



Week 4: Neonatology

Neonatal General

Thursday, July 23 2:30-4:00 pm EDT

Moderators

Rosemarie Tan
Shanthy Sridhar

EDT	Abstract	Title	Presenting Author
2:30 pm		Introduction & General Information	
2:35 pm	3378379	Association of Prophylactic Indomethacin and Antenatal Steroids with Spontaneous Intestinal Perforation.	Hemasree Kandraju
2:45 pm	3382338	Effect of Indomethacin Prophylaxis on Cerebral and Abdominal Tissue Oxygenation by Near-Infrared Spectroscopy in Preterm Neonates	Vivek Shukla
2:55 pm	3381413	Neonatal Determinants of the Fecal Mycobiome in Exclusively Breastfeeding Mother-Infant Dyads	Emily Skalla
3:05 pm	3380965	Individualized target fortification (TFO) of breast milk: Variation of macronutrient intake with different fortifiers and alternative approaches	Niels Rochow
3:15 pm	3378109	OroPharyngeal Therapy with Mother's Own Milk (OPT-MOM) Improves Feeding and Reduces Length of Stay in Premature Infants	Nancy Garofalo
3:25 pm	3374756	The anti-inflammatory properties of microRNA-125 limit the vasoobliteration in a rat model of oxygen-induced retinopathy	Maëlle Wirth
3:35 pm	3373468	Combined topical ocular ketorolac and oral omega-3 polyunsaturated fatty acids, Coenzme q10 or glutathione nanoparticles for oxidative stress in a rat model of intermittent hypoxia-induced retinopathy	Faisal Siddiqui
3:45 pm	3376385	Pulmonary Function Changes Before and After CDH Surgery in the Era of Gentle Ventilation	Brian Scottoline
3:55 pm		Wrap Up	

Note: Schedule subject to change based on presenter availability.

CONTROL ID: 3378379

TITLE: Association of Prophylactic Indomethacin and Antenatal Steroids with Spontaneous Intestinal Perforation.

PRESENTER: Hemasree Kandraju

AUTHORS (LAST NAME, FIRST NAME): Kandraju, Hemasree⁶; Kanungo, Jaideep¹; Lee, Kyong-Soon²; Daspal, Sibasis³; Nwaesei, Chuks⁴; Dorling, Jon⁵; Ye, Xiang Y.⁶; Lee, Shoo⁶; Shah, Prakesh⁶

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CURRENT CATEGORY: Neonatology

CURRENT SUBCATEGORY: Neonatal General

KEYWORDS: Antenatal steroids, intestinal perforation, preterm.

SESSION TITLE: Neonatal General | Neonatal General

SESSION TYPE: Webinar|Platform

ABSTRACT BODY:

Background: Indomethacin and steroids can both be associated with gastrointestinal adverse events. We hypothesized that the combination of antenatal steroids (ANS) and postnatal prophylactic indomethacin (PI) may be associated with spontaneous intestinal perforation (SIP).

Objective: To evaluate the association of the timing of exposure to ANS in conjunction with PI with the outcome of SIP among neonates with birth weight <750 grams or GA < 26 weeks.

Design/Methods: We retrospectively studied eligible infants admitted to NICUs participating in the Canadian Neonatal Network (CNN) during years 2010 to 2018. The timing of ANS was divided in 3 groups: (1) Partial ANS (**PS**), (2) Complete course of ANS ≤ 7 days prior to birth (**CS- $\leq 7d$**) or (3) complete course of ANS >7 days prior to delivery (**CS - >7d**). The exposure was defined as the timing of ANS with or without PI (6 Groups in total). PI was defined as indomethacin given within 24 hours of birth for prevention of IVH and not for the purpose of PDA treatment. The primary outcome was SIP defined as radiological finding of intestinal perforation, with absence of radiological features of intestinal ischemia such as fixed dilated bowel loops, pneumatosis intestinalis and/or intra-operative surgical report; and/or histopathological confirmation of perforation located in the ileum and on the antimesenteric border. Secondary outcomes were death within 14 days of birth and death within 14 days/SIP. The multivariable logistic regression models were used to compare the outcomes between the exposure groups adjusting for potential confounders.

Results: Among 6622 admitted infants, 4121 (62%) eligible infants who received partial or complete course of ANS were included in the analysis. Of these, PI was given in 917 (22.2%). Maternal and infants' characteristics are presented in [Table 1]. The raw incidences of SIP were lower in groups who did not receive PI compared to those who received PI in all 3 ANS groups. Adjusted OR, with CS- $\leq 7d$ and no PI group as the reference group (current standard of practice in most units), revealed that both PS and CS- $\leq 7d$ groups had higher odds of SIP if they also received PI. However, in the CS- $\leq 7d$ groups who received PI had lower odds of mortality [Table 3].

