Impact of morphine treatment with and without metoclopramide co-administration on myocardial and microvascular injury in acute myocardial infarction: insights from a randomized trial

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Background: Intravenous morphine administration in patients with acute myocardial infarction (AMI) can adversely affect platelet inhibition induced by P2Y12 receptor antagonists, potentially resulting in an increased risk of adverse clinical events. In contrast, some evidence suggests that opioid agonists may have cardioprotective effects on the myocardium. Currently available data in this regard are, however, sparse, inconsistent, and methodologically limited.

Purpose: The aim of this study was to investigate the impact of morphine with or without metoclopramide (MCP) co-administration on myocardial and microvascular injury after AMI assessed by cardiac magnetic resonance (CMR).

Methods: This prospective, randomized, single-center study assigned 138 patients with AMI in a 1:1:1 ratio to (a) ticagrelor 180 mg plus intravenous morphine 5 mg (morphine group); (b) ticagrelor 180 mg plus intravenous morphine 5 mg and MCP 10 mg (morphine + MCP group); or (c) ticagrelor 180 mg plus intravenous placebo (control group). Study drugs were administered before primary percutaneous coronary intervention. CMR was performed in 101 patients on day 1–4 after the index event to assess infarct size, microvascular obstruction, and left ventricular ejection fraction.

Results: Infarct size was significantly smaller in the morphine only group as compared to controls (15.5%LV [IQR 5.0 to 21.4%LV] vs. 17.9%LV [IQR 12.3 to 32.9%LV]; p=0.047). Furthermore, the number of patients with microvascular obstruction was significantly lower after morphine administration (10/36 [28%] versus 21/39 [54%]; p=0.022) and the extent of microvascular obstruction was smaller (0%LV [0 to 1.40%LV] versus 0.74%LV [0 to 3.10%LV]; p=0.037). In multivariable regression analysis, morphine administration was independently associated with a reduced risk for the occurrence of microvascular obstruction (odds ratio 0.37; 95% confidence interval 0.14 to 0.93; p=0.035). Left ventricular ejection fraction did not differ significantly between the morphine and the control group (p=0.970) and there was no significant difference in left ventricular ejection fraction (p=0.790), infarct size (p=0.491), and extent (p=0.753) or presence (p=0.914) of microvascular obstruction when comparing the morphine + MCP group to the control group.

Conclusions: In this randomized study, intravenous administration of morphine prior to primary percutaneous coronary intervention resulted in a significant reduction of myocardial and microvascular damage following AMI. This potential cardioprotective effect of morphine requires further evaluation in well-designed future trials with clinical endpoints.