PREMATÜRE BEBEKLERDE OKSİDATİF HASARI ÖNLEMEDE HANGİ LİPİD SOLÜSYONU DAHA ETKİLİ; SMOFLIPID Mİ, CLINOLEIC Mİ?

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22.12.2018

Uludağ Üniversitesi Tıp Fakültesi, Neonatoloji Bilim Dalı

Giriş

- Erken ve agresif total parenteral beslenme prematüre bebek bakımının esaslarından biridir
- Amaçlanan; intrauterin nutrient geçişinin devamlılığını ve istenen büyümeyi sağlamaktır

Giriş

- Ancak özellikle uzun süre kullanım ile artan, TPN ilişkili oksidatif hasar önemli bir sorun olmaya devam etmektedir
- Bu istenmeyen durum, daha çok lipid içerik ile ilişkili olarak karşımıza çıkmaktadır

Amaç

- Ülkemizde TPN içeriğinde kullanılan iki lipid solüsyonunun, ClinOleic (Zeytin ve soya yağı) ve SMOFlipid (Soya, zeytin ve balık yağı), prematüre bebeklerde, TPN ilişkili oksidatif hasarı önleme üzerine etkilerini araştırmaktır.

Gereç ve Yöntem

- Prospektif, randomize çalışma
- Uludağ Üniversitesi YDYB ünitesine yatırılan otuz iki hafta ve altındaki prematüre bebekler
- Tüm bebeklerin ailelerinden yazılı onam alındı
- Tüm bebeklere ilk gün 4-6 mg/kg/dakika glukoz, 3 gr/kg/gün protein ve 1 gr/kg/gün lipid solüsyonu içeren TPN başlandı

Gereç ve Yöntem

- Lipid içerik her gün 1 gr/kg/gün artırılarak, 3. günden itibaren 3 gr/kg/gün olarak devam edildi
- Bir gruba ClinOleic, diğer gruba SMOFlipid verildi
- Lipid infüzyonu enteral beslenme 75 ml/kg/gün olunca azaltılarak, 100 ml/kg/güne ulaşınca TPN ile birlikte sonlandırıldı

Gereç ve Yöntem

- Tüm bebeklerin serum örneklerinden 1, 7 ve 14. günlerde;
  - Total Antioksidan Kapasite (TAK)
  - Pro-inflamatuar sitokin düzeyleri
    - IL-6, IL-1beta, TNF-alfa
  - Anti-inflamatuar sitokin düzeyleri
    - IL-10

Gereç ve Yöntem

- Tüm bebeklerin serum örneklerinden 3. günlerinde;
  - Lipid peroksidasyon ürünü
    - MDA: malondialdehyde

Gereç ve Yöntem

- Her iki grupta yer alan hastalar:
  - TAK, lipid peroksidasyon ürünü, sitokin düzeyleri
  - Neonatal morbiditeleri ve mortaliteleri
    - BPD, NEK, İVK, ROP, solunum destek gereksinimi

Bulgular

TOPLAM: 89 bebek

Demografik özellikleri	SMOFlipid (n=42)	ClinOleic (n=47)	p
Gestasyonel hafta, ort±sd	28.1±1.2	28±1.1	0.4
Doğum ağırlığı (g), ort±sd	1397±602	1302±494	0.6

Bulgular

Demografik özellikleri	SMOFlipid (n=42)	ClinOleic (n=47)	p
Apgar skor[1], ort±sd	5.4±2.1	4.9±2.5	0.2
Apgar skor[5], ort±sd	7.5±1.4	6.9±1.8	0.1
Sezaryan doğum, n(%)	35 (83)	36 (76)	0.4
Düşük doğum ağırlığı (<10p), n(%)	3 (7.1)	4 (8.5)	0.8
Antenatal steroid, n(%)	30(71)	34(72)	0.9
Koryoamniyonit, n(%)	5 (12)	1 (2)	0.06
Preeklampsi, n(%)	23 (54.8)	26 (55.3)	0.9

Bulgular

NEONATAL SONUÇLAR	SMOFLİPİD GRUP n=42	CLİNOLEİC GRUP n=47	p
Respiratuar distres sendromu, n(%)	30 (71.4)	33 (70)	0.5
Patent duktus arteriozus, n(%)	25 (59.5)	31 (66)	0.3
İntraventriküler hemoraji, n(%)	6 (14.2)	6 (12.7)	0.3
Nekrotizan enterokolit, n(%)	1 (2)	2 (3.1)	0.4
Prematüre retinopatisi, n(%)	1 (2)	3(6.8)	0.3
Bronkopulmoner dislazi, n(%)	6 (14.1)	15 (31.2)	0.2