Conclusion(s): Antenatal steroid receipt closer to birth (partial or complete course of ANS ≤ 7 days prior to birth) followed by prophylactic indomethacin after birth was associated with SIP in extremely preterm neonates.

Table 1: Baseline characteristics

Characteristics	Partial steroid (PS)		Complete steroid within 7 days of birth (CS- <7d)		Complete steroid > 7 days before birth (CS- >7d)		P-value
	No PI	PI	No PI	PI	No PI	PI	
Maternal hypernatremia %	14.9 (n=57)	9.9 (n=32)	14.3 (n=129)	17.9 (n=154)	18.1 (n=164)	15.5 (n=178)	<0.01
Maternal diabetes %	4.1 (16)	6.5 (21)	7.5 (63)	6.3 (53)	8.8 (74)	10.2 (112)	0.21
Magnesium sulfate %	52.9 (203)	44.3 (142)	42.7 (353)	71.5 (577)	51.7 (434)	46.3 (483)	<0.01
Gestational age (weeks) mean (SD)	24.8 (1.51)	24.1 (1.4)	23.1 (1.33)	24.4 (1.49)	25.7 (1.71)	24.9 (1.49)	<0.01
Birth weight (kg) mean (SD)	2.5 (1.9)	2.6 (1.7)	2.9 (1.8)	4.1 (1.8)	3.1 (1.8)	2.9 (1.8)	<0.01
Male %	49.5	51.5	48.5	49.1	51.7	49.3	0.78
Apgar 7 at 5 min %	39.6	42	47.8	43.7	41.1	44.1	<0.01
Singleton %	70.9	74.6	78.9	74.9	70	67.5	<0.01
SGA %	19.2	9	24	22.9	29.8	15.3	<0.01
100% Cesarean %	46.2	45.6	36.9	40.8	39.9	45.5	<0.01
Inotropes within 3 days %	15.3	15.8	13	11.3	17.6	11.8	<0.01

Abbreviations: PI, prophylactic indomethacin; CS, complete steroid

Table 1: Baseline Characteristics

Table 2: Outcome rates according to groups

Outcomes	Partial steroid (PS)		Complete steroid within 7 days of birth (CS- <7d)		Complete steroid > 7 days before birth (CS- >7d)	
	No PI	PI	No PI	PI	No PI	PI
Number of infants	817	732	1723	515	664	170
SIP %	4.6	7.4	3.5	6.3	3	3.5
Mortality within 14 days of life %	20.7	16.4	10.6	8.4	7.5	7.7
SIP or Mortality within 14 days of life %	24.5	22.8	13.7	14.4	10.4	11.2

Abbreviations: PI, prophylactic indomethacin; CS, complete steroid

Table 2: Outcome rates according to groups

Table 3: Comparison of outcomes AOR (95% CI)

Outcomes	Partial steroid (PS)		Complete steroid within 7 days of birth (CS- <7d)		Complete steroid > 7 days before birth (CS- >7d)	
	No PI	PI	No PI	PI	No PI	PI
SIP	1.24 (0.86,2.07)	2.24 (1.24,4.02)	1	1.72 (1.08,2.75)	0.9 (0.53,1.53)	1.00 (0.42,2.36)
Mortality within 14 days	1.94 (1.51,2.51)	1.02 (0.66,1.56)	1	0.60 (0.41,0.87)	0.99 (0.7,1.41)	0.81 (0.44,1.40)
SIP or mortality within 14 days	1.88 (1.46,2.32)	1.35 (0.93,1.95)	1	0.86 (0.63,1.17)	0.95 (0.7,1.28)	0.86 (0.51,1.43)

Adjusted for potential confounders, including GA, maternal hypernatremia, MgSO4, Cesarean section, Apgar score <7 at 5 min, SGA, singleton and inotropes within 3 days of life

Abbreviations: PI, prophylactic indomethacin; CS, complete steroid

Table 3: Comparison of outcomes AOR (95% CI)

IMAGE CAPTION:

Table 1: Baseline Characteristics

Table 2: Outcome rates according to groups

Table 3: Comparison of outcomes AOR (95% CI)

CONTROL ID: 3382338

TITLE: Effect of Indomethacin Prophylaxis on Cerebral and Abdominal Tissue Oxygenation by Near-Infrared Spectroscopy in Preterm Neonates

PRESENTER: Vivek Vishwanath Shukla

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CURRENT CATEGORY: Neonatology

CURRENT SUBCATEGORY: Neonatal General

KEYWORDS: Near infrared spectroscopy, Outcomes, Indomethacin.

