PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Cochrane Neonatal

Dr. Álvaro Fredes

02-08-2020

INDISA - NEORED

Un Nuevo Concepto en Medicina Perinatal

INDISA
CLINICA DE FAMILIA

Neo Red

Transmitted Home Oximetry and Duration of Home Oxygen in Premature Infants

- < 28s con DBP el 28% utiliza O2 domiciliario (HOT).
- No existen guías basadas en evidencia y seguimiento por BP en controles ambulatorios mensuales.
- Exposición prolongada a O2, mayor estrés parental y mala calidad de vida.
- **Objetivo:** evaluar si registro de oximetría domiciliaria (RHO) comparado con cuidado estándar, disminuye días de O2 y mejora calidad de vida familiar.

INDISA - NEORED

Pediatrics August 2020, 146 (2) e20200079.

Transmitted Home Oximetry and Duration of Home Oxygen in Premature Infants

- **Diseño:** randomizado no ciego, 9 NICUs 2013-2017.
  - EG ≤ 37s con O2 al alta y en 1° control BP.
  - Exclusión: HP, O2 > 1L/min, laringo/traqueomalacia, cafeína.
  - Protocolo:
    - Ambos grupos: control mensual, 20 min challenge SpO2>93% al disminuir flujo O2 (50% del previo). Si flujo < 0.125 L/min pasa a O2 nocturno.
    - *Standard-care (control):* polisomnograma nocturno hospitalizado para decidir retiro de O2.
    - *Intervention:* oximetría continua en domicilio (RHO) mínimo 25h por reporte vía mail cada 4-7 días. Algoritmo y recomendaciones para mantener, aumentar o bajar O2.

INDISA CLINICA DE FAMILIA

Neo Red

Transmitted Home Oximetry and Duration of Home Oxygen in Premature Infants

- **Outcomes:**
  - Duración de O2 domiciliario
  - Calidad de vida de padres (PedsQL)
- **Outcomes 2arios:**
  - Eventos adversos (infecciones respiratorias, complicaciones GTT, intolerancia alimentaria)
  - Cambios en Z-peso y Z-peso/talla a los 6 meses

INDISA
CLINICA DE FAMILIA

Neo Red

TABLE 1 Baseline Demographic and Clinical Characteristics of the Randomly Assigned Sample for the RHO Trial

	Intervention (N = 97)	Standard Care (N = 99)
Sex, *n* (%)		
Male	64 (66)	58 (59)
Female	33 (34)	41 (41)
Race, *n* (%)		
White	59 (60)	57 (57)
African American	13 (13)	12 (12)
Asian American	4 (4)	1 (1)
Other	21 (22)	29 (29)
Hispanic	6 (6)	12 (12)
Multiplicity, *n* (%)		
Singleton	85 (88)	93 (94)
Twin	12 (12)	6 (6)
Very low birth wt (<33 wk, <1500 g)	82 (92)[a]	84 (90)[a]
Respiratory support (36 wk), *n* (%)		
Ventilator	6 (6)	3 (3)
CPAP or high-flow O_2	48 (49)	52 (53)
Low-flow nasal cannula	32 (33)	36 (36)
Room air	5 (5)	2 (2)
Unknown	6 (6)	6 (6)
Diuretics, *n* (%)		
Yes	38 (39)	41 (41)
No	51 (53)	52 (53)
Unknown	8 (8)	6 (6)

TABLE 1 Baseline Demographic and Clinical Characteristics of the Randomly Assigned Sample for the RHO Trial

	Intervention (N = 97)	Standard Care (N = 99)
Initial O_2 requirement, *n* (%)		
≤125 mL/min	61 (65)[b]	54 (56)[b]
250 mL/min	16 (17)	30 (31)
≥500 mL/min	16 (17)	11 (11)
Nocturnal	1 (1)	1 (1)
Birth wt, mean ± SD, g (*n*)	929 ± 443 (89)	938 ± 439 (93)
GA, mean ± SD, wk, (*n*)	26.9 ± 2.7 (97)	26.8 ± 2.5 (98)
Length of stay in neonatal intensive care, mean ± SD, d, (*n*)	104 ± 37 (88)	98 ± 33 (94)
CGA at discharge, mean ± SD, wk, (*n*)	42.0 ± 4.8 (92)	40.9 ± 3.2 (95)
NICU days on ventilator, mean ± SD, (*n*)	25 ± 22 (83)	24 ± 25 (83)
NICU days on CPAP or high-flow O_2, mean ± SD, (*n*)	39 ± 21 (71)	39 ± 22 (76)
NICU days on low-flow nasal cannula, mean ± SD, (*n*)	28 ± 24 (61)	24 ± 18 (68)

