

***INCIDENCE AND RISK FACTORS OF
LATE-ONSET HYPOGLYCEMIA
IN EXTREMELY PRETERM INFANTS***

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Background

- Preterm, low birth weight → risk of early hypoglycemia
- In our unit recurrently hypoglycemia in preterm on full enteral nutrition
- Retrospective cohort study¹: < 32 weeks and < 1500g (n = 98)
 - 44% < 1000g, 23% 1000-1499g
- Prospective cohort study²: continuous subcutaneous sensor for 72 h at 32-33 weeks in preterm < 1500g (n = 41)
 - 41% < 1500g

1. Staffler A et al. Very low birth weight preterm infants are at risk for hypoglycemia once on total enteral nutrition. J Matern Fetal Neonatal Med 2013
2. Mola-Schenzle E et al. Clinically stable very low birthweight infants are at risk for recurrent tissue glucose fluctuations even after fully established enteral nutrition. Arch Dis Child Fetal Neonatal Ed 2015

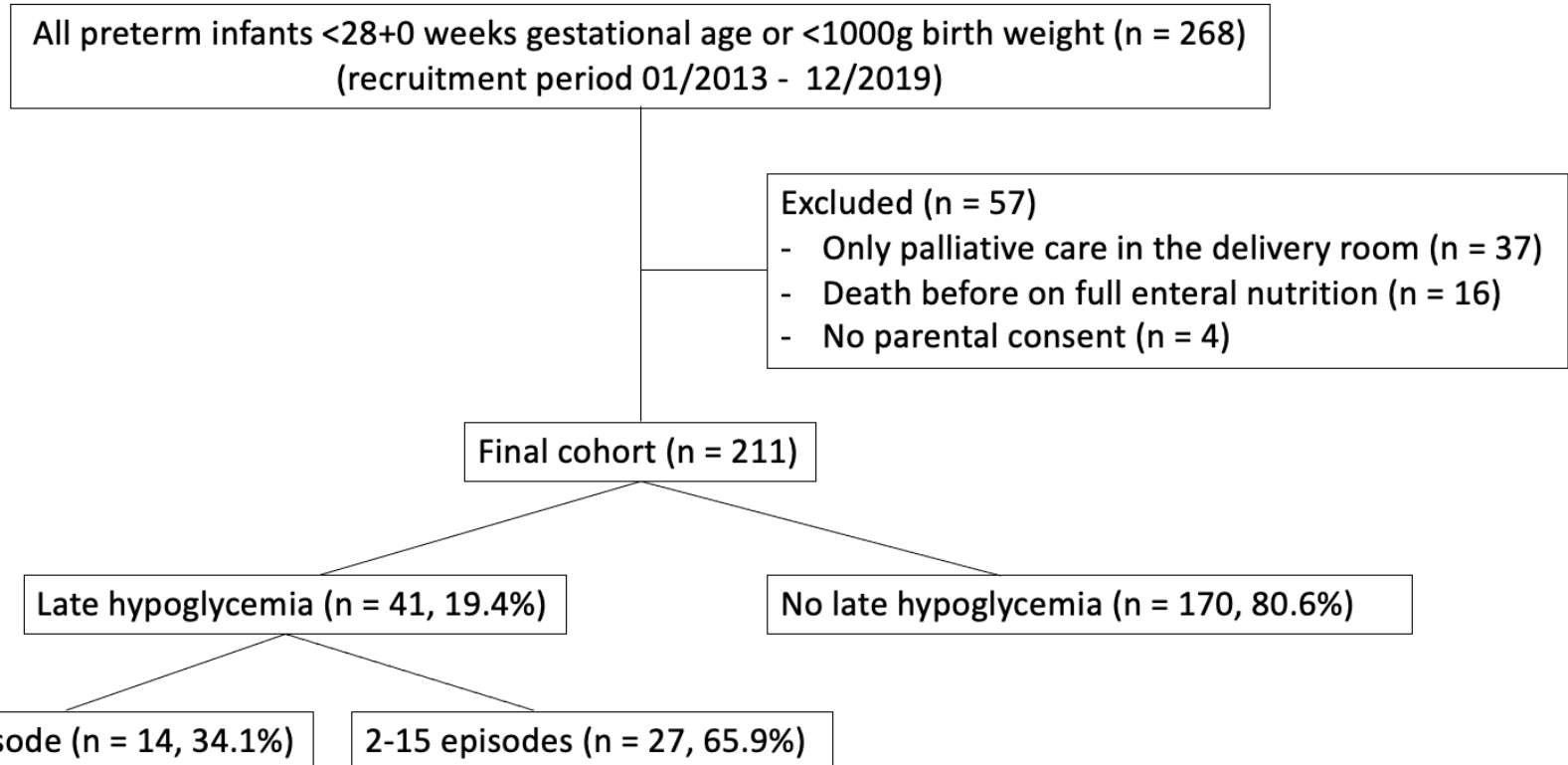
Objectives

Determine incidence and identify risk factors
of late hypoglycemia
in extremely preterm / extremely low birth weight infants

Methods

- Retrospective single center cohort study
- Inclusion:
 - Gestational age < 28 weeks and/or birth weight < 1000 g
 - Observation period 01/2013 - 12/2019 (7 years)
- Exclusion:
