Physicochemical stability and compatibility testing of Levetiracetam in all-in-one parenteral nutrition admixtures in daily practice

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Abstract

Objectives: Parenteral antiepileptic drugs are frequently used in critically ill patients for seizure control therapy or prevention. Many of these patients require additional parenteral nutrition (PN). Therefore, a parallel infusion of the frequently used antiepileptic drug levetiracetam (LEV) is interesting in terms of the restricted i.v. lines (e.g., neonates). The potential interactions of the complex PN admixture with the drug product and the appropriate admixing of a drug at effective dosages require physicochemical lab assessments to obtain specific and reliable pharmaceutical documentation for the intended admixing. To assess the of compatibility and stability of LEV, a neutral and hydrophilic drug, in commercial all-in-one (AiO) PN admixtures using simple validated tests to provide necessary data in a timely manner and to allow convenient, documented and safe treatment with PN as the drug vehicle.

Methods: Different concentrations of LEV were injected into two different AiO PN admixtures with no further additives. Stability and compatibility tests for the drug and the PN admixtures were performed over seven days at +4 °C, +23 ± 1 °C and +37 °C without light protection. Stability and sample characteristics were observed by visual inspection and the validated light microscope method. Moreover, the pH level of the admixture was checked, as were the concentrations of LEV over time in the PN admixtures, using an established LC-MS/MS method.

Results: The stability controls of LEV at different temperatures were within absolute ± 20% of the theoretical value in a concentration range of 98.91-117.84% of the initial value. No changes in pH occurred (5.55 ± 0.04) and no microscopic out of specification data or visual changes were observed. The mean value of the largest lipid droplet in each visual field over seven days was 2.4 ± 0.08 µm, comparable to that of the drug-free AiO admixture. Samples stored at +37 °C showed yellowish discolorations after 96 hours of storage.

Conclusions: LEV showed compatibility and stability over seven days in the selected PN admixtures, and the described methods represented a valuable and timely approach to determine the stability and compatibility of the highly hydrophilic, not dissociated LEV in AiO admixtures under conditions of use. Further studies with clinically relevant and representative examples of physicochemically different drug classes are needed.

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