Aspirin resistance in the early postoperative period: Pharmacokinetics may be part of the answer

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Platelet aggregation levels in the first 2 days after coronary artery bypass grafting.

Central Message

The apparent resistance to aspirin early after cardiac surgery may be due to poor gastrointestinal absorption. Therapeutic solutions may include a higher aspirin dose or adding a second agent such as clopidogrel.

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Despite aspirin therapy in the early postoperative period, cardiac surgical patients continue to be at risk for early and clinically important thrombotic events.^{1,2} This aspirin unresponsiveness has prompted platelet function testing to optimize dose adjustment in an effort to achieve therapeutic platelet inhibition timeously and thus escape thrombotic complications.^{3,4} The study by Hattesen and colleagues⁵ in this issue of the *Journal* sheds light on possible pharmacokinetic mechanisms

for the aspirin resistance observed early after cardiac surgery.

FIGURE 1. Platelet aggregation levels in the first 2 days after coronary artery bypass grafting. ARU, aspirin reaction units. Figure 1 for this commentary is taken from the article, Figure 3, A from Hattesen and colleagues,⁵ the subject of this editorial.

In this study of patients after coronary artery bypass grafting (N = 53), the gastrointestinal absorption of aspirin was impaired in the first 48 hours postoperatively as evidenced by low blood levels of salicylic acid and corresponding low levels of platelet inhibition (Figure 1).⁵ The pharmacokinetics of aspirin returned to the preoperative baseline within 48 hours after surgery with a return of both adequate salicylic acid levels and platelet inhibition.⁵ The investigators measured both free and protein-bound fractions of salicylic acid in the blood to highlight that the low levels of aspirin in the early postoperative period were likely due to reduced gastrointestinal absorption rather than to an increase in protein binding.⁵ This study thus highlights the gastrointestinal pharmacokinetics of aspirin as an important mechanism for apparent “aspirin resistance” in the first days after cardiac surgery.⁵

There has been a focus on aspirin resistance in the *Journal* in recent years because of its persistent incidence and serious sequelae both in pediatric and adult cardiac surgical practice.¹⁻⁷ This latest trial has focused attention on gastrointestinal absorption as a research and therapeutic target to restore aspirin responsiveness in the early postoperative period for our patients.⁶ Perhaps a higher aspirin dose could enhance absorption and restore a favorable pharmacokinetic profile.^{3,4} Perhaps adding clopidogrel to aspirin therapy even earlier in the postoperative period for dual antiplatelet blockade may provide a solution for adequate platelet blockade, as has been considered already for longer-term outcome enhancement after coronary artery bypass grafting.^{6,7}

Hattesen and colleagues⁵ are to be congratulated for highlighting gastrointestinal aspirin kinetics as a new target in their hypothesis-generating study. It seems that in the early postoperative period that an aspirin a day may not be enough for our patients. The opportunities

to restore platelet blockade may be best realized through further inquiry to standardize effective platelet blockade in the early postoperative period.^{8,9} Future trials will likely focus on aspirin kinetics as a function of dose and on combination therapy with additional agents such as clopidogrel. Clinical success in this aspect of perioperative care will require freedom from not only thrombotic events but also bleeding events, as the search for the optimal therapeutic approach to balanced platelet blockade in the early postoperative period evolves.⁷⁻⁹

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