Duración de O2 domiciliario

TABLE 2 Duration of HOT, as Influenced by Study Group and Initial Oxygen Requirement

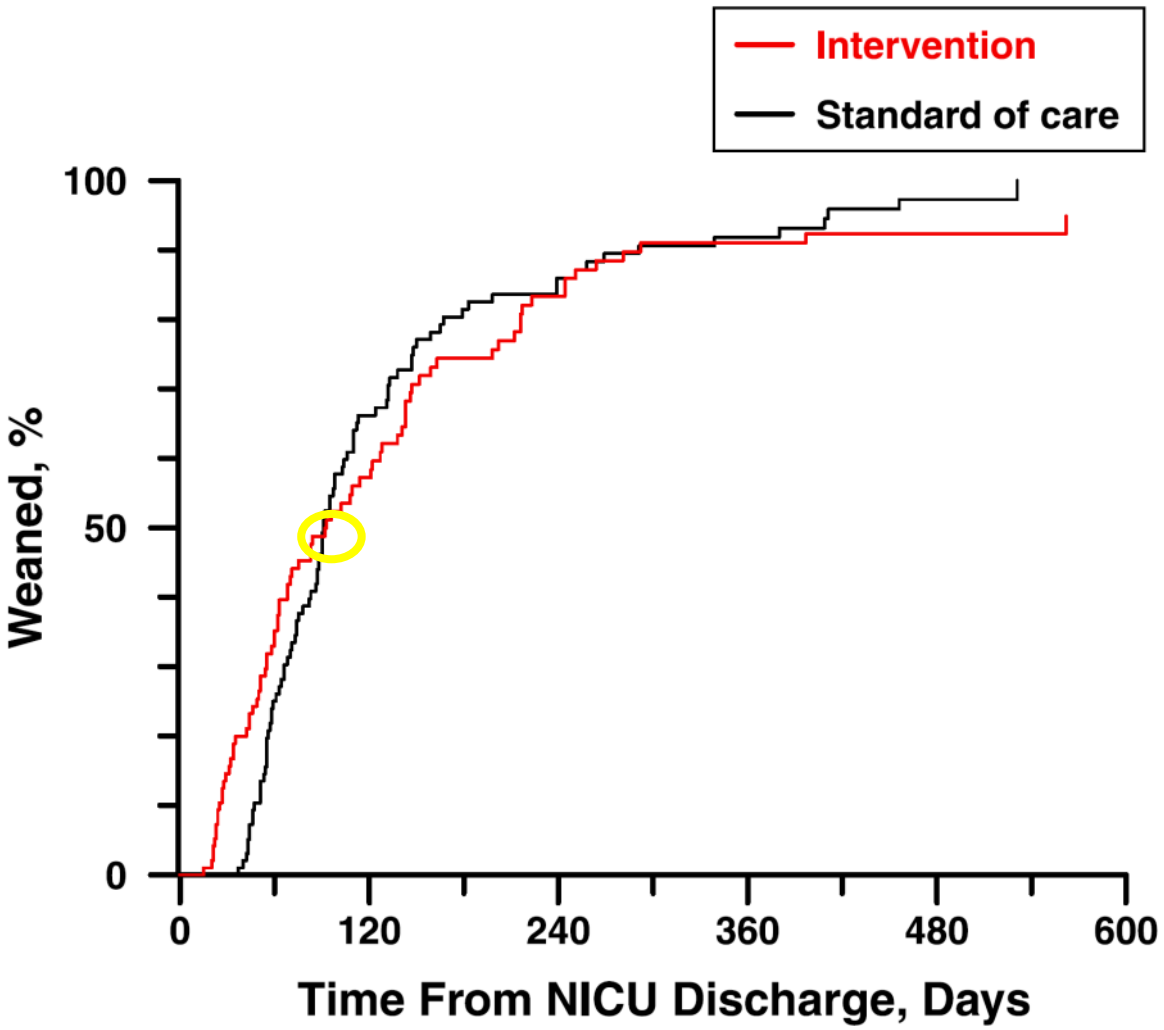
Influence	Duration, Adjusted Mean ± SE, d[a]	*P*[b]
Study group		
Intervention	78.1 ± 6.4	.03
Standard care	100.1 ± 8.0	—
Initial O_2		
≤125 mL/min	73 ± 5	<.0001
250 mL/min	98 ± 11	—
≥500 mL/min	149 ± 21	—
Nocturnal	80 ± 46	—

