Compatibility and stability of Sandimmun® in commercial all-in-one parenteral nutrition admixtures

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Abstract

Background: Parenteral nutrition (PN) is indicated if the gastrointestinal tract does not work sufficiently anymore. These patients often suffer from severe diseases and need several intravenously administered medications. Co-administration of a drug and PN or even admixing the drug inside the PN is not recommended but can often not be avoided. Due to the complex formulation of the PN admixture the addition of drugs could lead to interactions between the components which might be dangerous for the patient. One medication which is often used alongside PN is Cyclosporin A (Sandimmun®), an immunosuppressant. The i.v. formulation for Cyclosporin A (CsA) is an emulsion itself and the admixing of Sandimmun® requires physicochemical stability tests and documentation for the drug and the PN admixture.

Aim: The aim of this study was to test the stability and compatibility of CsA in two often used PN admixtures (NuTRIflex® Omega Special and NuTRIflex® Lipid Special). Further, an analysis was conducted to determine whether the emulsifier of Sandimmun® has an influence on the stability of PN admixtures.

Methods: The chosen analytical methods allow a quick investigation on the stability of these admixtures in clinical routine. Stability of CsA within the PN was tested with LC-MS/MS by adopting a similar method as is used for therapeutic drug monitoring. The lipid emulsion stability was observed using an established light microscopic method and by visual inspection. The observations were completed with pH measurements. The same method was used to determine the effect of the emulsifier. All analytical tests were performed for different concentrations, over a period of one week and under different storage conditions.

Results: It was shown that both lipid emulsions were stable over seven days. The LC-MS/MS method to control the CsA concentration turned out to be not repeatable enough and the results were difficult to analyse. Furthermore, it was found that the emulsifier itself has a significant influence on the lipid emulsion stability and that there are signs for overly stable lipid emulsions, which can have a negative impact on the lipid clearance.

Conclusion: Further investigations for the admixing of Sandimmun® into PN and especially its excipients are indicated. Results show that the focus of upcoming studies should not only consider physico-chemical stability but also pharmacokinetic aspects.

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