SESSION TITLE: Neonatal General |Neonatal General

SESSION TYPE: Webinar|Platform

ABSTRACT BODY:

Background: Early indomethacin prophylaxis (EIP) decreases severe intraventricular hemorrhage (IVH), hemodynamically significant patent ductus arteriosus (HS-PDA), and the need for PDA ligation in preterm neonates. The near-infrared spectroscopy (NIRS) is a non-invasive method for assessing cerebral (cNIRS) and abdominal tissue (aNIRS) oxygenation, metabolism, and perfusion. Cerebral and abdominal tissue oxygenation in preterm neonates following EIP may be associated with short-term neuro and gastrointestinal morbidities.

Objective: To determine the effect of a single dose of indomethacin given within the first 6 hours after birth (EIP) on cNIRS and aNIRS and the association of NIRS data with death and/or short-term neuro and gastrointestinal (GI) morbidities in preterm neonates.

Design/Methods: Cohort study (May 2018 to May 2019) of 100 consecutive very preterm neonates with gestational age between 25^{0/7}-29^{6/7} weeks receiving ≥40% FiO₂ on admission. Hourly cNIRS (birth-3 days), aNIRS (birth-7 days) values, short-term morbidities, and mortality were noted. Neonates were grouped by exposure to EIP.

Results: There were 66 neonates in the EIP group and 34 in the control group. cNIRS and aNIRS for the first three days were not different between groups (all p>0.05) but aNIRS values from day 4-7 were lower in the control group compared to the EIP group (all p≤0.01). EIP was associated with a decreased incidence of all IVH (p=0.01) and HS-PDA (p<0.01).

Conclusion(s): Early indomethacin prophylaxis in preterm neonates does not impact the cerebral and abdominal tissue oxygenation in the first three days after birth. However, early indomethacin prophylaxis is associated with higher abdominal tissue oxygenation between 4-7 days after birth. The role of aNIRS in early identification of HS-PDA could be further explored.

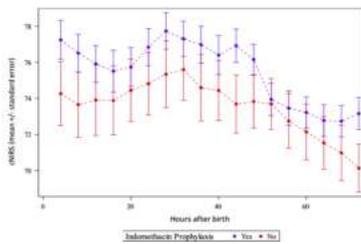


Figure 1: Trend of cNIRS values by group

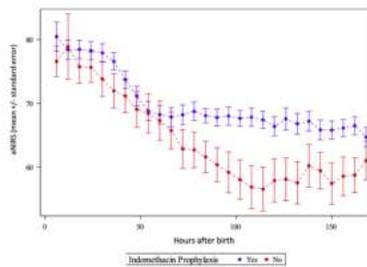


Figure 2: Trend of aNIRS values by group

Variables	Measures	Indomethacin (N=66)	Control (N=34)	Overall (N=100)
Gestational age	Weeks, Mean (SD)	26.75 (1.48)	27.01(1.40)	26.87 (1.46)
Sex	Male, N	33	15	50
	Female, N	33	19	50
Death	Yes, N	1	1	2(2)
	No, N	65	33	98
HS-PDA	Yes, N	6	11	17
	No, N	60	23	83
IVH	Grade I/2, N	37	22	59
	Grade 3/4, N	4	10	14
	Grade 3/4, N	5	2	7
PVL	Yes, N	3	1	4
	No, N	63	33	96
ROP	Stage 1/2, N	21	11	32
	Stage 3/4, N	8	5	13
Abnormal neuro exam at discharge or death	Yes, N	23	14	39
	No, N	43	20	63
Combined death and IVH grade 3/4, and/or intraventricular hemorrhage, and/or ROP stage 3/4, and/or abnormal neuro exam at discharge	Yes, N	12	17	29
	No, N	54	17	71
Neurologic sequelae	Yes, N	7	5	12
	No, N	59	29	88
Spontaneous intestinal perforation	Yes, N	0	1	1
	No, N	66	33	99
Combined death and/or NEC and/or SIP	Yes, N	7	6	13
	No, N	59	28	87

Table: Baseline characteristics and outcomes

IMAGE CAPTION:

Figure 1: Trend of cNIRS values by group

Figure 2: Trend of aNIRS values by group

Table: Baseline characteristics and outcomes

CONTROL ID: 3381413

TITLE: Neonatal Determinants of the Fecal Mycobiome in Exclusively Breastfeeding Mother-Infant Dyads

PRESENTER: Emily Skalla

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CURRENT CATEGORY: Neonatology

CURRENT SUBCATEGORY: Neonatal General

KEYWORDS: Microbiome, Infant, Fungi.