—, not applicable.

[a] Retransformed from log scale.

[b] Testing for equal means or for 0 rate of change.

- 87% (172/196) logró suspender O2.
- Disminución 22% del tiempo de uso O2 domiciliario con RHO.
- Ajuste por soporte ventilatorio NICU (VMI, CPAP, HFNC) disminución 11-18% de O2 domiciliario con RHO (p<0.4).
- Menor duración de HOT con menor O2 inicial.



Unweaned:											
Intervention	97	59	35	20	13	7	7	6	6	6	2
Standard care	99	71	32	17	12	8	7	3	2	0	0

FIGURE 2
Kaplan-Meier time-to-event curves: onset of weaning.

Score calidad de vida de los padres

TABLE 3 Parents' Quality-of-Life Scores (PedsQL) During and After Weaning

	Preweaning		3-mo After Weaning		Change	
	n	Mean ± SE	*n*	Mean ± SE	Estimate (95% CI)	*P*[a]
Intervention	80	72.6 ± 1.9	56	77.4 ± 2.1	4.8 (2.2 to 7.4)	.0004
Standard care	90	72.3 ± 1.8	52	76.5 ± 2.1	4.2 (1.6 to 6.8)	.002
Difference (*P*)	—	0.3 ± 2.6 (.91)	—	0.9 ± 2.9 (.77)	0.6 (−3.1 to 4.3)	.75

—, not applicable.

[a] *P* tests for significant differences between groups or significant change over time.

Antropometría

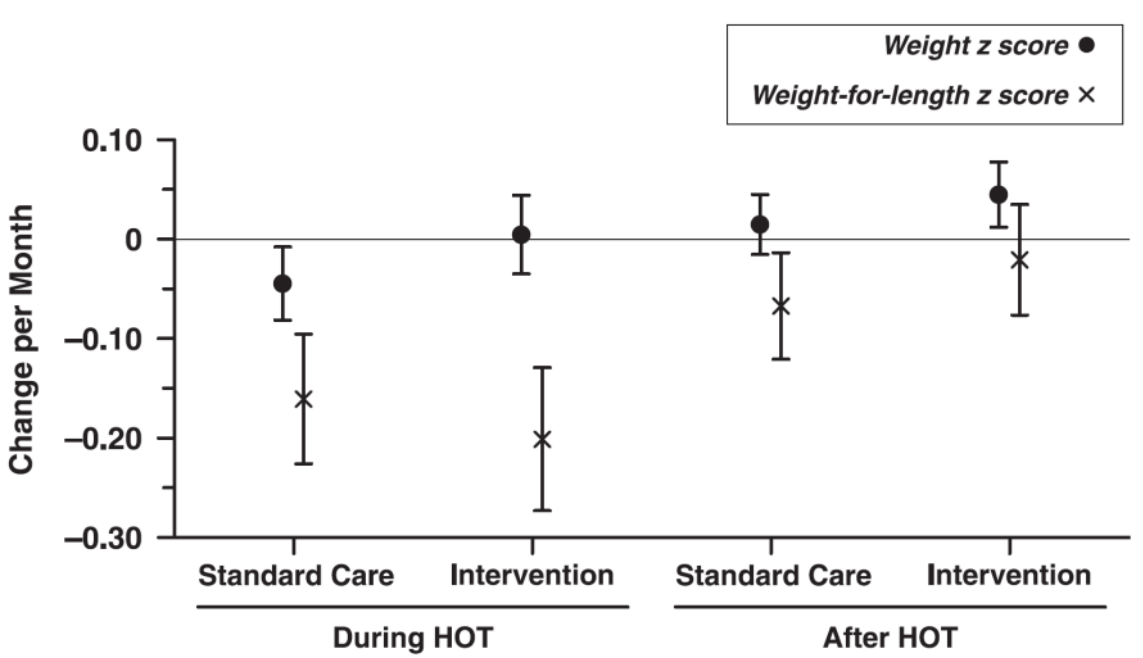


FIGURE 3
Weight and weight-for-length growth before and after weaning.

