O-203a Figure 2

Abstract O-203a Figure 2

(SD 0.06) mmol/L, p = 0.001). There were no important adverse effects. However, accelerated failure time analysis showed a non-significantly shortened time to medical readiness for discharge of 14% favouring the magnesium sulfate group, OR = 1.14, 95% CI 0.93 to 1.40, p = 0.20. Mean times until readiness for discharge were 14.6 h [SD 9.7] vs 15.6 h [SD 11.3] for the investigational and placebo groups, respectively, p = 0.9.

Conclusions Adding nebulised magnesium sulfate to combined nebulised bronchodilator and systemic steroid therapy fails to provide evident benefit for patients with moderate or severe status asthmaticus.

O-203b
PAEDIATRIC MICRODOSE STUDY OF [14C] PARACETAMOL TO STUDY DRUG METABOLISM USING ACCELERATED MASS SPECTROMETRY: PROOF OF CONCEPT

Rationale Microdosing is a promising new method to obtain pharmacokinetic data in children with minimal burden and minimal risk. The use of a labelled oral microdose offers the added benefit to study intestinal and hepatic drug disposition in children already receiving an intravenous therapeutic drug dose for clinical reasons.

Objective To present pilot data of an oral [14C]paracetamol (AAP) microdosing study as proof of concept for this method to study developmental pharmacokinetics in children.

Methods In an open microdose pharmacokinetic pilot study, infants (0–6 yrs of age) received a single oral [14C]AAP microdose (3.3 mg/kg, 60 Bq/kg) in addition to intravenous therapeutic doses of AAP (15 mg/kg IV q6 h) prescribed by the treating physician to provide analgesia. Blood samples were taken from an indwelling catheter at multiple time points. AAP blood levels were measured by LC-MS/MS and [14C]AAP and metabolites ([14C]AAP-Glu and [14C]AAP-4Sul) were measured by accelerator mass spectrometry.

Results Ten infants (ranging from 0.1 to 83.1 months of age) were included, one patient was excluded from PK analysis, as he vomited shortly after administration. In all 9 patients, [14C]AAP and metabolites in blood samples were detectable at expected concentrations. Dose normalised [14C]AAP C_max concentrations approached median C_mg intravenous concentrations: median 8.41 mg/L (range 3.75 to 23.78 mg/L) and 8.87 mg/L (range 3.45 to 12.9 mg/L), respectively.

Conclusions We demonstrate the practical and ethical feasibility to use a [14C]labelled microdose to study paracetamol pharmacokinetics, including metabolite disposition, in young children.