SESSION TITLE: Neonatal General |Neonatal General

SESSION TYPE: Webinar|Platform

ABSTRACT BODY:

Background: Colonizing bacteria within the infant gut (the "microbiome") are important for the development of long-term health. Diet and birth mode are key early-life exposures that affect microbiome composition. In addition to bacteria, fungi also colonize the gut (the "mycobiome"), with some fungi being implicated in health outcomes such as asthma and obesity. Despite the potential importance of fungi in health, there has been a lack of study regarding how infant mycobiomes develop and are affected by biological and environmental factors.

Objective: The goal of this study was to test the hypothesis that common neonatal factors affect gut mycobiome composition in a cohort of infants who are exclusively breastfeeding.

Design/Methods: We characterized mycobiomes from healthy mothers (milk) and their exclusively breastfeeding infants (feces) enrolled in the Mothers and Infants Linked for Healthy Growth (MILk) study (n=70 dyads) by sequencing the internal transcribed spacer region 2 (ITS2) of the fungal rDNA locus. Sequences were aligned to an ITS2 database to identify fungal taxa and statistical comparisons of mycobiome features (beta-diversity and relative abundances of fungal taxa) according to sample type, birth mode, and sex were performed using the R software package.

Results: Mycobiomes of breastmilk and feces were significantly different from each other ($p<0.01$) as were fecal mycobiomes of male versus female infants ($p<0.05$). Vaginally delivered one-month old infants had significantly different fecal mycobiomes than infants delivered by cesarean section ($p<0.05$), with a significantly higher relative abundance of *Malassezia restricta*, a skin-associated fungus, in the feces of infants born by cesarean section ($p<0.01$). These differences associated with birth mode were no longer observed at 6 months of age. Breastmilk mycobiomes were not affected by delivery mode.

Conclusion(s): In this cohort of mothers and infants where the diet of the infant was controlled (exclusively breastfed), infant gut mycobiomes were affected by sex and, in the short term, by birth mode. Because all mothers delivering by cesarean section also received intra-partum antibiotics, we cannot exclude antibiotics as a contributing co-variable of the mycobiome compositional differences seen according to birth mode. Continued study of how early-life exposures affect mycobiomes/microbiomes is needed to develop strategies that promote the development of healthy human-associated

microbial communities.

(No Image Selected)

CONTROL ID: 3380965

TITLE: Individualized target fortification (TFO) of breast milk: Variation of macronutrient intake with different fortifiers and alternative approaches

PRESENTER: Niels Rochow

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CURRENT CATEGORY: Neonatology

CURRENT SUBCATEGORY: Neonatal General

KEYWORDS: metabolism, human milk, breast milk analysis.

SESSION TITLE: Neonatal General | Neonatal General

SESSION TYPE: Webinar|Platform

ABSTRACT BODY:

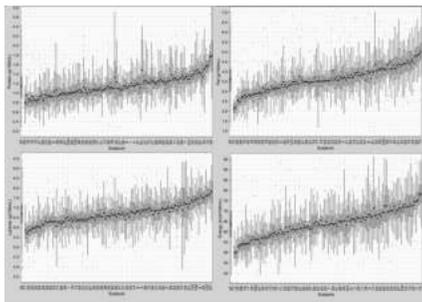
Background: Breast milk (BM) needs to be fortified for very low birth weight (VLBW) infants. Over 50% of VLBW infants fed BM with standard fortifier (SF) are growth restricted and risk metabolic and cardiovascular diseases. Using SF, nutritional deficits result from high variations of BM macronutrients (MN). TFO prevents nutritional deficits and leads to higher growth rates compared to SF. Based on native BM analysis, TFO adds to SF BM the lacking amounts of fat, protein or carbohydrates (carbs) to meet recommendations. However, over-fortified MNs by SF cannot be corrected by TFO. Commercial SF differ highly in MN composition affecting intake and growth.

Objective: 1) To test MN levels of 7 commercial fortifiers and 2 human milk (HM) based fortifier with SF or TFO, 2) To model new SF for 3 different settings, 3) To test the reduction of MN variation by batching according to BM analysis.

