P0276 Stability of generic brands of meropenem reconstituted in isotonic saline – a comparison to the reference product

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Introduction

Meropenem is a relatively unstable compound when dissolved. Currently all available data have been derived from tests on the original product from Astrazeneca, and it is unsure if these data can be extrapolated to the stability of other commercially available vials.

Objectives

The aim of this study was to assess the stability of four different brands of meropenem for use as a prolonged or continuous infusion.

Materials and methods

Meropenem was obtained as the commercial powder preparation for injection from four different brands available worldwide (Meronem Astrazeneca®, Meropenem Sandoz®, Meropenem Fresenius Kabi® and Meropenem Hospira®).

The vials were reconstituted and mixed with 0.9 % sodium chloride to produce solutions with concentrations of 10, 20 and 40 mg/mL in polypropylene syringes, which were kept at 25° C. Samples were taken immediately after preparation and up to 12 hours and were stored at -80° C until analysis.

Meropenem concentrations were determined using UPLC-MS/MS. Chromatographic separation was performed on a Waters Acquity UPLC system using a BEH C_{18} column (1.7 µm, 100 x 2.1 mm) applying a binary gradient elution of water and acetonitrile both containing 0.1 % formic acid. The total runtime was 5.5 minutes. Chromatographic analysis was carried out after diluting the samples to 50 mg/L in water containing meropenem-d_6, in order to reach the linear range of the assay (0.5 – 100 mg/L).

Two meropenem samples taken at each timepoint were independently assayed in duplicate, and the average of these concentrations was used for data analysis. Solutions retaining >90% of the initial concentration were considered stable.

Related samples Friedman's two way of analysis of variance by ranks (IBM, Chicago, IL) was used to compare the rate of meropenem degradation between different brands. A p value of < 0.05 was considered statistically significant.

Results

The stability was concentration dependent. At 25° C, all 10 and 20 mg/mL solutions were stable for 12 hours in 0.9% sodium chloride, while the 40 mg/mL solutions were stable for a maximum of 8 hours. Stability of the different vials of meropenem was comparable for the time period tested (related samples Friedman's two way of analysis of variance by ranks, p=0.282).

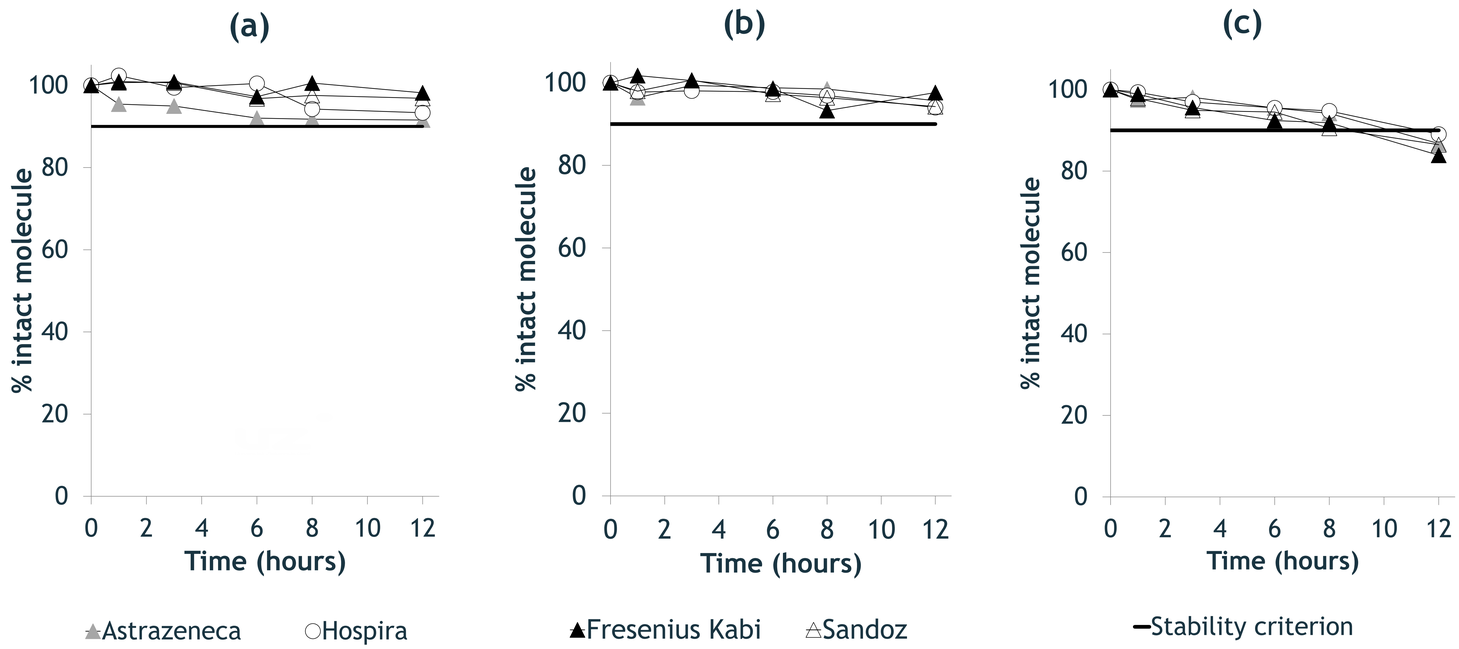

FIG. 1 : Stability over time for the 4 tested brands of meropenem in 3 different concentrations at 25° C.
(a) Percentage of intact molecule over time for the 4 tested brands of meropenem in a concentration of 10 mg/mL.
(b) Idem (a), but in a concentration of 20 mg/mL.
(c) Idem (a), but in a concentration of 40 mg/mL.

Conclusion

All tested vials of meropenem in a concentration of 10 and 20 mg/mL were stable for 12 hours at 25° C when diluted in 0.9% sodium chloride. The 40 mg/mL solutions were stable for a maximum of 8 hours. This report is the first to show equivalent stability between different commercially available vials of meropenem. Clinicians can safely use these generic forms of meropenem as 8-hour infusions if the concentration is ≤ 40 mg/mL and dissolved in 0.9 % sodium chloride.

References and acknowledgment
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