Stability of total parenteral nutrition admixtures for pediatric home care in the presence of high concentrations of electrolytes

D. Watrobska-Swietlikowska[1], A. Szlagatys-Sidorkiewicz[2]

[1]Department of Pharmaceutical Technology, Medical University of Gdansk, Hallera Av. 107, 80-416 Gdansk, Poland, Tel.: +48583491085, Fax.: +48583491090, email: dwatro@gumed.edu.pl

[2]Department of Pediatrics, Pediatric Gastroenterology, Hepatology and Nutrition, Medical University of Gdansk, Nowe Ogrody Str. 1-6, 80-803 Gdansk, Poland, Tel.: +48587460250, Fax.: +48583022591, email: aga1@gumed.edu.pl

Poster number TCH-041

INTRODUCTION

In a clinical practice electrolytes-enrichment of the parenteral nutrition admixtures is a usual demand, especially in the neonatal/pediatric wards [1]. The supplementation of parenteral nutrition with high concentration of electrolytes is a living problem due to decreased stability of lipid emulsions in nutrition admixtures caused by bivalent cations. When higher intakes of Ca^{2+} and phosphate are necessary an organic salts of calcium and phosphate (e.g. glucoso-1-phosphate or glycerophosphate) should be used [2]. Precipitation of calcium phosphate can be overcome by using organic salts [3]. It was found that glycerophosphate provided much better compatibility with Ca^{2+}, allowing the addition of up to 100 mmol/L phosphorus and 40 mmol/L Ca^{2+}, without any precipitation [4].

[1] Colomb, V., et al. J. Pediatr. Gastroenterol. Nutr. 44, 347-353 (2007)
[2] Pertkiewicz, M., et al. e-SPEN 4, e117-e119 (2009)
[3] Bouchoud, L., et al. Clin. Nutr. 29, 808-812 (2010)
[4] Ronchera-Oms, C.L., et al. Clin. Nutr. 14, 373-380 (1995)

The aim of study was to examine the stability of 48 different pediatric admixtures designed for home parenteral nutrition. Investigated admixtures were characterized by high concentration of electrolytes (20-61 mmol/l K^+, 9-21 mmol/l Ca^{2+}, 6-20 mmol/l Mg^{2+}).
Three types of emulsions: Intralipid, ClinOleic and SMOFlipid and organic calcium salt (gluconolactobionate) were used for preparation of TPN admixtures.

EXPERIMENTAL METHODS

TPN pre-admixtures were prepared at the clean room using Multicomp II pump (Fresenius Kabi, Uppsala, Sweden) (Fig. 1). The compositions of TPN admixtures were prescribed by physicians in the Copernicus Specialist Hospital of Gdansk (Tab.1).

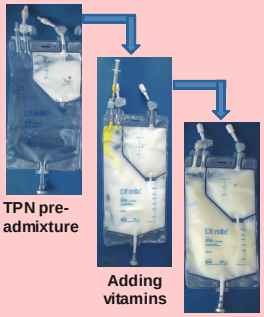
Figure 1. Preparation of TPN pre-admixtures.

Table 1. Content of electrolytes in TPN admixture [mmol/l]

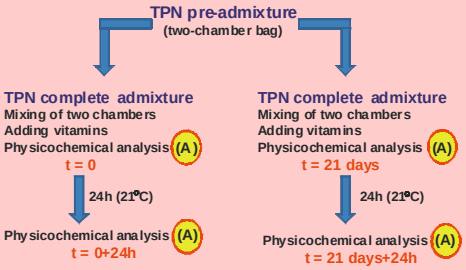
TPN	Na^+	K^+	Mg^{2+}	Ca^{2+}	PO_4^{3-}
1	58.0	41.2	13.8	14.3	14.1
2	46.1	32.9	10.9	11.6	11.2
3	59.4	39.6	11.1	12.9	11.7
4	39.9	26.7	7.4	8.6	8.1
5	69.5	49.5	8.7	12.9	9.9
6	58.2	41.2	7.4	10.8	8.4
7	46.3	32.9	5.7	8.6	6.5
8	49.4	29.7	11.1	17.2	16.7
9	41.2	25.2	9.1	14.3	14.1
10	32.9	19.9	7.4	11.6	11.2
11	48.7	29.7	8.7	12.9	9.9
12	41.4	25.2	7.4	10.8	8.4
13	33.1	19.9	5.7	8.6	6.5
14	86.4	61.4	20.3	21.5	20.8
15	69.3	49.5	16.2	17.2	16.7
16	46.1	32.9	10.9	11.6	11.2

Each of compositions of 16 of TPN admixutres were prepared using different lipid emulsion and aminoacid:
a - Intralipid and Aminoven Infant
b - SMOFlipid and Aminoven Infant
c - ClinOleic and Primene

Scheme of preparation of complete TPN admixture



Scheme of storage and analysis of TPN admixtures



(A) Physical analysis:
- visual observations
- globule size measurements (optical microscopy and laser diffractometry)
- pH analysis
- zeta potential measurements

RESULTS AND DISCUSSION

Visual inspection of all completed TPN admixtures did not reveal other changes but very slight creaming after 24 h of storage at room temperature (t=0+24h).

