年の間に43ヵ国862施設から組み入れられた。1年間の経過観察期間中にticagrelor群患者の9.3%が一次エンドポイント（心臓発作、脳卒中または血管死の合計）に合致したのに対し、クロピドグレル群においては11%であった；つまり、治験薬において相対リスクが15%低かった。総死亡率もticagrelorにより、6.0%から4.9%に低下し、相対リスクは18%低下した。同様に、新たな心筋梗塞およびステント血栓のリスクも軽減した。重大な出血の発現率上昇は認められなかった。

Full Text

Acutely ill myocardial infarction patients who received both aspirin and a new reversible oral anti-platelet medication had fewer cardiac events than patients on aspirin and the most commonly used, irreversible anti-platelet drug, researchers reported in a late-breaking clinical trial presentation at the American Heart Association's Scientific Sessions 2009.

In the PLATelet Inhibition and Patient Outcomes (PLATO) trial, a subset of 8,430 patients who were in the midst of ST-elevation heart attacks (STEMI) and were scheduled for primary percutaneous coronary intervention (PCI) with stenting received the investigational drug ticagrelor or clopidogrel in addition to aspirin. Participants for the randomized, double blind trial were recruited from 862 sites in 43 countries between 2006 and 2008.

The ticagrelor group suffered fewer cardiovascular events from the onset of the trial, and the benefits continued the longer patients took the drug during the year-long follow-up, said Philippe Gabriel Steg, M.D., lead investigator of the study. "The results are very clear and actually very consistent with the overall trial results of the larger PLATO trial, namely that there's a reduction in the primary endpoint - a composite of incidence of heart attack, stroke or vascular death - with no increase in major bleeding complications compared to clopidogrel," said Steg, professor of cardiology and director of the coronary care unit at H?pital Bichat-Claude Bernard in Paris, France.

Bleeding is usually a concern with new antiplatelet agents. Since ticagrelor is a more potent agent than one of the American Heart Association/American College of Cardiology guidelines recommended medications, clopidogrel, bleeding was a concern. "The good news is that there was no sign of increased major bleeding regardless of how we defined it," he said.

Following up to one year, 9.3 percent of the ticagrelor group met the primary endpoint, compared to 11 percent of the clopidogrel group - a 15 percent relative risk reduction for the investigational group. The patients in Steg's analysis had STEMI and were scheduled to receive primary PCI - also known as angioplasty - and stenting during the acute phase of their heart attacks. The 4,201 patients randomized to the test group received 180 milligrams (mg) of ticagrelor during PCI, followed by 90 mg twice daily for six to 12 months. The other 4,229 patients received 300 mg of clopidogrel with a provision for an additional 300 mg during PCI, followed by 75 mg daily for six to 12 months. All patients in the trial also received daily aspirin therapy.

"STEMI is really the most acute form of coronary disease and represents roughly 40 percent of the patient group enrolled in the larger PLATO trial," Steg said. "It is a common condition, and it is a high-risk condition for which the standard of care, clopidogrel, has clear drawbacks."

"Clopidogrel's drawbacks include a slower onset of effectiveness, which is not suited to the need for rapid effect in STEMI, and a modest and inconsistent anti-platelet effect - many patients respond well, but a sizeable unresponsive group remains at high risk of blood clots despite therapy," Steg said. Clopidogrel also binds permanently to the platelets' P2Y12 receptors, so its effect lasts seven to 10 days after the medication is stopped. In contrast, ticagrelor's effect is direct and reversible, he said.

"With ticagrelor, there is an actual disassociation between the drug and the P2Y12 receptor so that the drug does not bind permanently to the receptor, and the receptor and the platelet can regain function, with normal platelet clotting ability returning in about four days, which may explain the absence of increased bleeding with ticagrelor" Steg said. "However, ticagrelor does have off-target effects, which probably explain a side effect more commonly seen with ticagrelor than clopidogrel: dyspnea, or breathlessness, which affected 12.9 percent of ticagrelor patients and 8.3 percent of the clopidogrel group."

Overall mortality was reduced with ticagrelor - from 6.0 percent to 4.9 percent, a relative reduction of risk of 18 percent. Likewise, the risk of new myocardial infarction and the risk of stent thrombosis were also reduced. "Furthermore, the benefit is not solely achieved during the acute phase, the first 30 days after angioplasty, but the benefit accrues over time so that the longer you treat, the greater the difference in event rates," Steg said. "There is a strong rationale to prefer this new agent both in the acute (first 30 days) and in the late phase after a heart attack."

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