 - death before reaching full enteral feeds
 - no parental consent
- Definition of late hypoglycemia:
 - Any blood glucose level < 2.6 mmol/L from 8 DOL
 - Full enteral nutrition
- Matched control group by gestational age (\pm 2 days) and sex

Results



	Late hypoglycemia (n=41)
Age, weeks (SD, range)	7.0 (3.2, 1.3-13.7)
Post-menstrual age, weeks (SD, range)	33.3 (2.8, 26.9-38.6)
Body weight, g (SD, range)	1450 (440, 440-2510)

Results

Demographic and clinical characteristics of study participants at birth

	All (n = 211)	No late hypoglycemia (n = 170)	Late hypoglycemia (n = 41)
Male sex, n (%)	112 (53)	84 (49) [†]	28 (68) [†]
Gestational age, weeks, median (IQR)	27.0 (2.7)	27.1 (2.3) [§]	26.0 (2.9) [§]
Birth weight, g, mean (SD)	810 (270)	855 (240) [*]	650 (220) [*]
Birth weight z-score, mean (SD)	-0.75 (1.22)	-0.66 (1.09) [*]	-1.1 (1.25) [*]
Prenatal steroids, n (%)			
incomplete	27 (13)	21 (12)	6 (15)
complete	176 (83)	142 (84)	34 (83)
Chorioamnionitis, n (%)	90 (44)	74 (45)	16 (41)
Cesarean section, n (%)	195 (92)	156 (92)	39 (95)
Gestational diabetes mellitus, n (%)	15 (7)	14 (8)	1 (2)
Preeclampsia, n (%)	38 (18)	30 (18)	8 (20)
Maternal arterial hypertension, n (%)	10 (5)	4 (2) [§]	6 (15) [§]
Maternal body mass index, kg/m ² , mean (SD)	27 (7)	27 (7)	27 (8)

