Stability study of a ternary parenteral nutrition admixture after addition of human insulin

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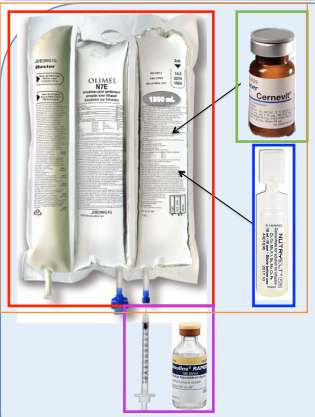
Introduction and objectives

Parenteral nutrition admixture (PNA) induces administration of high dextrose amounts. Hyperglycaemia is a frequent side effect, with potential deleterious effects. Consequently, human insulin is sometimes directly added into the PNA bag. Drug mixing with PNA is strongly discouraged, especially in the case of ternary parenteral nutrition (TPN). Indeed, TPN admixtures corresponding to emulsions, are supposed to be potentially destabilized, even broken down by the addition of drugs or any other external nutrients.

The main goal of this work was to study the *in vitro* stability of a TPN admixture after addition of human insulin into the bag.

Materials and methods



Tested mediums of work

1) PNA = Olimel N7E® (ternary industrial PNA in EVA bag) supplemented with vitamins (1 Cernevit® vial) and trace elements (1 Nutryelt® vial)

2) PNA + 20 IU/L of human insulin (Umuline rapide®)
Each assay performed in triplicate

Storage conditions : room temperature during 24 hours

Measured parameters
- pH (pH-meter measurement)
- PFAT5 (light obscuration system, analysis range : 1.8-50 µm)
- Osmolality (osmometer measurement)

Sampling times : 0 and 24 hours after medium mixing ± insulin addition

Descriptive analysis of pH, PFAT5[1] and osmolality values

Results

Results (mean ± SD) obtained for the 3 parameters of interest are detailed in the table below.

Parameter	PNA		PNA + human insulin 20 IU/L	
	t_0	t_{24}	t_0	t_{24}
pH	6.35 ± 0.01	6.32 ± 0.01	6.36 ± 0.01	6.32 ± 0.01
PFAT5 (%)	0.018 ± 0.007	0.005 ± 0.000	0.017 ± 0.001	0.004 ± 0.000
Osmolality (mOsm/kg)	1700.3 ± 14.0	1709.7 ± 15.5	1718.7 ± 15.9	1710.0 ± 6.1

Initial values and their variation over time were comparable whatever the medium (with or without insulin) for the 3 parameters.

Discussion - Conclusion

All PFAT5 values were below the threshold of 0.05%[1] with and without insulin. This hypothesis is confirmed by the constancy of both pH and osmolality values. The addition of human insulin in TPN admixtures seems a good solution to avoid hyperglycaemia in patients treated with TPN. Indeed, both dextrose and insulin are rigorously administered together. However, further studies are needed to demonstrate that admixtures of both TPN and insulin remains stable. Physicochemical stability of lipid injectable emulsion is paramount to their safety. **In the present work, stability of a TPN emulsion has been demonstrated**. These results could be strengthened by measurements of zeta potential and size distribution of lipid droplets. Moreover, insulin stability studies in real conditions have to be performed to complete these experiments.

Reference

1. United States Pharmacopeia, USP37/NF32. Chapter <729> Globule size distribution in lipid injectable emulsions. Rockville, MD: United States Pharmacopeia; 2014:360-363.