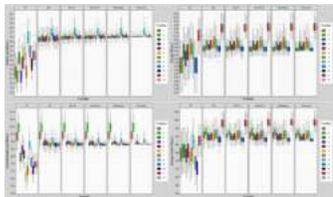
Design/Methods: An RCT using TFO (n=103 preterm infants <30 wk) provided 3,349 daily native BM samples. Validated BM analysis was performed daily for fat, protein, and carbs (Fusch G. ClinNutr. 2015). The target BM intake and composition followed the ESPGHAN recommendations with 150 mL/kg/d and 3.0, 8.8, and 4.4 g/100mL for protein, carb and fat, respectively. MN levels were simulated for SF and TFO using 5 different milk testing schedules. BM's intra-individual MN variation was presented as quantile distance (90th-10th%ile). Growth rates were predicted considering MN composition (Kashyap S. et al. 1994, 2001) and standardized intake of 130 kcal/kg/d of SF or TFO BM.

Results: MNs showed high variation in native BM (Fig 1). SF did not meet ESPGHAN targets. Protein targets were not reached in most SFs (Fig 2,3). SFs rich in carb or fat exceeded fat or carb targets. The MN variation of SF was reduced by TFO (Fig 2,3). TFO BM analysis 2x/wk reached mean recommended intake, 3x/wk or more reduce significantly MN variation. Composition of modelled SF was different whether used for SF or TFO. Batching of BM based on MN reduced the variation. Batching BM with high MN levels did not reach ESPGHAN targets for VLBW.

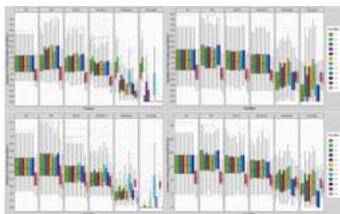
Conclusion(s): Commercial SFs provide different composition and need TFO to reach recommended intake. When TFO is performed, the SF composition is crucial. TFO can only correct lacking MN content and is not effective when SF exceeds target values. The high fat contents of HM-based fortifier provide fat globules (e.g. phospholipids) which cannot be considered equally with non-human fat of fortifier.



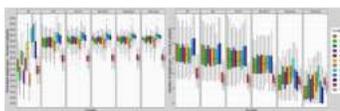
Content of macronutrients and composition in native breast milk sorted by median. Boxplots display median values of all subjects and of individual subjects. Circles present mean values. Dots present Outliers.



Macronutrient content and composition in BM after fortification with 12 fortifiers using different approaches. Fortifier #8 modelled for (SF), #9 for (Mo), #10 for (Mo, We, Fr) schedule; fortifier #11 and #12 are human milk based fortifiers. The boxplots display mean values after BM analysis of 103 subjects. Dots present outliers. SF- standard fortification, Mo, Tu, We, Th, Fr – weekdays



Confidence interval 10.-90. To demonstrate variation of macronutrient content and composition in fortified BM using 12 fortifiers in different approaches. Fortifier #8 modelled for (SF), #9 for (Mo), #10 for (Mo, We, Fr) schedule; fortifier #11 and #12 are human milk based fortifiers. The boxplots display mean values after BM analysis of 103 subjects. Dots present outliers. SF- standard fortification, Mo, Tu, We, Th, Fr – weekdays



Growth rate g/kg/d ((left) and variation of individual growth rate (90th – 10th percentile) achieved when 130 kcal/kg/d is fed of fortified breast milk. Fortifier #8 modelled for (SF), #9 for (Mo), #10 for (Mo, We, Fr) schedule. The boxplots display mean values after BM analysis of 103 subjects; fortifier #11 and #12 are human milk based fortifiers. Dots present outliers. SF- standard fortification, Mo, Tu, We, Th, Fr – weekdays

IMAGE CAPTION:

Content of macronutrients and composition in native breast milk sorted by median. Boxplots display median values of all subjects and of individual subjects. Circles present mean values. Dots present Outliers.

Macronutrient content and composition in BM after fortification with 12 fortifiers using different approaches. Fortifier #8 modelled for (SF), #9 for (Mo), #10 for (Mo, We, Fr) schedule; fortifier #11 and #12 are human milk based fortifiers. The boxplots display mean values after BM analysis of 103 subjects. Dots present outliers. SF- standard fortification, Mo, Tu, We, Th, Fr – weekdays

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CONTROL ID: 3378109

TITLE: OroPharyngeal Therapy with Mother's Own Milk (OPT-MOM) Improves Feeding and Reduces Length of Stay in Premature Infants

PRESENTER: Nancy Adrianna Garofalo

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CURRENT CATEGORY: Neonatology

CURRENT SUBCATEGORY: Neonatal General

KEYWORDS: Oropharyngeal therapy, mother's milk, feeding.

