The influence of pH and buffering on the stability of meropenem 6.25-25 mg/ml at 32°C
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INTRODUCTION

• Drug stability is an important consideration for the use of continuous infusion of antibiotics in ambulatory devices for outpatient parenteral antimicrobial therapy (OPAT) services.
• Recent work1 has identified a lack of stability data to support the use of agents in this way, which would meet the requirements of the NHS Yellow Cover Document (YCD).2
• Meropenem is a broad-spectrum antipseudomonal carbapenem, but its use is limited in OPAT services by a multiple daily dosing schedule.
• A continuous infusion could improve outcomes by optimising PK/PD, but meropenem is known to be unstable in aqueous solution. pH and drug concentration also have an influence on the stability of meropenem.
• We have tested the stability of meropenem at two concentrations in unbuffered and buffered solutions at different pH values in order to determine if these factors can be adjusted to optimise the stability of meropenem for continuous infusion for OPAT services.

METHODS

• Two concentrations of meropenem (6.25 and 25 mg/ml) were diluted in a variety of aqueous solutions including:
  - 0.9% sodium chloride (unbuffered control)
  - 5.0% sodium citrate buffer pH 6
  - 5.0% phosphate buffer pH 6
• pH concentrations were adjusted with citric acid.
• 20 ml aliquots were stored in universal containers at 32°C for 24 hours.
• A continuous infusion could improve outcomes by optimising PK/PD, but meropenem is known to be unstable in aqueous solution. pH and drug concentration also have an influence on the stability of meropenem.
• We have tested the stability of meropenem at two concentrations in unbuffered and buffered solutions at different pH values in order to determine if these factors can be adjusted to optimise the stability of meropenem for continuous infusion for OPAT services.

RESULTS

• Meropenem, after reconstitution and dilution in aqueous solution, is unstable with the degradation rate resulting in between approx. 20 and 30% loss after 24 hours at 32°C (Tables 1 and 2).

CONCLUSIONS

• Meropenem is unstable in aqueous solutions.
• The degradation rate is influenced by drug concentration, pH and buffering agent.
• Attempts to improve stability by the use of buffering have failed to make any noticeable improvement to degradation rates.
• Meropenem is too unstable to be used as a continuous infusion at 32°C in ambulatory devices for OPAT services.
• Degradation rates mean that an infusion period of less than 6 hours would be necessary to avoid loss of more than 5% of the drug, rendering it impractical for most OPAT services.
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REFERENCES