Background

Meropenem is a broad spectrum carbapenem with useful activity against a number of organisms resistant to other antibiotics. Like all β-lactams, the time during which its concentration remains above the MIC of the offending organism is the main driver for activity and needs to be optimized. In this context, administration of meropenem by prolonged or even continuous infusion has been advocated [1-3].

Meropenem, as MERONEM® (the original branded product) has limited stability (approx. 5-8h) when prepared in concentrated solutions such as those used in Intensive Care Units for prolonged (3h) or continuous infusion [5,6]. No detailed information, however, is publicly available for generics. Since Hospital Pharmacies are increasingly forced to purchase antibiotics based on minimal cost acquisition considerations (and to select generics) without real analytical capabilities for checking key quality properties (and to select generics) without real analytical capabilities for checking key quality properties, this work aimed at monitoring β-lactams serum concentrations in patients with nosocomial pneumonia, we undertook to compare 4 generics of meropenem to the original branded product for stability and visible release of degradation products.

Methods

Solutions were prepared at 1g/48mL and 2g/48mL in 0.9% NaCl (pharmaceutical grade), mimicking the procedure used in Intensive Care Units when using meropenem by prolonged or continuous infusion.

1. Stability at low and high concentrations and low and high temperatures

Solutions were incubated at 25°C, 30°C, 37°C for up to 8h with samples taken at 0, 0.5, 1, 2, 3, 4, 5, 6, 7, and 8 h.

2. Stability of visible degradation product(s):

Detailed analytical studies beyond those giving legal rights of the chosen product(s). Meropenem is known for its limited stability considered for monitoring purposes in the clinical setting and not as a routine test for choosing the appropriate antibiotic.

Results

Meropenem degradation proceeded on a time-, concentration- and temperature-dependent fashion, together with the appearance of a yellow color. The full results are presented in the poster but can be summarized as follows. Sandoz and Sanofi-Aventis generics degraded more rapidly when tested at the lowest concentration, and Sandoz generic produced a more intense yellow color than the other generics tested.

Conclusions

Meropenem from different sources vary in stability when tested in concentrated solutions, and some may generate more colored degradation products. Detailed analytical studies are required for proper companion and rational choice of the source of meropenem offered for clinical use especially if extended or continuous infusion is used.

References

1. MERREM IV® Product information (10/06) - [1]
4. Fonds de la Recherche Scientifique (F.R.S.-FNRS); [4]
5. Liberation of visible degradation product(s):
6. EU pharmacopoeia [7]

Funding

This work is part of the MOIN4STRAT project (European Union’s 7th Framework Programme for research, technological development and demonstration grant no. 226000). F.V. is Senior Research Associate of the Belgian Fonds de la Recherche Scientifique F.R.S.-FNRS.

Main messages and Key Conclusion

We confirm that meropenem is unstable in concentrated solutions, calling for caution when stored and/or used for infusion for more than 8h at temperature exceeding 35°C (see practical guide).

- Generics from Fresenius Kabi and Sandoz, are less stable than the original (MERONEM®) or the other generics tested. The Sanofi-Aventis generic releases more colored products than all other compounds tested.

- Detailed analytical studies beyond those giving legal rights of commercialisation to generics of meropenem are needed to fully assess their quality when intended for use by prolonged or continuous infusion.

Key words

Meropenem, Meropenem degradation, Meropenem stability, Meropenem concentration, Meropenem visibility, Meropenem in hospital pharmacy.