SESSION TITLE: Neonatal General | Neonatal General

SESSION TYPE: Webinar|Platform

ABSTRACT BODY:

Background: OroPharyngeal Therapy with Mother's Own Milk (OPT-MOM) can serve as a natural ex-utero substitute for (biofactor-rich) amniotic fluid exposure, providing sustained oropharyngeal immunostimulation until per oral (PO) feedings can be provided to extremely preterm (EP) infants. We hypothesized that OPT-MOM improves immune function and promotes intestinal health thereby improving feeding tolerance and reducing length of stay.

Objective: To measure the effects of OPT-MOM on (1) reducing length of stay, time to full enteral feedings and to full PO feeds and (2) reducing the incidence of NEC, late-onset sepsis (L-OS), and death in EP infants <1250 grams.

Design/Methods: A double-blind, placebo-controlled, randomized safety and efficacy trial of OPT-MOM among EP infants in 5 NICUs (Group A, OPT-MOM, n=105 v. Group B, placebo, n=101). Infants were randomized to receive 0.2 mL of 'study substance' every 2 hours for 48 hours (beginning < 96 hours of life), then every 3 hours until 32 weeks CGA.

Results: There were no differences in birthweight (881±219 v 890±190 gm), GA (27.2±2.1 v.27.4±1.8 wk), or Snappe Score (28.0±20.7 v.25.8±21.8) for groups A and B, respectively. Compared to B, A had a shorter length of NICU stay (mean +/- SD: 77 ± 33 v. 86 ± 38 d, d=0.25, p=0.23), a shorter time to reach full enteral feedings (21 ± 15 v. 28 ± 35 d, d=0.26, p=0.40), and reduced time to reach full PO feeds (23 ± 16 v. 29 ± 31 d, d=0.24, p=0.18). The incidence of L-OS was similar (15.1% v. 15.6%), as was mortality (1.2 % vs. 1.1%), but there was a trend towards less NEC (1.2% v. 3.4%, p=0.37) in A v. B, respectively. Sample size using PASS 14.0 software (NCSS, LLC. Kaysville, UT), with a two-tailed alpha of 0.05 and a 20% attrition rate was estimated at 548 infants (n=274 in each group) to detect a minimum effect size of 0.24 with 80% power. Thus, findings from this pilot study are clinically relevant and suggest that results may have reached statistical significance, with a larger sample size.

Conclusion(s): In this pilot study, our data showed a 9-day reduction in length of stay, 7-day reduction in time to full

enteral feedings, a 6-day reduction in time to full PO feedings, as well as lower NEC in OPT-MOM-treated infants, compared to controls. We speculate that less inflammation and improved commensal microbiome contributed to these improved outcomes. A 9-day reduction in stay for EP infants is a potential savings of 1.8 billion in USD yearly.

(No Image Selected)

CONTROL ID: 3374756

TITLE: The anti-inflammatory properties of microRNA-125 limit the vasoobliteration in a rat model of oxygen-induced retinopathy

PRESENTER: Maëlle Wirth

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CURRENT CATEGORY: Neonatology

CURRENT SUBCATEGORY: Neonatal General

KEYWORDS: Oxygen-Induced Retinopathy, microRNA-125, inflammation.

SESSION TITLE: Neonatal General | Neonatal General

SESSION TYPE: Webinar|Platform

ABSTRACT BODY:

Background: High sustained inflammation is a hallmark in the pathogenesis of oxygen-induced retinopathy (OIR) leading to retinal vasoobliteration, like in the retinopathy of prematurity. Dysregulation of microRNAs (miRs), key regulators of genes expressions, has been implicated in the regulation of ocular inflammation. However, the role of miRs in inflammatory process during OIR, and especially on activated-microglial cells, a key producer of pro-inflammatory cytokines, remains to explore.

Objective: This study aimed to investigate the potential anti-inflammatory role of miR-125 in OIR.

Design/Methods: qRT-PCR and western blot were performed respectively to analyze the expression of miR-125 and inflammatory cytokines in retinal/choroidal tissues of OIR rat and also in activated microglial cells (SIN9) subjected to hyperoxia and LPS. *In vitro*: miR-125 function on inflammation in LPS or hyperoxic-activated microglial cells was performed using a miR-125 mimic. *In vivo*: OIR rat pups were intravitreally supplemented with miR-125 mimic (0,5 mg/kg) or a control-miR at P5 before hyperoxic cycling (50-10% O₂ from P1 to P14). Retinal and choroidal tissues were collected between P10 to P17 to analyze the inflammatory markers and the vascular density by retinal immunostaining.