Eventos Adversos

TABLE 4 AEs and Serious AEs From NICU Discharge to 6 Months After Oxygen Discontinuation

Event Type	Intervention (N = 97), n (%)	Standard Care (N = 99), n (%)	P[a]
All events	25 (26)	42 (42)	<.0001
Serious AEs	19 (20)	30 (30)	.0005
Life-threatening, intensive care admission, or intubation (grade 4)	6 (6)	8 (8)	.002
Hospitalization[b]	19 (20)	32 (32)	.0002
Intervention without hospitalization drug or nondrug therapy[c]	25 (26)	40 (40)	.0001
Emergency department visits	17 (18)	19 (19)	.02
October through April (respiratory virus season)	17 (18)	31 (31)	<.0001
May through September	15 (15)	26 (26)	.0002
Respiratory-related events	20 (21)	27 (27)	.003
Nonrespiratory-related events	14 (14)	26 (26)	.0001

[a] Small P value from Farrington-Manning noninferiority test indicates intervention group did not incur a significantly worse AE rate than the standard-care group by the prespecified margin of 10%.

[b] Hospitalization (grade 3+) includes grade 4 events.

[c] Intervention without hospitalization drug or nondrug therapy (grade 2+) includes grade 3.

Conclusiones

- El registro de oximetría (RHO) acorta la duración del uso de O2 domiciliario (“dosis dependiente”).
- RHO permitiría identificación temprana de pacientes preparados para retiro de O2.
- RHO no disminuyó estrés parental, se asoció a menos efectos adversos comparado con cuidado estándar y el retiro precoz de O2 no empeoró outcomes nutricionales.
- Duración O2 domiciliario promedio: 3 meses con cuidado estándar y 2.5 meses con RHO (recordar que se excluyen HP y malacias).
- Con el uso de protocolos de manejo seguro y eficiente de pacientes con O2 domiciliario, se podrían realizar altas y destetes de O2 más precoces.

INDISA
CLINICA DE FAMILIA

INDISA - NEORED

Neo Red

Variation in Car Seat Tolerance Screen Performance in Newborn Nurseries

- Recomendación AAP: < 37s, 90-120 min (o duración de viaje).
- Gran variabilidad criterios de falla, momento del test y seguimiento.
  - Encuestas NICUs: falla SpO2 <80 a <93%, bradicardia <70 a <120.
- Poca información sobre test en PT tardíos de alta desde nurseries.
- **Objetivo:** evaluar protocolos y variación prácticas en test de silla.
  - Better Outcomes through Research for Newborns (BORN) network
  - Encuesta Febrero-Junio 2019, 106 nurseries.

INDISA - NEORED

Pediatrics. August 2020, 146 (2) e20193593

Resultados

- 79.2% de respuesta (35 estados)
- 3100 (2200-4500) partos al año
- 90.5% realiza test de silla pre alta
- Criterios de inclusión:
  - 98.7% realiza test a todos los < 37s
  - 81.6% incluye criterio de peso, la mayoría < 2.5 K (82.3%)
  - 7.6% no tiene criterios adicionales, pero la mayoría incluye otros diagnósticos y comorbilidades.

