Morphine in acute coronary syndrome: systematic review and meta-analysis

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Abstract
Objective Morphine is frequently used in acute coronary syndrome (ACS) due to its analgesic effect, it being recommended in the main cardiology guidelines in Europe and the USA. However, controversy exists regarding its routine use due to potential safety concerns. We conducted a systematic review of randomised-controlled trials (RCTs) and observational studies to synthesise the available evidence. Design Systematic review and meta-analysis. Data sources CENTRAL, MEDLINE, EMBASE and trial registries. Eligibility criteria for selecting studies We included RCTs and observational studies evaluating the impact of morphine in cardiovascular outcomes or platelet reactivity measures. Data extraction and synthesis Data were screened, extracted and appraised by two independent reviewers. The data were pooled results using a random-effects model. Outcomes included in-hospital mortality, major adverse cardiovascular events (MACE), platelet reactivity (using VerifyNow) and bleeding, reported as relative risk (RR) with 95% CI. We assessed the confidence in the evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework. We followed the Metaanalysis Of Observational Studies in Epidemiology and Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Results Five RCTs and 12 observational studies were included, enrolling 69 993 participants. Pooled results showed an increased risk of in-hospital mortality (RR 1.45 [95% CI 1.10 to 1.91], low GRADE confidence), MACE (RR 1.21, 95% CI 1.02 to 1.45) and an increased platelet reactivity at 1 and 2 hours (59.37 platelet reactivity units [PRU], 95% CI 36.04 to 82.71; 68.28 PRU, 95% CI 37.01 to 99.55, high GRADE confidence) associated with morphine. We found no significant difference in the risk of bleeding. We found no differences in subgroup analyses based on study design and ACS subtype. Conclusions Morphine was associated with an increased risk of in-hospital mortality and MACE but the high risk of bias leads to low result confidence. There is high confidence that morphine decreases the antiplatelet effect of P2Y12 inhibitors.

Keywords
acute coronary syndrome; meta-analysis; morphine; platelet reactivity; stemi; systematic review