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Review

Review of drug stability in parenteral nutrition admixtures

Daniel Cardona [a,*], Maria Nadal [b], Joan Estelrich [c], M. Antònia Mangues [a]

[a] Pharmacy Department, Hospital Santa Creu i Sant Pau, 167-08025 Barcelona, Spain
[b] Primary Care Pharmacist, Catalan Health Institute, Girona, Spain
[c] Physicochemical Department, Universitat de Barcelona, Spain

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SUMMARY

Background and aims: The addition of drugs to parenteral nutrition admixtures (PNA) or simultaneous Y-site administration is a concern in daily practice. We present a literature review studies on the physicochemical stability of drugs using both methods.
Methods: We performed a search of electronic databases and publications about drug stability in PNA. We prioritized studies that used two methods for obtaining samples: the reproduction of clinical administration conditions or centrifugation.
Results: Forty-two studies met all inclusion criteria and covered a total of 118 drugs with the following characteristics: simultaneous Y-site administration [20 studies and 115 drugs], and administration in PNA [24 studies and 13 drugs]. Eighty drugs administered in PNA via Y-site were compatible and 26 incompatible, while 9 results depended on the study conditions. Twelve out of 13 drugs included in the PNA were compatible for more than 24 h at room temperature.
Conclusions: The results of drug stability tests depend on the sampling methodology. Most of the results were obtained by the centrifugation method. Although the clinical method is much more reliable and offers a higher reproducibility of physicochemical stability, we found it was used by very few studies.
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1. Introduction

Two methods are used to administer drugs with parenteral nutrition admixtures (PNA): simultaneous Y-site infusion or inclusion in the PNA. The former normally consists of an intermittent infusion of drugs with PNA in simultaneous Y-site administration. The liquid content in the nutrient admixture is used as a vehicle for introducing the drugs into the patient. Once the admixture is prepared, the contact time between drugs and admixture can range from 10 min to 12 h. In the second method, the drug is mixed with the PNA and the period of co-infusion is the same, usually up to 24 h. However, this method is not usual in daily clinical practice due to the problems arising from a possible lack of physicochemical stability of the nutrients included in the PNA or absence of chemical stability data.

Separate administration of drugs and PNA is not always possible, even though multi-lumen catheters are used, since some situations require a high number of intravenous administrations (polypharmacy).

Although pharmacists are frequently consulted about the administration of drugs via PNA there is a lack of information about compatibility due to the high variability in PNA composition. Therefore, pharmacists are required to interpret the results of existing stability studies, since working conditions cannot always be guaranteed to be the same.

Before adding a drug to a PNA or delivering it by simultaneous Y-site infusion, its physicochemical stability must be reviewed in order to maintain the stability of the nutritive admixture (avoiding emulsion breaking, creaming or precipitations) and the concentration of the drug in the mixture must be ≥90% of the initial concentration.[1]

There are several reviews about drug compatibility with PNA and drug stability in ternary mixtures (containing amino acids, dextrose, lipids, with electrolytes, trace elements and vitamins).[2–4]

The aim of the current work was to review the literature about physicochemical stability of drugs administered by simultaneous Y-site infusion or in PNA. We also focused on peripheral and central administration.

Abbreviations: CC, Coulter Counter®; CR, counted radioactivity recovered after ^{125}Iodine labelling; EMIT, enzyme multiple immunoassay; EVA, ethylene vinyl acetate; FACS, fluorescence activated cell sorter; FPI, Fluorescence polarization immunoassay; HPLC, high-performance liquid chromatography; LD, laser diffraction; PCS, photon correlation spectroscopy; PN, parenteral nutrition; PNA, parenteral nutrition admixtures; PPNA, peripheral parenteral nutrition admixures; PVC, polyvinyl chloride; RIA, radioimmunoassay; RT, room temperature.

* Corresponding author. Tel.: +34 93 553 74 58; fax: +34 93 553 74 71.
E-mail address: dcardona@santpau.cat (D. Cardona).

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2. Methodology

2.1. Search strategy

We performed a search in MEDLINE/PubMed (January 1967–May 2011) and EMBASE (January 1974–May 2011) for articles published in English and Spanish using the search terms ["total parenteral nutritition admixtures" or "3-in-1 parenteral nutrition" or "total parenteral nutrition"] and ["drugs" or "medication"] and ["incompatibility" or "compatibility" or "stability" or "instability"] and ["physical" or "chemical"].

Additionally, we searched in nutrition-specific journals (*Clinical Nutrition, The Journal of Parenteral and Enteral Nutrition*) and also reviewed Pharmacy-specific journals (*Nutrición Hospitalaria or American Journal of Health-System Pharmacists, Pharmacy World & Science and Farmacia Hospitalaria*) and abstracts from scientific meetings in parenteral nutrition.

