Scoping the stability of amoxicillin for use in Outpatient Parenteral Antimicrobial Therapy (OPAT) services in accordance with the requirements of the UK NHS Yellow Cover Document

Fekade B. Sime[1], Steven C. Wallis[1], Conor Jamieson[2], Tim Hills[3], Mark Gilchrist[4], Mark Santillo[5], R. Andrew Seaton[6], Felicity Drummond[7], Jason A. Roberts[1] on behalf of the BSAC OPAT Drug Stability Testing Programme.

1 The University of Queensland Centre for Clinical Research, Brisbane, Australia; 2 NHS England & Improvement, Birmingham, UK; previously at Pharmacy Department, Sandwell and West Birmingham NHS Trust, UK; 3 Pharmacy Department, Nottingham University Hospitals, Nottingham, UK; 4 Department of Pharmacy/Infection, Imperial College Healthcare NHS Trust, London, UK; 5 Torbay & South Devon NHS Foundation Trust, Torquay, UK; 6 Department of Infectious Diseases, Queen Elizabeth University Hospital, Glasgow, UK; 7 British Society for Antimicrobial Chemotherapy, Birmingham, UK

P1461

INTRODUCTION

Administering continuous amoxicillin by infusion presents an attractive choice for OPAT in particular for enterococcal infections. However, its aqueous stability has limited its value. In the UK, the National Health Service Pharmaceutical Quality Assurance Committee Yellow Cover Document (YCD)[1] standards for stability assessment of small molecules apply for antibiotics in elastomeric devices. The aim of our study was to scope the impact of buffering on stability of amoxicillin solutions for continuous infusion assessed under YCD standards.

METHODS

Amoxicillin solutions at 4.17 mg/mL, 50 mg/mL and 66.6 mg/mL were prepared using 0.3% citrate buffered saline (CBS) pH 7, water for injection (WFI) and 0.9% w/v saline. Samples were stored in a refrigerator, 2-8°C, for 10 days followed by 24 hours at 32°C to reflect the 'in-use' period. Triplicate samples in sterile glass containers were assayed at 7 time points during fridge storage and at 6 points during in-use storage using a stability indicating assay method and pH monitoring.

CONCLUSIONS

Our results indicate that the buffering capacity of 0.3% citrate buffer was inadequate to maintain the pH and stability of amoxicillin at clinically relevant concentrations for use in OPAT services and is insufficient to meet YCD[1] or international standards. These test conditions mimic the potential use of pre-formulated solutions of amoxicillin in elastomeric devices with procurement and fridge storage of filled devices prior to administration to a patient in an OPAT service. The known instability of amoxicillin in aqueous solution, and the failure of buffering with citrate buffer to prevent unacceptable losses, indicates that further testing of amoxicillin for OPAT remains challenging.

ACKNOWLEDGEMENTS

The authors would like to thank: B. Braun Medical Ltd. and Vygon Ltd. for funding and in-kind provision of elastomeric devices.

ENQUIRIES

Contact Email: OPAT@bsac.org.uk

REFERENCE

1. NHS Pharmaceutical Quality Assurance Committee. A standard protocol for deriving and assessment of stability: part 1 - aseptic preparations (small molecules). Edition 5, 2019.

RESULTS

The lowest concentration of amoxicillin in WFI and CBS (Figure 1) was the most stable during fridge storage, but still lost >5% of amoxicillin after 168 hours, while in saline losses >5% occurred within 24 hours. There was accelerated degradation at intermediate and high concentrations irrespective of the solution tested. A similar trend was seen at the in-use temperature of 32°C with the low dose amoxicillin being most stable in WFI and CBS; losses at intermediate and high dose exceeded 75% within 20 hours (Figure 2). At the in-use temperature of 32°C there was marked degradation of amoxicillin in all solutions, with saline again being the least stable. All solutions demonstrated marked pH changes during the study, both during fridge and in-use storage temperatures.