Despite the various composition and type of lipid emulsions in microscopic observations all TPN admixtures were characterized by size of oily particles not larger than 1 µm, which is safe for a patient (Fig. 2). Microscopic observations were confirmed by using PCS and LD methods.

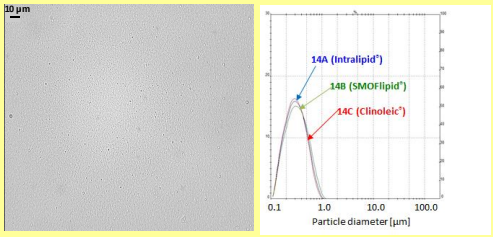


Figure 2. Microscopic observation and droplet size distribution of complete TPN 14 at t=0+24h.

The median ($d_{0.5}$) of oily droplets in TPN was 310-330 nm and 90% of oily droplets ($d_{0.9}$) were under 580-670 nm (LD method) whereas Z-avarage was in range 250-310 nm (PCS method). These parameters remained unchanged after storage for 24 h at room temperature. It was noted that type of the lipid emulsion has no influence on droplet size distribution of the TPN admixtures (Fig. 2). Oily droplet size did not also change despite the storage of the pre-admixtures in two-chamber bags (Fig. 3).

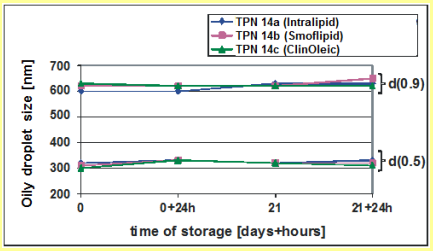


Figure 3. Oily droplet size of complete admixtures TPN 14 - the effect of storage of pre-admixture for 21 days.

Only in two of the complete admixtures (TPN 15b and 16a) at t=21 days+24h few oily droplets up to 8-10 µm and some agglomerates of these droplets were observed in microscopic observations despite the fact that no oily globules lager than 1 µm were detected in these admixtures by using laser diffractometry and PCS methods (Fig. 4). This observation was confirmed in another independent experiment, so these admixtures was classified as unstable.

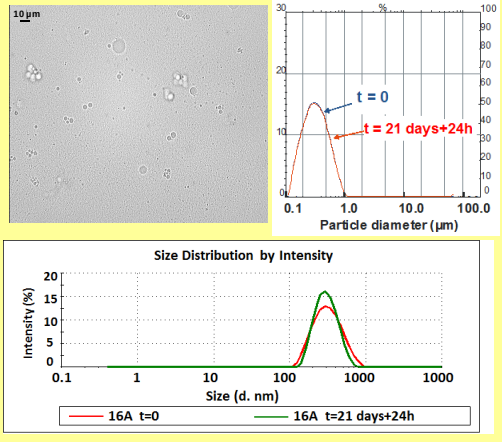


Figure 4. Microscopic observation and droplet size distribution of complete admixture TPN 16a - effect of storage for 24 days.

The pH values of TPN admixtures were in range 6.2 - 6.5. These values did not change during storage (Fig. 5).

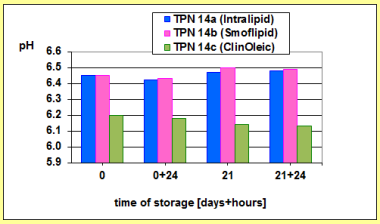


Figure 5. The pH values of the complete TPN 14 - the effect of various composition.

Despite the high electrolytes concentration zeta potential values in TPN admixtures were in range -35.0 to -47.0 mV. These values did not change during storage (Fig. 6).

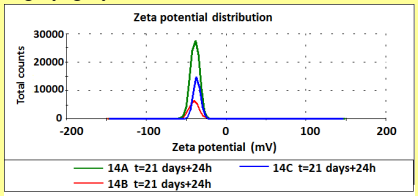


Figure 6. Zeta potential of complete TPN 14 - the effect of various composition.

CONCLUSIONS

TPN pre-admixtures with proposed compositions may be stored for at least 21 days at 4°C. The complete TPN admixtures demonstrated stability for at least 24 h at room temperature. Type of the lipid emulsion has no influence on stability of the studied admixtures. It was possible to obtain stable admixtures despite of the high concentration of electrolytes. Laser diffractometry did not show destabilization of complete admixtures which were visually or microscopically observed as unstable. Oily droplet size distribution measured by laser diffractometry should always be verified by microscopic observations.

The authors wish to thank Fresenius Kabi for financial support, and we also thank B/Braun and Baxter for giving their products for the study.