* $P < 0.001$; § $P < 0.01$; † $P < 0.05$

Results

Clinical characteristics of infants after preterm birth

	All (n = 211)	No late hypoglycemia (n = 170)	Late hypoglycemia (n = 41)
Early hypoglycemia, n (%) (> 10 mmol/L in the first week)	83 (39)	60 (35)*	23 (56)*
Early hyperglycemia, n (%) (< 2.6 mmol/L in the first week)	96 (46)	68 (40)**	28 (68)**
Parenteral nutrition, days, median (IQR)	9 (6)	9 (5)	9 (5)
Patent ductus arteriosus, n (%)	44 (21)	35 (21)	9 (22)
Bronchopulmonary dysplasia at 36 weeks, n (%)	28 (13)	17 (10)**	11 (27)**
Retinopathy of prematurity, n (%)	34 (16)	25 (15)	9 (22)
Necrotizing enterocolitis, n (%)	2 (1)	0 (0)	2 (5)
Sepsis, n (%)	95 (45)	70 (41)*	25 (61)*
Intraventricular hemorrhage, n (%)	47 (22)	10 (24)	9 (22)
Posthemorrhagic hydrocephalus, n (%)	8 (4)	8 (5)	0 (0)

* $P < 0.05$, ** $P < 0.01$

Results

Multivariable logistic regression analysis:

- Gestational age
- Birth weight z-score
- Maternal arterial hypertension

Results

No significant differences of infants with late hypoglycemia and matched controls in:

- Enteral intake (fluid, protein, carbohydrates, fat, energy)
- Milk type (>95% human milk)
- Concentration of milk fortifier
- Feeding interval
- Daily weight gain

Discussion

Incidence higher than expected and likely to be underestimated

Causes:

- Lower glycogen reserve? Impaired gluconeogenesis?
- Increased need for catch-up growth?
- Higher energy demand (BPD)?
- Impaired responsiveness of β -cells to glucose¹?

Clinical relevance unknown (long-term neurodevelopment?)

1. Boehmer, B. H. et al. (2017). The impact of IUGR on pancreatic islet development and β -cell function, *J Endocrinol*, 235(2), R63-R76

Conclusions

Risk factors for late hypoglycemia in extremely preterm

- low gestational age
- growth retardation
- maternal arterial hypertension

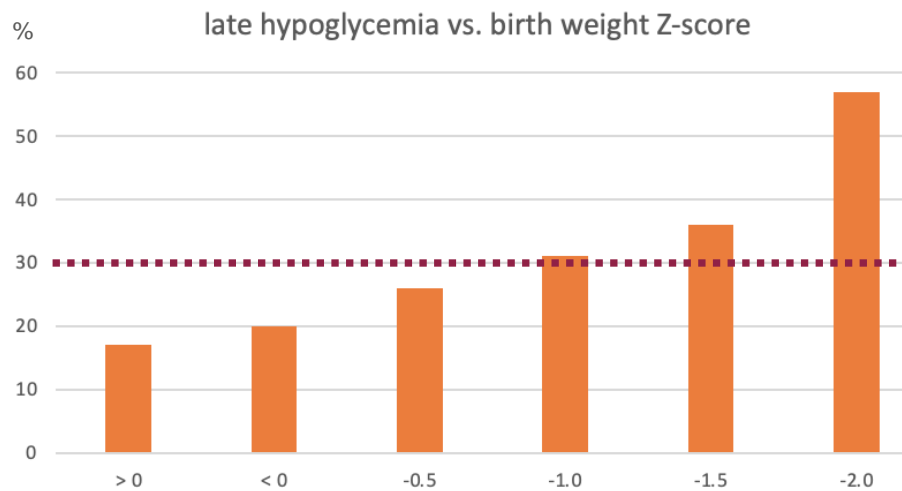
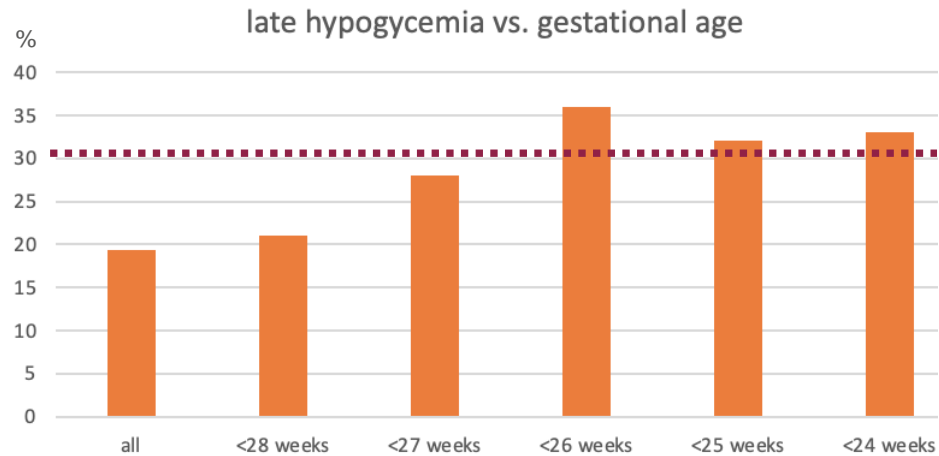
Regular blood glucose measurements are necessary
in infants at risk even if clinically stable and on full
enteral nutrition