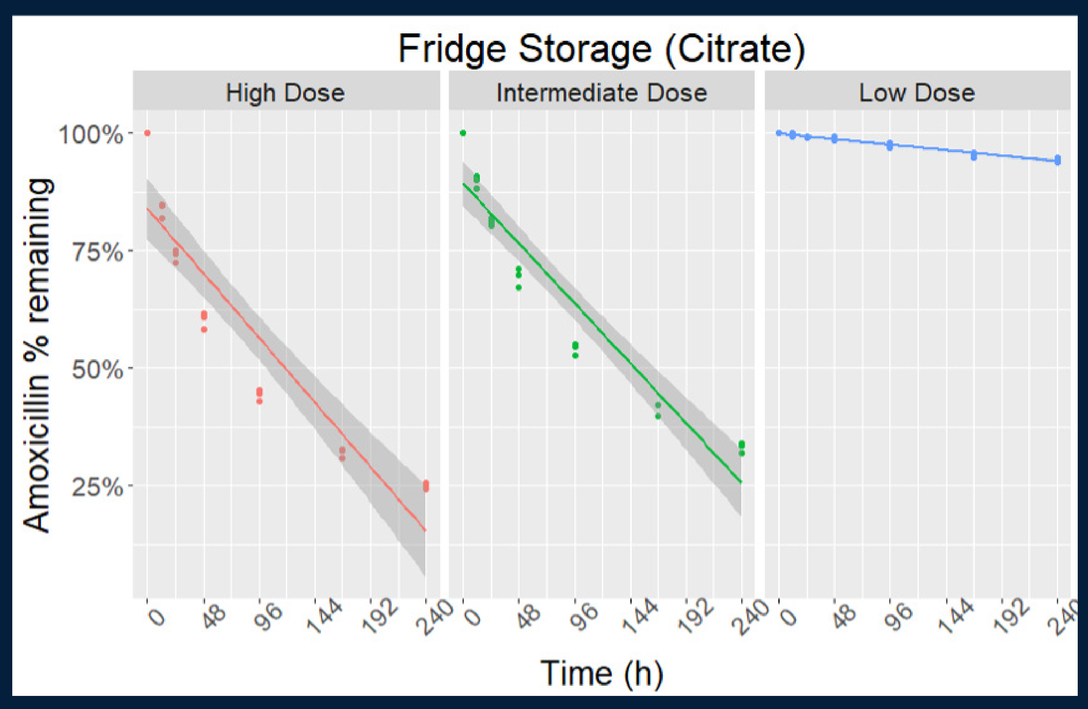

FIGURE 1. Stability of amoxicillin solution in 0.3% citrate buffer pH 7 at high (66.6 mg/mL), intermediate (50 mg/mL) and low (4.17 mg/mL) dose, during fridge storage (2-8°C) for ten days (0-240 hours). The degradation pattern was the same for WFI and normal saline.

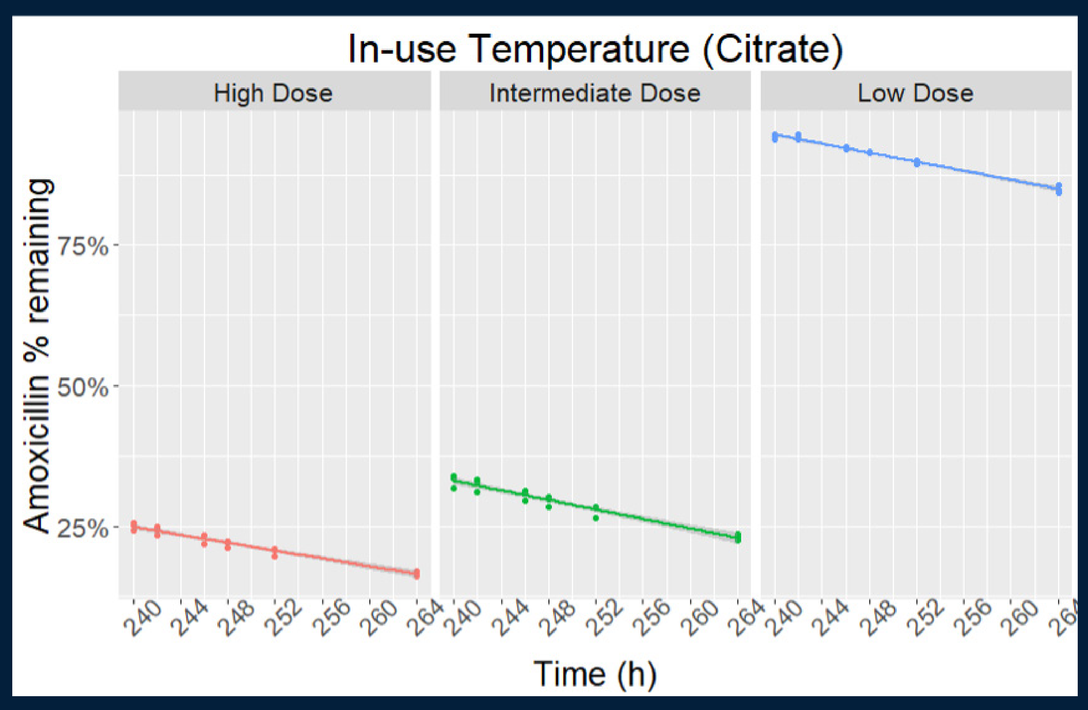

FIGURE 2. Stability of amoxicillin solution in 0.3% citrate buffer pH 7 at high (66.6 mg/mL), intermediate (50 mg/mL) and low (4.17 mg/mL) dose concentrations, during 24 hour 'in-use' temperature exposure at 32°C, following 10 days (0-240 hours) fridge storage at 2-8°C. The degradation pattern was the same for WFI and normal saline.