Morphine in myocardial infarction: balancing on the tight rope

Dan Atar* and Stefan Agewall

Department of Cardiology, Oslo University Hospital Ullevål, and Faculty of Medicine, University of Oslo, Norway

Online publish-ahead-of-print 21 October 2015

This editorial refers to ‘Morphine delays and attenuates ticagrelor exposure and action in patients with myocardial infarction: the randomized, double-blind, placebo-controlled IMPRESSION trial’, by J. Kubica et al., on page 245.

In the current issue of the journal, Kubica and co-workers present findings of attenuated platelet inhibition by ticagrelor induced by the concomitant administration of morphine. The authors tested a 5 mg intravenous dose of morphine against placebo in 70 patients with acute myocardial infarction (AMI), followed by a 180 mg loading dose of ticagrelor. The measured parameters included ticagrelor plasma concentrations and several platelet function tests. All assessments showed a delayed ticagrelor plasma appearance as well as a weaker antiplatelet effect in the morphine group.

From the consistency of the data and the methodologically sound approach, it appears that this discovery is founded on solid grounds, and it may trigger an immediate supposition in the cardiovascular community: to avoid the administration of morphine in AMI.

During the last two decades, the treatment of acute coronary syndrome (ACS) patients has changed dramatically; however, a few recommended actions, such as giving morphine to those patients, prevail. Morphine as a therapeutic principle is actually a long-established routine, as we can think back to history’s first description by A. Hammer in Vienna in 1878 of a survived myocardial infarction. Are we now entering a time where the pinnacle on morphine in patients with STEMI undergoing primary percutaneous coronary intervention (PCI)

Do we have evidence that contributes to our understanding of this critical interaction? There are no direct studies from the manufacturers addressing this issue. However, in the recent ‘Administration of Ticagrelor in the Cath Lab or in the Ambulance for New ST Elevation Myocardial Infarction to Open the Coronary Artery’ (ALANTIC) trial, the subgroup that did not receive morphine responded more strongly to out-of-hospital ticagrelor loading (the early intervention arm) than the patients who received morphine. One of the explanations might be that the direct morphine effect on intestinal motility results in a delayed absorption of ticagrelor. Another explanation may well be that patients who received morphine in a non-randomized fashion—hence based on physician assessment—had a stronger affliction from a larger ST-segment elevation myocardial infarction (STEMI), including stronger pain and compromised circulation. In fact, ticagrelor is not alone in this interaction issue: similar findings have been reported in the literature for all the other ADP receptor blockers: Hobl and co-workers found a decreased clopidogrel response in healthy volunteers who received morphine. Further, Parodi et al. found that both prasugrel and ticagrelor displayed a delayed activity when given concomitantly with morphine in patients with STEMI undergoing primary percutaneous coronary intervention (PCI). As mentioned, the underlying pathological explanation of this observation is not known. Apart from a supposed morphine-induced effect on absorption, vomiting as a morphine side effect may be an important aspect. Figure 1 depicts some of the possible interactions.

To draw an interesting parallel, the use of morphine has been criticized not only in myocardial infarction, but also in treatment of acute pulmonary oedema. In a retrospective study from 2008 based on the ‘Acute Decompensated Heart Failure National Registry’ (ADHERE) records, morphine given in acute decompensated heart failure was an independent predictor of increased hospital mortality, with an odds ratio of 4.8 (95% confidence interval 4.52–5.18, P < 0.001). In a retrospective study from Israel comprising 2336 patients, morphine administration was associated with an increased mortality; however, after propensity score matching, this association
became non-significant. Morphine is still widely used for pulmonary oedema in spite of a poor scientific evidence base.

Taken together, one is left with a therapeutic dilemma in AMI patients which at present is not resolved. One aspect to consider is whether there are alternative means to reduce chest pain in patients with AMI, as proposed by Parodi in a recent review article. Yet, apart from the pain relief, morphine administration is associated with decreased sympathetic activity which may have beneficial effects. Without doubt we need more randomized studies, both such as that presented by Kubica and co-workers and also trials reporting hard endpoint outcomes. Meanwhile—as an intermediate step to increase our knowledge base—we may take advantage of existing registries on P2Y12 inhibitors in patients with ACS. In conclusion, until we have these data, an increased awareness of a more selective use of morphine in clinical praxis appears warranted.

**Conflict of interest:** none declared.

**References**