Questions?



Thank you
for your attention

Results



Results

Nutritional characteristics and weight gain of infants with late hypoglycemia and matched controls (at first hypoglycemia, n=41)

	Late hypoglycemia (n = 41)	No late hypoglycemia (n = 41)
Total fluid intake, mL/kg/d, mean (SD)	147.7 (14.2)	149.1 (12.3)
Caloric intake, kcal/kg/d, mean (SD)	124.1 (14.2)	124.2 (9.8)
Protein intake, g/kg/d, mean (SD)	4.6 (0.8)	4.5 (0.8)
Carbohydrate intake, g/kg/d, mean (SD)	15.0 (1.9)	15.2 (1.3)
Fat intake, g/kg/d, mean (SD)	5.3 (0.6)	5.3 (0.5)
Feeding interval, h, mean (SD)	2.6 (0.5)	2.8 (0.7)
Human breast milk, n (%)	40 (98)	39 (95)
Human breast milk & formula milk, n (%)	1 (2)	2 (5)
Milk fortification, n (%)	39 (95.1)	39 (95)
Concentration of milk fortifier, % (SD)	4.8 (1.6)	5.0 (1.4)
Protein supplement, n (%)	30 (73.2)**	21 (51)**
Carbohydrate supplement, n (%)	1 (2.4)	0 (0)
Fat supplement, n (%)	7 (17.1)	2 (4.9)
Change in feeding regimen*, n (%)	23 (56)	17 (42)
Daily weight gain per kg*, g/kg/d, mean (SD)	17 (7)	18 (6)

*in antecedent 7 days. **P = 0.040

Results

Nutritional intake of infants with late hypoglycemia and matched controls (all episodes, n=157)

	No late hypoglycemia (n =157)	Late hypoglycemia (n=157)	P value
Total fluid intake, mL/kg/d, mean (SD)	148.1 (15.0)	153.1 (15.2)	0.0002
Caloric intake, kCal/kg/d, mean (SD)	122.2 (14.1)	132.6 (15.3)	<0.0001
Protein intake, g/kg/d, mean (SD)	4.3 (0.9)	4.7 (0.8)	0.001
Carbohydrate intake, g/kg/d, mean (SD)	14.6 (1.8)	16.6 (2.5)	<0.0001
Fat intake, g/kg/d, mean (SD)	5.4 (0.8)	5.6 (0.7)	0.0003
Feeding interval, h (SD)	3.2 (0.8)	2.6 (0.5)	<0.0001
Human milk, n (%)	137 (87)	147 (94)	0.055
Preterm formula milk, n (%)	26 (13)	10 (6)	0.055
Milk fortification, n (%)	133 (85)	145 (92)	0.034
Concentration of milk fortifier (%)	4.3 (2.0)	4.7 (1.8)	0.0199
Protein supplement, n (%)	86 (55)	85 (54)	0.910
Carbohydrate supplement, n (%)	0 (0)	59 (38)	<0.0001
Fat supplement, n (%)	11 (7)	30 (19)	0.001