Bulgular

BRONKOPULMONER DİSPLAZİ EVRE, n(%)	SMOFLİPİD GRUP n=42	CLİNOLEİC GRUP n=47	p
HAFİF, n=0			
ORTA, n=9	3 /42 (7.1)	6/47 (12.8)	0.06
AĞIR, n=12	3 /42 (7.1)	9/47 (19.1)	0.02

Bulgular

NEONATAL SONUÇLAR	SMOFLİPİD GRUP n=42	CLİNOLEİC GRUP n=47	p
Mekanik ventilatör gün, ort±sd	10.7±2.6	10.2±2.8	0.8
Toplam oksijen gün, ort±sd	30±22.1	34±24.2	0.2
Total parenteral nütrisyon gün, ort±sd	13.1±2.2	13.1±2.7	0.9
Mortalite, n(%)	6 (14.3)	5 (10.6)	0.4
Kolestaz	0	0	
Non-invaziv ventilatör gün, ort±sd	10.3±2.6	18.5±2.1	0.01

Bulgular

Parametre	Örnek günü	SMOFLİPİD GRUP n=42	CLİNOLEİC GRUP n=47	p
Total antioksidan kapasite (U/ml)	1	9.0±1.6	5.5±1.5	>0.05
IL-6 (pg/ml)	1	118±21	74.6±17	>0.05
IL-10 (pg/ml)	1	50.7±38	15.5±6.0	>0.05
IL-1 BETA (pg/ml)	1	37.2±21.4	22.1±14.7	>0.05
TNF-ALFA (pg/ml)	1	112±76	17±11	>0.05

Bulgular

Parametre	Örnek günü	SMOFLİPİD GRUP n=42	CLİNOLEİC GRUP n=47	p
Total antioksidan kapasite (U/ml)	7	17.4±2.7	8.7±2.3	0.01
IL-6 (pg/ml)	7	60.9±10.7	40.6±10.6	>0.05
IL-10 (pg/ml)	7	18.4±3.0	13.1±7.2	>0.05
IL-1 BETA (pg/ml)	7	5.0±1.1	11.5±9.4	>0.05
TNF-ALFA (pg/ml)	7	2.1±1.6	3.7±3	>0.05

Bulgular

Parametre	Örnek günü	SMOFLİPİD GRUP n=42	CLİNOLEİC GRUP n=47	p
Total antioksidan kapasite (U/ml)	14	10.3±2.2	9.7±2.5	>0.05
IL-6 (pg/ml)	14	19.4±3.8	21.3±8.0	>0.05
IL-10 (pg/ml)	14	19.9±5	13.4±11	>0.05
IL-1 BETA (pg/ml)	14	5.2±1.9	1.9±1.3	>0.05
TNF-ALFA (pg/ml)	14	3.8±2.2	4.5±4.3	>0.05

Bulgular

Parametre	Örnek günü	SMOFLİPİD GRUP n=42	CLİNOLEİC GRUP n=47	p
Lipid peroksidasyon ürünü (MDA) (nmol/mL)	3	12.7±9.6	11.7±10.5	>0.05

Tartışma

- TPN ilişkili oksidatif stresin de etiyolojisine katkı sağladığı ROP, BPD gibi morbiditeler neonatologların önemli uğraşlarından biri olmaya devam etmektedir.
- Bu morbiditeleri azaltmaya yönelik çalışma alanlarından biri de TPN ilişkili oksidatif hasarı azaltmak üzerinedir.

Tartışma: Intralipid & SMOFlipid

Early Hum Dev. 2014 Jan;90(1):27-31. doi: 10.1016/j.earlhumdev.2013.11.002. Epub 2013 Dec 4.

The influence of fish-oil lipid emulsions on retinopathy of prematurity in very low birth weight infants: a randomized controlled trial.

Beken S[1], Dilli D[2], Fettah ND[2], Kabataş EU[3], Zenciroğlu A[2], Okumuş N[2].

Author information

Abstract

OBJECTIVE: To compare the effect of two lipid emulsions on the development of retinopathy of prematurity in very low birth weight infants.

DESIGN: Randomized controlled study.

PATIENTS AND METHODS: Eighty very low birth weight infants receiving parenteral nutrition from the first day of life were evaluated. One of the two lipid emulsions were used in the study infants: Group 1 (n=40) received fish-oil based lipid emulsion (SmofLipid®) and Group 2 (n=40) soybean oil based lipid emulsion (Intralipid®).

MAIN OUTCOME MEASURES: The development of retinopathy of prematurity and the need for laser photocoagulation were assessed.