2.2. Study findings

2.2.1. Sampling methods

The articles selected for this review describe the use of at least one of the following sampling methods: 1) simultaneous Y-site administration conditions (Fig. 1); 2) centrifugation of an admixture of the drug and PNA (Fig. 2); and 3) an injection of drugs within the PNA (Fig. 3).

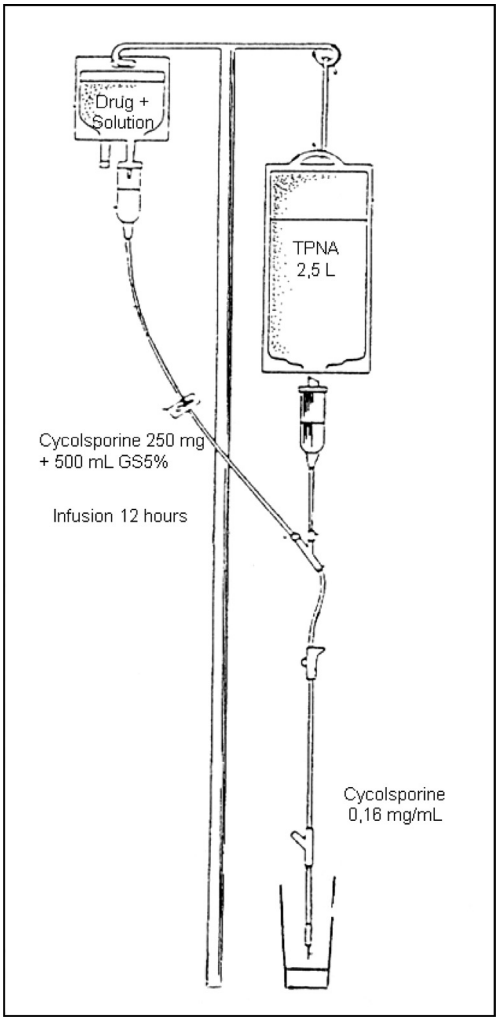

Fig. 1. Clinical method simulating Y-site administration of drug (previously diluted or not) with TPNA.

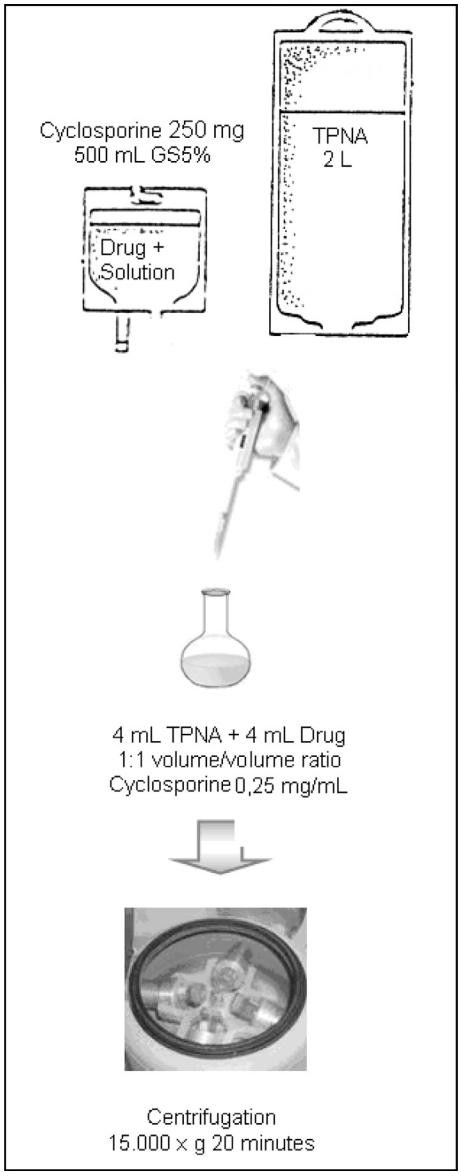

Fig. 2. Centrifugation method. Clinical method simulating Y-site administration of drug (previously diluted or not) with TPNA more centrifugation 1:1 V/V ratio.

For the simultaneous Y-site infusion, two procedures are described. On one hand, Baptista *et al* simulated clinical administration conditions by infusing a volume of the PNA into 14 mini-bottles of different antibiotics for 30 min,[5] while the other method reproduced administration conditions used in daily clinical practice.[6–8] The samples were obtained from a Y-site administration of drugs via a running PNA line. All the tested drug solutions were infused in the appropriate time (ranging from 10 min to 12 h). The PNA was administered for a period of 24 h. The volume analysed corresponded to the amount of administered drug plus the simultaneous PNA volume administered.

Najari *et al*[6] studied 3 drugs, which were administered by a Y-site technique with the PNA, in accordance with common practices in bone marrow transplant units. A filter system with a gridded 0.8 μm membrane filter disk was placed at the end of the intravenous set to collect any precipitates. The drug was considered