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Addendum: Drug Interaction between Opioids and Oral P2Y₁₂ Platelet Inhibitors

Opioids delay gastric emptying and the absorption of many oral drugs, including the P2Y₁₂ inhibitors clopidogrel (*Plavix*, and generics), prasugrel (*Effient*, and generics), and ticagrelor (*Brilinta*), which are commonly used for initial treatment of acute coronary syndrome (ACS). An article in our February 25, 2019 issue reviewed studies showing that coadministration of opioids delayed and decreased absorption of oral P2Y₁₂ inhibitors and increased platelet reactivity.¹ Recently published clinical outcomes data may add to these concerns.

In a post-hoc subgroup analysis of the EARLY ACS trial, the effects of morphine were evaluated in 5,438 patients with non-ST-elevation ACS (NSTEMI) treated with clopidogrel and in 3,462 NSTEMI patients not treated with a P2Y₁₂ inhibitor. In the clopidogrel group, the primary composite endpoint of death, myocardial infarction, recurrent ischemia, or thrombotic bailout at 96 hours occurred significantly more often in patients who received morphine than in those who did not (adjusted odds ratio 1.40; 95% CI 1.04-1.87). Morphine use was not associated with an increased incidence of adverse cardiovascular events in patients who did not receive a P2Y₁₂ inhibitor.²

Although this was only a post-hoc analysis and not a randomized controlled trial of morphine use in clopidogrel-treated patients, it does provide some additional evidence that caution should be used with coadministration of oral P2Y₁₂ inhibitors and opioids, and that use of the IV P2Y₁₂ inhibitor cangrelor (*Kengreal*)³ should be considered in patients with ACS who require or are already taking an opioid agonist.

1. Drug interaction: opioids and oral P2Y₁₂ platelet inhibitors. *Med Lett Drugs Ther* 2019; 61:31.
2. RHM Furtado et al. Morphine and cardiovascular outcomes among patients with non-ST-segment elevation acute coronary syndromes undergoing coronary angiography. *J Am Coll Cardiol* 2020; 75:289.
3. Cangrelor (Kengreal) — an IV antiplatelet drug for PCI. *Med Lett Drugs Ther* 2015; 57:145.

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