September 22nd, 2023 09:00 - 11:00

PARALLEL SESSION 23 - I&I&I Sepsis

ID 281. Antibiotic exposure for presumed culture-negative early-onset sepsis is predominant in Europe, North America and Australia

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Background:

Due to the potentially fulminant nature of neonatal early–onset sepsis (EOS), there is a low threshold to initiate empirical antibiotics. Predominantly, blood cultures remain negative, allowing antibiotics to be discontinued within 48 hours. As the sensitivity of blood cultures is not 100%, a subset of patients are given prolonged antibiotic treatment for presumed "culture negative EOS" (CN–EOS). Our goal was to

determine the incidence of presumed CN-EOS and related antibiotic exposure during the first postnatal week.

Methods:

We conducted a secondary analysis of a retrospective study of late-preterm and term infants born between January 2014 and December 2018 in 13 networks from 11 countries in Europe, North America and Australia. Culture-proven EOS (CP-EOS) was defined as positive blood and/or cerebrospinal fluid culture and antibiotic treatment for ≥5 days. In the absence of positive cultures, newborns were considered as having a presumed CN-EOS when treated with antibiotics for ≥5 days, and considered as having culture-negative ruled-out sepsis (CN-ROS) when treated <5 days. We determined the incidence of CP-EOS, CN-EOS and CN-ROS and related antibiotic exposure.

Results:

Among 757'979 late-preterm and term infants born in the participating networks during the study period, 21'703 were treated with antibiotics (2.86%, 95%CI 2.83%-2.90%). The number of infants classified as CN-EOS, CP-EOS and CN-ROS was 7'996 (36.8%), 375 (1.7%) and 13'330 (61.4%). The incidence of CN-EOS, CP-EOS and CN-ROS was 10.55 (95% CI 10.32-10.78), 0.49 (95% CI 0.44-0.54) and 17.58 (95% CI 17.29-18.88) cases per 1000 livebirths. The median (IQR) duration of treatment for CN-EOS, CP-EOS and CN-ROS was 6 (5-8), 9 (7-14) and 3 (3-4) days. The median (IQR) number of antibiotic days (per 1000 livebirths) administered for CN-EOS, CP-EOS and CN-ROS was 77 (76-78), 5 (5-5.5), and 53 (52-53). There was a positive correlation between the incidence of CP-EOS and CN-EOS in each network (R = 0.79, 95% CI 0.43-0.94).

Conclusions:

Presumed CN–EOS was responsible for over half of the total number of antibiotic days administered to late–preterm and term newborns. Implementing restrictive diagnostic criteria for CN–EOS may lead to a more targeted and reduced use of antibiotics in early life.

None declared

ID 345. ANTIBIOTIC USE IN SWEDISH NEONATAL UNITS: A NATIONWIDE POPULATION-BASED COHORT

Mr Johan Gyllensvärd[1,2], Mrs Marie Studahl[3,4], Mr Lars Gustavsson[3,4], Mrs Elisabet Hentz[5], Mrs Karin Åkesson[1,6], Mr Huiqi Li[7], Mr Mikael Norman[8,9,10], Mr Anders Elfvin[2,5]
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Background: Antibiotic use varies between neonatal units. The magnitude of this variation, and its relation to outcome, have not been studied in Sweden.

Methods: All hospital live births from 34 weeks' gestation (n=1 025 515) during 2012–2020 were included in this nationwide population–based cohort. Data were collected from the Swedish Neonatal Quality Register and the Swedish Medical Birth Register.

The primary outcome was the usage of systematic antibiotics in the first week of life. Secondary outcomes were the duration of antibiotic treatment, the incidence of culture-proven EOS, and EOS-associated mortality.

Results: A total of 19 286 (1.9%; 95% CI: 1.85% – 1.91%) newborns (7686 girls [39.9%], median [IQR] gestational age 40 [38 — 41] weeks, median [IQR] birth-weight 3610 [3140 — 4030] g) received antibiotics during the first week of life with a range between different neonatal units from 0.9% to 4.3% ($p<0.001$). Antibiotic use was lower in level I units (1.6%) than in level II and level III units (1.9% and 1.9%, respectively, $p<0.001$) and the duration of antibiotic treatment was 102 days per 1000 live births in level I, 114 days in level II and 113 days per 1000 live births in level III units. In contrast, the incidence of EOS was higher in level I (1.1 newborns per 1000 live births) than at level II (0.71) and III hospitals (0.39 newborns per 1000 live births). The majority of EOS was caused by group B streptococci (0.34 per 1000 live births). Mortality associated with EOS was 1.39% (9 of 647 newborns). For each infant with EOS, 30 infants were started on antibiotics and 179 antibiotic days were administered. The median (IQR) duration of antibiotic treatment in infants without EOS was 5 (3 – 7) days, with a range between neonatal units from 3 (2 – 6) to 7 (3 – 10) days.

Conclusions: To our knowledge, this large study report the lowest rate of antibiotic use among late preterm and term newborns in a nationwide population.
The incidence of culture-proven EOS was in line with other international reports and the mortality rate associated with EOS was low.

None declared

ID 482. Variation in antibiotic consumption in very preterm infants - a 10-year population-based study in Norway

Doctor Zuzana Huncikova[1,2], Dr. Hans Jørgen Stensvold[3], Prof. Knut Øymar[1,2], Dr. Anlaug Vatne[1], Dr. Astri Lang[4], Dr. Ragnhild Støen[5], Dr. Anne Karin Bringtsen[3], Prof. Dag Moster[6], Dr. Beate Henriksen[7,8], Dr. Terje Selberg[9], Dr. Arild Rønnestad[3,10], Prof. Claus Klingenberg[11,12]

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Background: Wide variations in antibiotic use in preterm infants have been reported across centers despite similar rates of infection. Prolonged antibiotics use in uninfected infants is associated with increased risk of necrotizing enterocolitis, bronchopulmonary dysplasia and death. