Letters to Editor

Opioids during coronary interventions in cath lab – Need reconsideration?

Sir,

Patient presenting with chest pain and acute coronary syndrome is rushed to the cardiac catheterisation lab for percutaneous coronary interventions and receives opioids such as morphine for pain relief. This is a very common scenario in routine clinical practice. However, recent studies have seriously questioned the peri-procedural use of opioids with adverse cardiac events.

A post-hoc subanalysis from the EARLY ACS (Early Glycoprotein IIb/IIIa Inhibition in Patients With Non-ST-Segment Elevation Acute Coronary Syndrome) trial is recently published. In this trial, 5438 patients were administered clopidogrel before undergoing percutaneous coronary intervention (PCI) and 11.3% of these patients received morphine prior to the procedure. Patients receiving clopidogrel and morphine showed higher rates of ischaemic events at day 4 [adjusted odds ratio (OR), 1.40; $P = 0.026$ and higher rates of death or myocardial infarction at 30 days. In this trial, 3462 patients did not recieve clopidogrel, and the use of morphine in these patients was not related with raised ischaemic events at 96 h or any increase in myocardial infarction or death at 30 days.[1]

Similarly, single-centre, randomised PACIFY trial (Platelet Aggregation With Ticagrelor Inhibition and Fentanyl) showed that fentanyl administration reduces the plasma concentrations of ticagrelor and retards its antiplatelet effects.[2,3] Previously also few studies indicated the possibility of malabsorption of clopidogrel after morphine use and reduces P2Y12 inhibition.[4,5] PERSEUS (Platelet Inhibition after Pre-hospital Ticagrelor using Fentanyl compared to Morphine in patients with ST-segment elevation Myocardial Infarction undergoing Primary Percutaneous Coronary Intervention) is a prospective, single-centre, open-label, randomised controlled trial is presently undergoing. This study includes the patients treated with ticagrelor and undergoing primary PCI. Platelet reactivity will be assessed in patients randomised to receive fentanyl versus morphine.[6]

Drugs such as P2Y12 inhibitors - clopidogrel, ticagrelor and prasugrel are entirely absorbed through intestine. Opioids slow the gastric emptying into small intestine. This can effectively trap these antiplatelet drugs within stomach till the opioid effect subsides and gastrointestinal peristaltic movement improves. Recent evidences suggest that this pharmacodynamic interaction between opioids and oral antiplatelet drugs can have serious clinical implications.

Adequate and optimal analgesia for acute pain cannot be neglected or unaddressed. At the same time, ineffective oral P2Y12 inhibitors in presence of opioid may potentially risk the patient to catastrophic acute stent thrombosis.

What should be our balanced strategies to be implemented in such cases?

CAN WE MODIFY OR OPT FOR DIFFERENT ANTIPLATELET REGIME?

Concurrent administration of opioids creates a dangerous window of about 8 h between the intake of oral P2Y12 inhibitor and its onset of action. Intravenous cangrelor or GP IIb/IIIa antagonist (high-dose bolus tirofiban followed by a 6-h infusion) can be potentially useful to cover this window. Subcutaneous enoxaparin with 6 h regimen effectively prohibits thrombin-induced platelet activation and can be considered as a good option. The subcutaneous P2Y12 inhibitor selatogrel can be helpful in future owing to its longer half-life than cangrelor and ease of administration. Repeat loading dose of oral antiplatelet drug after 6 to 8 h of the last dose of opioids has also been suggested to optimise therapeutic levels of antiplatelet effect.

CAN WE HAVE NON-OPIOID ANALGESICS?

Intravenous acetaminophen can help in muscular back pain due to lying down on the table but its efficacy in treating chest pain is not established. Midazolam and propofol can provide anxiolysis and sedation but hardly any analgesic effect. Ketamine has been successfully tried in paediatric cardiac cath lab procedures. Future studies regarding its use in percutaneous coronary interventions are mandated. Recent studies have demonstrated the safety and efficacy of ketofol (1:1 mixture of ketamine and propofol) in paediatric patients undergoing cardiac cath lab procedures.[7] Use of ketofol in adult cardiac cath lab procedures

needs to be investigated. Dexmedetomidine can give good analgesia with conscious sedation. Although it is associated with haemodynamic stability, its propensity to cause bradycardia and heart block can be detrimental in patients with proximal right coronary lesions. Tramadol (atypical opioid) at an analgesic dose of 1 $mg.kg^{-1}$ does not retard gastric emptying as compared to morphine. Its emetic potential is an issue for concern, however, pre-emptive use of antiemetics can mitigate this side effect.

Present findings mandate the new investigation on alternative non-narcotic options for pain management in acute coronary syndrome patients in presence of oral antiplatelet agents.

Glossary of terms - PCI - percutaneous coronary intervention, EARLY ACS trial - Early Glycoprotein IIb/IIIa Inhibition in Patients With Non-ST-Segment Elevation Acute Coronary Syndrome trial, PACIFY trial - Platelet Aggregation With Ticagrelor Inhibition and Fentanyl, PERSEUS trial - Platelet Inhibition after Pre-hospital Ticagrelor using Fentanyl compared to Morphine in patients with ST-segment elevation Myocardial Infarction undergoing Primary Percutaneous Coronary Intervention

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Dr Monish S Raut - This author helped in conceptualising the manuscript.

Dr Vijay M. Hanjoora - This author helped in supervising the manuscript.

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Conflicts of interest

There are no conflicts of interest.

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