INDISA
CLINICA DE FAMILIA

Neo Red

Resultados

TABLE 1 CSTS Inclusion Criteria and Performance Characteristics

	n (%)
Additional inclusion criteria	
BW used	
<2.5 kg	51 (67.1)
<5 lb	6 (7.9)
<2 kg	5 (6.6)
Not used	14 (18.4)
Other criteria	
Hypotonia and/or neuromuscular disorder	42 (55.3)
Supplemental oxygen requirement	26 (34.2)
CHD	17 (22.4)
Trisomy 21	8 (10.5)
Cleft palate or micrognathia	7 (9.2)
Physician discretion	7 (9.2)
History of NICU admission for respiratory issues	4 (5.3)
Airway anomalies	3 (3.9)
History of apnea, bradycardia, and/or desaturation events	2 (2.6)
Small for GA or in utero growth restriction	2 (2.6)
Discharged with apnea monitor	2 (2.6)
Orthopedic issues (poor fit risk)	2 (2.6)
Neurologic abnormalities	1 (1.3)
Hydrocephalus	1 (1.3)
Maternal opiate exposure	1 (1.3)

Resultados

TABLE 1 CSTS Inclusion Criteria and Performance Characteristics

	n (%)
CSTS performance	
Location	
Central location in NBN	62 (81.5)
Patient's room	6 (7.9)
NICU	5 (6.6)
Either patient's room or NBN	3 (3.9)
When performed	
Day shift	2 (2.6)
Night shift	3 (3.9)
When convenient for staff	71 (93.4)
Staff performing CSTS	
Nurse	76 (100)
Medical assistant	8 (9.5)
Child passenger safety tech	5 (6)
Physical and/or occupational therapist	1 (2.1)
Respiratory therapist	1 (2.1)
CPST available to assist	
Yes	24 (31.6)
No	50 (65.8)
Unsure	2 (2.6)
Who places infant into car seat?	
Trained staff	64 (84.2)
Parent or guardian	6 (7.9)
Either staff or parent or guardian	6 (7.9)

Resultados

TABLE 1 CSTS Inclusion Criteria and Performance Characteristics

	n (%)
CSTS duration	
Minimum duration	
<60 min	2 (2.6)
60–89 min	9 (11.8)
90–120 min	63 (82.9)
Duration of car ride home	2 (2.6)
Maximum duration (*n* = 48)	
30 min	1 (2.1)
60 min	2 (4.2)
90 min	21 (43.8)
2 h	15 (31.3)
2–3 h	1 (2.1)
2.5 h	1 (2.1)
3 h	4 (8.3)
Case-by-case basis	1 (2.1)
Physician discretion	1 (2.1)
Half the time to home	1 (2.1)

Resultados

TABLE 2 CSTS Failure Criteria

	n = 74, *n* (%)
$Sp0_2$ failure criteria	
<93%	4 (5.4)
<92%	2 (2.7)
<91%	1 (1.4)
<90%	45 (60.8)
<89%	1 (1.4)
<88%	8 (10.8)
<85%	10 (13.5)
Varies by birth GA	2 (2.7)
Not specified in policy	1 (1.4)
Desaturation duration	
Any drop below threshold	12 (16.2)
>5 s	2 (2.7)
>10 s	14 (18.9)
>15 s	6 (8.1)
>20 s	28 (37.8)
>30 s	6 (8.1)
>60 s	1 (1.4)
Not specified	5 (6.8)
Bradycardia failure criteria	
<100 bpm	6 (8.1)
<90 bpm	11 (14.9)
<80 bpm	48 (64.9)
<60 bpm	1 (1.3)
Not specified in policy	8 (10.8)
Bradycardia duration	
Any drop below threshold	20 (27)
>5 s	3 (4.1)
>10 s	22 (29.7)
>15 s	5 (6.8)
>20 s	14 (18.9)
>30 s	1 (1.4)
>60 s	1 (1.4)
Not specified	8 (10.8)
Apnea definition	
>20 s	62 (83.8)
>15 s	1 (1.3)
>10 s	2 (2.7)
Not specified	9 (12.2)
Additional failure definitions	
Respiratory distress	25 (33.8)
Tachypnea	9 (12.2)
Cyanosis or color change	4 (5.4)

