Separating and Shielding Multivitamins to Reduce Toxic Peroxides contaminating the Parenteral Nutrition (SMART-PN): in vitro study

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BACKGROUND

Parenteral nutrition contamination with peroxides:

- Due to their gastrointestinal immaturity, virtually all preterm infants < 29 weeks of gestational age will need PN for the first few days/weeks of their lives.
- Peroxides were reported to contaminate the PN solution.
- The photo-excitable riboflavin catalyzes the oxidation of electron donors by oxygen in this light-dependent reaction. That is why Multivitamins (MV) added to PN solution and PN exposure to light were found to be the 2 main inducers of peroxide contamination.

The in vitro effect of photoprotection:

- Complete photoprotection of the PN solution (starting from PN compounding till its infusion to infants) resulted in significant reduction of contaminating peroxides (146 ± 15 vs 215 ± 24 μM)

Biological effects of peroxides contaminating PN

- In animal model, infusion of photo-exposed PN led to increased oxidative stress, more oxidized redox potential and significant lung remodeling with hypoalveolarization which is one of the main pathological changes in Bronchopulmonary dysplasia (BPD).

PN photoprotection in preterm infants:

- The antioxidant defenses are still poorly developed in preterm infants.
- With PN photoprotection, single-center studies showed a reduction of urinary peroxide levels by about 50% as well as a reduction of BPD by 25 -30%.
- Recent meta-analysis off all photo-protection studies found a 50% reduction in mortality in the photo-protected group compared to light exposure.
- Complete PN photo-protection is not feasible with the current set-up in clinical settings.

HYPOTHESIS AND OBJECTIVES

We hypothesize that shielding and infusing MV in a separate line is a readily applicable and effective method of photo-protection. Our objective is to compare the quantity of peroxides contaminating PN with this intervention compared to the standard of care (no photo-protection).

METHODS

To insure complete photoprotection of multivitamins since its sampling till its completed infusion through intravenous line:

- The MV (Multi-12 pediatrics, Sandoz) preparations comes already in amber vials (Figure 1-A).
- It is sampled in a syringe that is photo-protected with a white label (Figure 1-B) indicating the subject study name, protocol number and the infusion rate.
- The MV is allowed 30 min as transport time from the pharmacy to the Neonatal intensive care unit (NICU).
- In neonatal unit, this syringe is installed in the pump and connected to photo-protected extension (Figure 1-C, LS688 Light-Safe® Minibore Extension Set, ID: 71.7511, Codan, USA) that is connected to a trifurcate connection (Figure 1-D, one for PN without MV, second for lipids, the third is a photoprotected one and it is for the MV) that directly infuse to the patient intravenous line (LS230 Trifurcated Light-Safe® Minibore Extension Set, ID: 72.7514, Codan, USA), Figure 2.

A: MV already comes in amber vial

B: Photo-protected syringe with a white label

C: Amber extension line (LS688 Light-Safe® Minibore Extension Set, ID: 71.7511, Codan, USA)

D: Amber trifurcate (LS230 Trifurcated Light-Safe® Minibore Extension Set, ID: 72.7514, Codan, USA).

- The whole set up is depicted in Figure 2 showing current set up (Figure 2-A) compared to the intervention set up (Figure 2-B).
- Five samples were obtained from each solution:
 - At times 0 infusion (after 30 minutes of sampling to simulate the time of transport between the pharmacy and the NICU)
 - After infusion by 30 minutes, 1, 3 and 5 hours.
- Samples of 0.5 ml were used for peroxide determination using ferrous oxidation/xylenol orange technique. H_2O_2 served for the standard curve. The results were expressed as μM equivalent H_2O_2 .
- For each group (control and intervention) 3 solutions were made and peroxides were measured on the previously indicated times.
- Results represent Mean $\pm$ SEM.

Actual set-up for PN administration

Intervention set-up

Figure 2

Results

- In absence of photo-protection, peroxides in the syringe increased from 97 ± 10 μM at vial opening to 198 ± 18 μM at time of connection to the intravenous line (30 min later); with this MV photo-protection method peroxides remained stable with a limited increase to 109 ± 11 μM .
- When adding the generated peroxides over 5 hours (5 samples: at times 0, 30 minutes, 1, 3 and 5 hours), the total peroxides were 1270 ± 47 μM without photo-protection vs. 710 ± 16 μM with this new method (about 45% reduction of peroxide contamination). Results are depicted in (Figure 3).

Figure 3

CONCLUSION

Shielding and infusing MV in a separate line provide a readily applicable and effective method of photo-protection with a 45% reduction of peroxides' contamination of PN.