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The HEAT trial: a protocol for a multicentre randomised placebo-controlled trial of IV paracetamol in ICU patients with fever and infection.

Young PJ, Saxena MK, Bellomo R, Freebairn RC, Hammond NE, van Haren FM, Henderson SJ, McArthur CJ, McGuinness SP, Mackle D, Myburgh JA, Weatherall M, Webb SA, Beasley RW; ANZICS Clinical Trials Group.

Erratum in

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Abstract

BACKGROUND AND OBJECTIVE:

Paracetamol is commonly administered to febrile critically ill patients with infection. However, there is limited information on the efficacy and safety of using paracetamol in this setting. We describe the study protocol for a Phase IIb multicentre randomised controlled trial (the Permissive Hyperthermia Through Avoidance of Paracetamol in Known or Suspected Infection in ICU [HEAT] trial) comparing intravenous paracetamol to placebo in the treatment of fever in critically ill adults with known or suspected infection.

DESIGN AND SETTING:

A pilot study followed by the main trial from November 2012. 700 patients will be recruited for concealed, random, parallel assignment of either 1 g of intravenous paracetamol or placebo (100mL of 5% dextrose) 6-hourly to treat fever while they remain on antimicrobial therapy in the intensive care unit. The primary end point will be ICU support-free survival at 28 days after randomisation. Secondary end points will include peak daily and mean daily body temperatures, prevalence of liver dysfunction requiring cessation of study treatment, degree of renal injury (based on delta creatinine), other organ failures, and Day 28 and Day 90 mortality. All analyses will be conducted on an intention-to-treat basis.

RESULTS AND CONCLUSIONS:

The HEAT trial should generate results that will inform and influence the prescribing of paracetamol. It will also determine if a large-scale Phase III trial of paracetamol is required in this patient group and whether such a trial is feasible.

TRIAL REGISTRATION:

Australian and New Zealand Clinical Trials Registry (ACTRN12612000513819).

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