Resultados

TABLE 3 Follow-up of a Failed CSTS and Use of Car Beds

	n (%)
Follow-up of failed CSTS (*n* = 74)	
Duration between repeat CSTS?	
Not specified	3 (4.1)
Can repeat immediately	6 (8.1)
Minimum 6 h	14 (18.9)
Minimum 12 h	21 (28.4)
Minimum 24 h	1 (1.4)
Minimum 72 h	2 (2.7)
Minimum 7 d	22 (29.7)
Varies on the basis of how quickly infant failed CSTS	3 (4.1)
NICU team decides	2 (2.7)
How many repeat CSTSs before alternative discharge plans (NICU, car bed, etc)?	
Do not repeat CSTS	4 (5.4)
After 2 failed CSTSs	52 (70.3)
After ≥3 failed CSTSs	10 (13.5)
Unlimited (repeat until pass)	8 (10.8)
Consideration of a sleep study for failed CSTS?	
Never	68 (91.8)
After 2 failed CSTS	3 (4.1)
After ≥3 failed CSTS	3 (4.1)
Use of car beds at discharge	
Policy for use of car beds after failed CSTS (*n* = 74)	
Never discharge in car bed	15 (20.3)
Routinely used after 1 failed CSTS	1 (1.4)
Routinely used after ≥2 failed CSTSs	21 (28.4)
Occasionally use after repeated failed CSTSs	37 (50)

Resultados

TABLE 4 Provider Attitudes Regarding CSTS in NBN Patients

	Perform Routine CSTS (n = 74)	Do Not Perform Routine CSTS (n = 8)	P
Is the CSTS a good way to assess cardiorespiratory readiness for discharge in at-risk infants? n (%)			.0001
Yes	29 (39.2)	0	
No	19 (25.7)	8 (100)	
Unsure	26 (45.1)	0	
Under what birth GA should neonates be screened with CSTS before discharge? n (%)			<.0001
N/A (should not be considered)	8 (10.8)	5 (62.5)	
<37 wk	47 (63.5)	0	
<36 wk	8 (10.8)	0	
<35 wk	7 (9.5)	1 (12.5)	
<34 wk	3 (4)	1 (12.5)	
<33 wk	0	0	
<32 wk	0	1 (12.5)	
All neonates should be tested	1 (1.4)	0	
Under what BW should neonates be screened with CSTS before discharge? n (%)			.0089
N/A (should not be considered)	13 (17.6)	5 (62.5)	
<2500 g	39 (52.7)	0	
<2000 g	14 (18.9)	2 (25)	
<1500 g	2 (2.7)	1 (12.5)	
<5 lb	1 (1.4)	0	
Unsure	5 (6.8)	0	

Conclusiones

- Mayoría de las NBNs realizan test de silla pre alta, siguiendo recomendaciones de la AAP.
- Gran variabilidad en criterios de falla (SpO2 85-93% y FC), mayoría lo repite con variabilidad en el timing.
- NICUs 96.5% realiza test de silla en 2020.
- NBNs 90.% realiza test de silla en 2019 vs 22% en 2003.
- Importancia por el aumento de pretérminos tardíos que no ingresan a Neo y requieren cuidados en sala cuna.

Changes in the Preterm Heart From Birth to Young Adulthood: A Meta-analysis

- **Objetivo:** evaluar efecto de prematurez sobre remodelamiento miocárdico desde nacimiento hasta adultez.
- 32 estudios observacionales (preterm=1471; term=1665).
- **Resultados:**
  - Menores tamaños ventriculares desde nacimiento hasta adulto.
  - Menor función diastólica VI y sistólica VD en todas las edades.
  - Mayor velocidad de hipertrofia VI desde infancia hasta adultez.
  - Fenotipo miocárdico morfológico y funcional del PT hasta vida adulta.

- Miocardio sería más vulnerable a injuria, menor respuesta a estrés, y riesgo de insuficiencia cardíaca e isquemia.
- Prematurez como factor de riesgo cardiovascular y problema de salud pública por aumento de sobrevida.

INDISA - NEORED

Pediatrics August 2020, 146 (2) e20200146.

Cochrane Neonatal Reviews

Julio 2020

INDISA
CLINICA DE FAMILIA

INDISA - NEORED

Neo Red

Early fortification (EF) of human milk versus late fortification (LF) to promote growth in preterm infants

- RCT, EF < 100 mL/kg/d enteral feed volume or < 7 days ***VS*** LF ≥ 100 mL/kg/d feeds or ≥ 7 days.
  - 2 trials (237 infants), < 1500 g. EF: 20 mL/kg/d and 40 mL/kg/d. LF 100 mL/kg/d.

