Signal of harm in Morphine use in adults with pulmonary oedema: A rapid systematic review





REPUBLIC OF SOUTH AFRICA

BACKGROUND







recurrent hospital admissions

substantial healthcare expenditure

The use of **morphine** in the management of **acute pulmonary** oedema remains controversial, with conflicting guidance and significant variation in practice. Synthesised evidence is needed to inform standard treatment guidelines and clinical practice.

OBJECTIVES

To determine whether morphine should be used in the treatment of acute pulmonary oedema in adults.



A rapid review of systematic reviews of randomised controlled trials, then randomised controlled trial was conducted searching three electronic databases (PubMed, Embase, Cochrane Library) and one clinical trial registry on February 12, 2022. We used a prespecified protocol following Cochrane rapid review methods and aligned to the National Standard Treatment Guidelines and Essential Medicines List methodology. We first considered relevant high-quality systematic reviews of randomised controlled trials, then (if required) randomised controlled trials to inform time-sensitive or urgent evidence requests, clinical practice, policy or standard treatment guidelines.



RESULTS

We identified four systematic reviews of observational studies. The two most relevant, up-to-date, and highest quality reviews were used to inform evidence for critical outcomes. Morphine may increase in-hospital mortality (OR 1.78; 95% CI 1.01 to 3.13, low certainty of evidence, six observational studies, n=151 735 participants) resulting in 15 more per 1000 hospital deaths, ranging from 0 fewer to 40 more hospital deaths. Morphine may result in a large increase in invasive mechanical ventilation (OR 2.72; 95% CI 1.09-6.80, low certainty of evidence, four observational studies, n=167 847 participants), resulting in 45 more per 1000 ventilations, ranging from 2 more to 136 more. Adverse events and hospital length of stay was not measured across reviews or trials.



according to opioid use. IV, inverse variance:

Study or Subgroup	Weigh
Inhospital mortality	
Caspi 2019	17.8%
Dominguez-Rodriguez 2016	16.29
Gray (3CPO trial) 2010	16.8%
lakobishvili 2011	14.49
Miró (EAHFE registry) 2017	16.29
Peacock (ADHERE study) 2008 Subtotal (95% CI)	18.79 100.0 9
Heterogeneity: Tau ² = 0.44; Chi ² =	= 64.48,
Test for overall effect: Z = 1.99 (P	= 0.05)
30-day mortality	

44.7% lakobishvili 2011 55.3% Miró (EAHFE registry) 2017 100.0% Subtotal (95% CI) Heterogeneity: Tau² = 0.00; Chi² = 0.17, df = 1 (P = 0.68); l² = 0% Test for overall effect: Z = 2.78 (P = 0.006)

Source: Gao et al (2021)

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Forest plot of the pooled analysis evaluating in-hospital and 30-day mortality



No morphine compared to morphine for pulmonary oedema...



NO MORPHINE



MORPHINE (current standard of care)



Certainty of the evidence (GRADE): Low

(6 observational studies)



SAE (invasive mechanical ventilation)











CONCLUSION

Based on the most recent, relevant, and best available evidence, morphine use in adults with acute pulmonary oedema:



may increase in-hospital and all-cause mortality

may result in a large increase in the need for invasive mechanical ventilation

Recommending against the use of morphine in pulmonary oedema may improve patient outcomes.

Disinvesting in morphine for this indication may result in cost-savings, noting the possible accrued benefits of fewer patients requiring invasive ventilation and management of morphine-related side-effects.

What is a rapid review?

A rapid review is a form of knowledge synthesis that accelerates the process of conducting a traditional systematic review through streamlining variety of methods to produce evidence in a resource-efficient manner. For our rapid review, we streamlined the process by first searching for high-quality, relevant and up-to-date Systematic Reviews of RCTs, then followed by RCTs.

Where does our rapid review fit into National Standard **Treatment Guidelines and Essential Medicine List Process?**



Funding: MM, CH and IK are partly supported by the Research, Evidence and Development Initiative (READ-It). READ-It (project number 300342-104) is funded by UK aid from the UK government; however, the views expressed do not necessarily reflect the UK government's official policies. Research reported in this publication is the sole responsibility of the researchers and do not reflect the official views or position of the South African Medical Research Council or the University of Stellenbosch.