Medication Safety: Switching $P2Y_{12}$ Inhibitors

AMERICAN COLLEGE of CARDIOLOGY
Advancing Heart Care Worldwide

PROBLEM

- ✖ Oral $P2Y_{12}$ inhibitors vary in potency and pharmacokinetic and dynamic parameters
- ✖ A meta-analysis of 22,500 patients reported 19.1% rate of switching $P2Y_{12}$ inhibitors during hospitalization for ACS
  - 79.5% of these were an escalation of therapy and 18.5% a de-escalation
  - No significant difference in 30 day outcomes for cardiac events but increased risk of bleeding (OR 1.6, CI 1.22-2.10)
- ✖ Switching $P2Y_{12}$ inhibitors during hospitalization for acute coronary syndrome patients (ACS) has been reported at rates ranging from 9 to 24%
- ✖ Drug interactions between $P2Y_{12}$ inhibitors can lead to inadequate platelet inhibition and risk of thrombotic complications
- ✖ Inappropriate overlap of $P2Y_{12}$ inhibitors can lead to excessive platelet inhibition and risk of bleeding complications

SOLUTION

In the absence of clear evidence, a 2017 international expert consensus provides recommendations for switching between $P2Y_{12}$ inhibitors based on:

- ✔ Timing of switch relative to index event that led to initiation of $P2Y_{12}$ inhibitor
- ✔ Rationale for switch – particularly if related to bleeding or bleeding risk
- ✔ Unique pharmaco-dynamic and -kinetic properties of each agent (i.e. potency, reversibility of receptor binding, pro-drug)

TREATMENT TABLES:

Switching Between Intravenous and Oral $P2Y_{12}$ Inhibitors	
Intravenous to Oral	
Cangrelor to P	Load P 60 mg immediately after discontinuing cangrelor
Cangrelor to T	Load T 180 mg during infusion or immediately after discontinuing cangrelor
Cangrelor to C	Load C 600 mg immediately after discontinuing cangrelor
Oral to Intravenous (consider platelet function testing to time initiation of cangrelor)	
P to cangrelor	Start cangrelor 0.75 mcg/kg/min (without bolus) 3 – 4 days after last P dose
T or C to cangrelor	Start cangrelor 0.75 mcg/kg/min (without bolus) 2 – 3 days after last T or C dose

Switching Among Oral P2Y12 Inhibitors		
Switch	**Within 30 days of index event**	**> 30 days after index event**
Escalation in Potency		
C to P	Re-load with P 60 mg irrespective of timing of last dose	Administer P 10 mg MD 24 hrs after last C dose
C to T	Re-load with T 180 mg irrespective of timing of last dose	Administer T 90 mg bid MD 24 hrs after last C dose
De-escalation in Potency		
P to C	Re-load with C 600 mg 24 hrs after last P dose*	Administer C 75 mg MD 24 hrs after last P dose
T to C	Re-load with C 600 mg 24 hrs after last T dose* †	Re-load with C 600 mg 24 hrs after last T dose* †
Change Between High Potency		
P to T	Re-load with T 180 mg 24 hrs after last P dose	Administer T 90 mg bid MD 24 after last P dose
T to P	Re-load with P 60 mg 24 hrs after last T dose	Re-load with P 60 mg 24 hrs after last T dose

C = clopidogrel, P = prasugrel, T = ticagrelor, MD = maintenance dose
*Consider de-escalation with C 75 mg MD (24 hours after last P or T dose) in patients with bleeding or bleeding concerns.
†May consider re-loading C 600mg 12 hours (instead of 24 hours) after the last T dose

PREVENT POTENTIAL ERRORS

- ✔ Educate providers on pharmacodynamic differences between $P2Y_{12}$ inhibitors and current consensus recommendations for general escalation/de-escalation of these agents.
- ✔ Prior to the initiation or switch of a $P2Y_{12}$ inhibitor, obtain past medical history to identify contraindications, current medication list to identify drug interactions, pharmacy benefits to ensure drug cost/coverage, timing of index event, and when the patient received or will receive the last dose of the current $P2Y_{12}$ inhibitor.

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