- **Meta-analysis**

1. EF growth outcomes: mean time to regain BW (MD -0.06 days, -1.32 to 1.20), linear growth (MD 0.10 cm/week, 95% -0.03 to 0.22), head growth (MD -0.01 cm/week, -0.07 to 0.06 cm/week)
2. EF risk of NEC: MD -0.01 (-0.07 to 0.06).

- **Conclusions**

- Evidence is insufficient to support or refute early fortification of human milk in preterm infants.
- Further large trials would be needed.

INDISA
CLINICA DE FAMILIA

DOI: 10.1002/14651858.CD013392.pub2.

Neo Red

Higher versus lower protein intake in formula-fed low birth weight infants preterm infants

- RCT formula protein intake: LOW (< 3 g/k) vs HIGH (3-4 g/k) VS VERY HIGH (≥ 4 g/k).
  - Formula-fed hospitalized neonates < 2.5 k, excluded if PN or formula as supplement to HM.
  - 6 trials, 218 infants. 5 compared low VS high. 3 were small, all had methodological limitations.

- **Meta-analysis**

1. Improved weight gain (2.36 g/k/d, 1.31 -3.40) and NU accretion with HIGH vs LOW.
2. Uncertain effect on head growth (0.37 cm/w, 0.16 - 0.58; n = 18) and length gain (0.16 cm/w, -0.02 to 0.34; n = 48).
3. Moderate evidence shows no differences in weight or length gain to discharge, term, and 12 weeks from VERY HIGH. 3/24 infants receiving VH protein intake developed uremia.
4. No significant differences: NEC, sepsis or diarrhea.

- **Conclusions**

- Protein intake ≥ 3.0 g/kg but < 4.0 g/kg from formula accelerates weight gain.
- Limited information is available regarding the impact of higher formula protein intake on long-term outcomes such as neurodevelopment.
-

INDISA
CLINICA DE FAMILIA

DOI: 10.1002/14651858.CD003959.pub4

Neo Red

Head midline position for preventing the occurrence or extension of IVH in preterm infants

- 3 RCTs, 290 infants (< 30 weeks or < 1000 g)
  - 2 trials: midline head position VS head rotated 90° with the cot flat.
  - 1 trial: midline head position VS head rotated 90° + bed tilted at 30°.

- **Meta-analysis**

1. No effect on IVH (RR 1.11, 0.78-1.56; I^2 = 0%) and severe IVH (RR 0.71, 0.37-1.33; I^2 = 0%).

2. Neonatal mortality (RR 0.49, 0.25-0.93; I^2 = 0%; RD −0.09, −0.16 a −0.01)

3. Mortality until hospital discharge (RR 0.50, 0.28 -0.90; I^2 = 0%; RD −0.10, −0.18 a −0.02).

- **Conclusions**

- Certainty of the evidence was very low for all outcomes.

- Mortality might be reduced, certainty of the evidence is very low and it is unclear whether any effect is due to co-interventions (bed tilt).

INDISA
CLINICA DE FAMILIA

INDISA - NEORED
Un Nuevo Concepto en Medicina Perinatal

DOI: 10.1002/14651858.CD013392.pub2.

Neo Red

Use of reflective materials during phototherapy for newborn infants with unconjugated hyperbilirubinaemia

- Term or PT, phototherapy with curtains of reflective materials (plastic, linen or aluminium) VS phototherapy without curtains or other intensified photo.
  - 11 studies (10 reflective materials VS none, 1 reflective curtains and a single bank of lights VS double bank).
- **Meta-analysis**

- 3 studies (n=281) decline in SB at 4-8 h (-0.85, -1.15 to -0.55; I^2 = 57%; moderate-certainty evidence.

- 9 (n=893) decline in SB at 24 h and faster decline, (I^2 = 97%) was too high.

- Exchange transfusion reported by 2 studies, none in either group.

- 4 studies (n=466) reduction in mean duration of PT, (I^2 = 88%) was too high.

- 2 studies showed reduction in mean duration of hospital stay in hours (-41.08, -45.92 to -36.25; I^2 = 0; moderate-certainty evidence.

- **Conclusions**

- Moderate evidence reflective curtains may result in greater decline in SB.

- Very low evidence duration of phototherapy is reduced, and moderate evidence duration of hospital stay is reduced.

DOI: 10.1002/14651858.CD013392.pub2.