RESULTS: The maternal and perinatal characteristics were similar in both groups. The median (range) duration of parenteral nutrition [14days (10-28) vs 14 (10-21)] and hospitalization [34days (20-64) vs 34 (21-53)] did not differ between the groups. Laboratory data including complete blood count, triglyceride level, liver and kidney function tests recorded before and after parenteral nutrition also did not differ between the two groups. In Group 1, two patients (5.0%) and in Group 2, 13 patients (32.5%) were diagnosed with retinopathy of prematurity (OR: 9.1, 95% CI 1.9-43.8, p=0.004). One patient in each group needed laser photocoagulation, without significant difference. Multivariate analysis showed that only receiving fish-oil emulsion in parenteral nutrition decreased the risk of development of retinopathy of prematurity [OR: 0.76, 95% CI (0.06-0.911), p=0.04].

CONCLUSIONS: Premature infants with very low birth weight receiving an intravenous fat emulsion containing fish oil developed less retinopathy of prematurity.

Tartışma: ClinOleic & Omegaven

Pediatrics. 2011 Feb;127(2):223-8. doi: 10.1542/peds.2010-2427. Epub 2011 Jan 3.

Fish-oil fat emulsion supplementation may reduce the risk of severe retinopathy in VLBW infants.

Pawlik D[1], Lauterbach R, Turyk E.

⊕ Author information

Abstract

OBJECTIVE: The retina contains rods and cones that have membranes highly enriched with docosahexaenoic acid (DHA). Infants born prematurely are at risk of DHA insufficiency, because they may not have benefited from a full third trimester of the mother's lipid stores. Moreover, within the first 2 to 3 weeks of life, the main sources of lipids for premature infants are fat emulsions, which do not contain DHA.

PATIENTS AND METHODS: This observational study was designed to compare the safety and efficacy outcomes of an intravenous fat emulsion that consists of fish-oil emulsion (contains DHA) with soybean and olive oil, administered from the first day of life to 40 infants who weighed <1250 g; results were obtained from a historical cohort of 44 preterm neonates who were given an emulsion of soybean and olive oil. The primary study outcomes were the occurrence of retinopathy and need for laser therapy and cholestasis. Infants in the 2 groups were comparable with regard to demographic and clinical characteristics and were subjected to the same conventional therapy.

RESULTS: There was a significantly lower risk of laser therapy for infants who received an emulsion of soybean, olive oil, and fish oil ($P = .023$). No significant differences were found in acuity and latency of visual evoked potentials between infants in the 2 groups. There was no infant with cholestasis among those who received fish-oil emulsion, and there were 5 subjects with cholestasis in the historical group ($P = .056$).

CONCLUSION: Fish-oil-based fat emulsion administered from the first day of life may be effective in the prophylaxis of severe retinopathy.

Tartışma:

NEONATAL SONUÇLAR	SMOFLİPİD GRUP n=42	CLİNOLEİC GRUP n=47	p
Prematüre retinopatisi, n(%)	1 (2)	3(6.8)	0.3

Tartışma: Intralipid & SMOFlipid

Nutr Clin Pract. 2012 Dec;27(6):817-24. doi: 10.1177/0884533612454547. Epub 2012 Aug 9.

Cholestasis, bronchopulmonary dysplasia, and lipid profile in preterm infants receiving MCT/ω-3-PUFA-containing or soybean-based lipid emulsions.

Skouroliakou M[1], Konstantinou D, Agakidis C, Delikou N, Koutri K, Antoniadi M, Karagiozoglou-Lampoudi T.

⊕ Author information

Abstract

BACKGROUND: This study aimed to compare the effect of 2 lipid emulsions (LEs), a medium-chain triglyceride (MCT)/ω-3-polyunsaturated fatty acid (PUFA)-containing LE and a soybean-based LE, on the incidence of neonatal cholestasis, bronchopulmonary dysplasia (BPD), and lipid profile of preterm infants. Patients and

METHODS: In this prospective, observational study, 2 groups of preterm neonates, the very low birth weight (VLBW) (n = 129) and the low birth weight (LBW) groups (n = 153), which received parenteral LEs for at least 7 days, were included. Infants received either MCT/ω-3-PUFA-containing LE (SMOFlipid, subgroup I) or soybean-based LE (Intralipid, subgroup II) according to the attending neonatologist's preference and availability. Full biochemical assessment was performed on days of life 15, 30, and 45 and on discharge.