Results: We found that miR-125 expression is significantly reduced in the retina and choroid of OIR rats compare to control rats, and also in activated-SIN9 subjected to hyperoxia or LPS correlated with upregulation of keys pro-inflammatory cytokine including TNF-a and IL-6. Interestingly, we observe significant lower level of TNF-a and IL-6 in activated-SIN9 transfected with miR-125. *In vivo*, OIR rat pups intravitreally supplemented with miR-125 mimic displayed a significantly decrease of inflammatory markers (TNF-a and IL-6) associated with lower vasoobliteration area compared to the control at P10.

Conclusion(s): This study demonstrates that miR-125 acting as an inflammatory suppressor of activated-microglial cells protecting microvascular density during OIR. miR-125-based therapy could potentially constitute a novel therapeutic strategy to limits retinopathies-dependent inflammation.

(No Image Selected)

CONTROL ID: 3373468

TITLE: Combined topical ocular ketorolac and oral omega-3 polyunsaturated fatty acids, Coenzme q10 or glutathione

nanoparticles for oxidative stress in a rat model of intermittent hypoxia-induced retinopathy

PRESENTER: faisal j siddiqui

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KEYWORDS: Oxygen induced retinopathy , Intermittent hypoxia, Oxidative stress and antioxidants .

SESSION TITLE: Neonatal General |Neonatal General

SESSION TYPE: Webinar|Platform

ABSTRACT BODY:

Background: Neonatal intermittent hypoxia (IH) leads to oxidative distress and increased risk for severe oxygen induced retinopathy (OIR). Coenzyme Q10 (CoQ10), n-3 polyunsaturated fatty acids (n-3 PUFAs) and glutathione are potent antioxidants that protect against oxidative injury. Non-steroidal anti-inflammatory drugs (NSAIDs) and n-3 PUFAs individually, have been shown to reduce the severity of OIR.

Objective: To test the hypothesis that combined use of antioxidants and NSAIDs targeting oxidative stress and inflammation simultaneously, is an effective therapeutic combination to prevent severe OIR.

Design/Methods: Newborn rats were exposed to brief IH episodes (12%) during hyperoxia (50% O₂) from the first day of life (P0) until P14 during which they received daily oral supplementation with: 1) n-3 PUFAs in 50 μ L fish oil; 2) CoQ10 in 50 μ L olive oil; 3) glutathione nanoparticles (24 μ g in 50 μ L olive oil); 4) n-3 PUFAs+CoQ10; or 5) olive oil (placebo control) from P0-P14; or topical ocular ketorolac (Acuvail) or placebo saline from P5-P14. At P14, pups were placed in RA until P21. Control littermates remained in RA from birth to P21 with all treatments identical. Ocular and systemic levels of catalase, superoxide dismutase (SOD), total glutathione (GSH), 8-hydroxy-2'-deoxyguanosine (8-OHdG), and hydrogen peroxide (H₂O₂) were determined.

Results: Catalase, SOD, H₂O₂, 8-OHdG were higher in the choroid as compared to retina. n-3 PUFAs+Acuvail effectively reducing SOD in the choroid, but not in the retina. Of all treatment combinations, n-3 PUFAs+Acuvail was most effective for reducing retinal and choroidal 8-OHdG (biomarker for oxidative DNA damage), H₂O₂, and SOD (likely due to reductions in superoxide anion) in the groups exposed to neonatal IH.

Conclusion(s): Supplementation with the combination of antioxidants and treatment with topical ocular NSAIDs may have synergistic benefits for reduction of IH-induced ocular oxidative stress.



8-OHdG levels compared between Room Air and Intermittent Hypoxia



H₂O₂ levels compared between Room Air and Intermittent Hypoxia



SOD levels compared between Room Air and Intermittent Hypoxia



Catalase levels compared between Room Air and Intermittent Hypoxia

IMAGE CAPTION:

8-OHdG levels compared between Room Air and Intermittent Hypoxia

H₂O₂ levels compared between Room Air and Intermittent Hypoxia

SOD levels compared between Room Air and Intermittent Hypoxia

Catalase levels compared between Room Air and Intermittent Hypoxia

CONTROL ID: 3376385

TITLE: Pulmonary Function Changes Before and After CDH Surgery in the Era of Gentle Ventilation

PRESENTER: Brian Scottoline

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CURRENT CATEGORY: Neonatology

CURRENT SUBCATEGORY: Neonatal General

KEYWORDS: Congenital Diaphragmatic Hernia, CDH, Pulmonary Function Testing.