RESULTS: Of the VLBW infants, 7.4% and 13.3% of infants in subgroups I and II, respectively, developed cholestasis (P = .39; odds ratio [OR], 0.52; 95% confidence interval [CI], 0.15-1.76). The duration of LE administration was independently associated with cholestasis (P < .001; OR, 0.925; 95% CI, 0.888-0.963). The maximum amounts of lipids administered ranged between 1.6 and 3.6 g/kg/d in both VLBW subgroups. The VLBW subgroup I had lower incidence of BPD, lower alkaline phosphatase and phosphate, higher high-density lipoprotein (HDL), and lower cholesterol-to-HDL ratio on discharge than the VLBW subgroup II. The type of LE was independently associated with BPD and alkaline phosphatase. In the LBW group, the type of LE was not associated with clinical and biochemical parameters.

CONCLUSION: In VLBW infants, the MCT/ω-3-PUFA-containing LE administration is associated with decreased BPD and more favorable lipoprotein profile. Although a trend toward a lower incidence of cholestasis was observed, a preventive effect of MCT/ω-3-PUFA-containing LE on parenteral nutrition-associated cholestasis is not supported.

Tartışma:

BRONKOPULMONER DİSPLAZİ EVRE, n(%)	SMOFLİPİD GRUP n=42	CLİNOLEİC GRUP n=47	p
Bronkopulmoner dislazi, n(%)	6 (14.1)	15 (31.2)	0.2
HAFİF, n=0			
ORTA, n=9	3 /42 (7.1)	6/47 (12.8)	0.06
AĞIR, n=12	3 /42 (7.1)	9/47 (19.1)	0.02

Tartışma: ClinOleic & SMOFlipid

J Pediatr Gastroenterol Nutr. 2014 Feb;58(2):177-82. doi: 10.1097/MPG.0000000000000174.

Fish Oil (SMOFlipid) and olive oil lipid (Clinoleic) in very preterm neonates.

Deshpande G[1], Simmer K, Deshmukh M, Mori TA, Croft KD, Kristensen J.

Author information

Abstract

OBJECTIVES: Fat emulsions used in Australia for parenteral nutrition in preterm neonates have been based on either soybean oil or olive oil (OO). OO lipid Clinoleic has a high ratio of n-6 to n-3 fatty acids (9:1); this may not be ideal for long-chain polyunsaturated fatty acids supply. Newly available SMOFlipid has an appropriate ratio of n-6 to n-3 fatty acids (2.5:1). SMOFlipid also contains OO (25%), coconut oil (30%), and soybean oil (30%). The aims of the study were to evaluate the safety of the SMOFlipid and to test the hypothesis that SMOFlipid would lead to increased omega-3 long-chain polyunsaturated fatty acid levels and reduced oxidative stress as compared with Clinoleic in preterm neonates (<30 weeks).

METHODS: Preterm neonates (23-30 weeks) were randomised to receive Clinoleic or SMOFlipid emulsion for 7 days. Investigators and outcome assessors were masked to allocation. Plasma F2-isoprostanes (lipid peroxidation marker), red blood cell fatty acids, and vitamin E were measured before and after the study. Blood culture positive sepsis and growth were monitored for safety.

RESULTS: Thirty of 34 participants completed the study. Both emulsions were well tolerated without any adverse events. F2-isoprostane levels were reduced in the SMOFlipid group as compared with baseline. Eicosapentanoic acid and vitamin E levels were significantly increased in the SMOFlipid group. Oleic acid and linoleic acid levels were increased in both groups. No significant differences were noted in poststudy docosahexaenoic acid levels in both groups despite higher levels of docosahexaenoic acid in SMOFlipid.

CONCLUSIONS: SMOFlipid was safe, well tolerated, and showed beneficial effect in terms of reduction of oxidative stress by reducing lipid peroxidation levels in high-risk preterm neonates.

Tartışma:

Parametre	Örnek günü	SMOFLİPİD GRUP n=42	CLİNOLEİC GRUP n=47	p
Lipid peroksidasyon ürünü (MDA) (nmol/mL)	3	12.7±9.6	11.7±10.5	>0.05

- Ağır BPD görülmesi açısından farklılık gözlenmiştir
- Kolestaz (PNALD) her iki grupta da gözlenmemiştir.

Sonuç

- Çalışmamızda ClinOleic kullanımına göre, SMOFlipid kullanımı;
  - Neonatal morbiditeler, sitokin düzeyleri, oksidan ve antioksidan ürünler açısından karşılaştırılmıştır.
  - SMOFlipid kullanımının, artmış TAK ve istatistiksel olarak anlamlı olmasa da azalmış ROP ve BPD sıklığı ile birlikte olduğu,
  - Ağır BPD yi ise istatistiksel olarak anlamlı düzeyde azalttığı gösterilmiştir.

Sonuç

- Sonuç olarak bütün bu bilgiler ışığında;
  - Prematüre bebeklerde ilk seçenek lipid solüsyonu olarak SMOFlipid önerilebilir.

Teşekkürler…

22.12.2018