SESSION TITLE: Neonatal General |Neonatal General

SESSION TYPE: Webinar|Platform

ABSTRACT BODY:

Background: Congenital Diaphragmatic Hernia (CDH) is accompanied by lung hypoplasia, respiratory insufficiency, and pulmonary hypertension, and carries a significant risk for mortality and morbidity in survivors. A previous publication (Antunes, Pediatrics; 1995) reported that an FRC of < 9 mL/kg correlated significantly with mortality. There have been no studies of preoperative or immediate postoperative pulmonary function in the contemporary era of CDH management.

Objective: To define changes in pulmonary function test (PFT) measures in preoperative and postoperative CDH patients in the current era of management.

Design/Methods: This is a prospective observational study of PFTs performed on all CDH patients at the OHSU NICU as part of a CDH care pathway. Patients had PFTs prior to surgery, shortly after surgery, and prior to discharge, if possible. Functional residual capacity (FRC) was measured by nitrogen washout, and passive respiratory resistance (Rrs) and compliance (Cr) were measured with the single breath occlusion technique as per standardized criteria. The PFTs were performed by trained neonatal respiratory therapists and interpreted by a single expert.

Results: Patient characteristics are shown in Table 1. 28 infants with CDH were studied. PFTs were obtained preoperatively on all patients (96%), shortly after surgery on 24 patients (86%), and 13 patients (46%) had preoperative, postoperative, and pre-discharge studies. Three patients required preoperative ECMO; one required ECMO after surgery (14%). Four patients died due to CDH (14%). Preoperative FRC averaged 10.5 mL/kg (unmeasurable - 20.1), increasing by 70% postoperatively to 17.6 (11.1 - 28.4) (p<0.05). Mean Crs was 0.37 mL/cmH₂O/kg (unmeasurable- 0.69) before surgery, and increased 1.5-fold to 0.59 (p<0.05), while mean Rrs decreased 25% from 0.16 cmH₂O/mL/sec (unmeasurable - 0.71) preoperatively to 0.12 (0.038 - 0.32) postoperatively (p<0.05) (Table 2). Smaller improvements in PFTs from postoperative measures were noted in those with pre-discharge studies. In this cohort, a preoperative FRC < 5mL/kg was associated with death; 8/11 patients with FRC ≤ 9 mL/kg before surgery survived long term.

Conclusion(s): In this cohort, CDH patients demonstrated preoperative FRCs reflective of pulmonary hypoplasia, but demonstrated significant improvement in post-repair FRC, Crs, and Rrs. While this is a small cohort, it is the largest perioperative CDH PFT data extant, and demonstrates improved survival with low preoperative FRC in the gentle ventilation era.

Table 1: Patient Data

Item	Data (n=28)
Birth weight mean, (range) (g)	3146 (1099, 4195)
Gestational age: mean, (range) (wks)	37.3 (26.7, 42.4)
Male	53%
Caucasian	68%
Outborn	21%
LHR, mean, (range)	1.34 (0.6, 2.6) ^f
MRI O:E ratio, mean (range)	0.49 (0.29, 0.6)
Left defect	82%
Right defect	14%
Liver up	35%
Multiple anomalies	25%
ECMO Preoperative	11%
ECMO Postoperative	3.5%
Died (CDH)	14%
Died (non-CDH)	7%*
Discharge on oxygen	21%
Oxygen at 1 year	0%

^f Available for 19/28. * (expired due to 1. MRSA sepsis, 2. liver failure)

Table 2: Pre- vs. Postoperative PFTs

	Pre	Post
FRC (mL/kg)	10.1 ± 4.1 ^a	17.6 ± 4.5 ^{***b}
Crs/kg (mL/cmH ₂ O/kg)	0.37 ± 0.14 ^c	0.59 ± 0.24 ^{**d}
Rrs (cmH ₂ O/mL/sec)	0.16 ± 0.13 ^e	0.12 ± 0.06 ^{**f}

Mean, (SD); ** p<0.05 by ANOVA

^a measured on 27/28

^b measured on 22/28

^c measured on 24/28

^d measured on 22/28

^e measured on 21/28

^f measured on 19/28

IMAGE CAPTION:

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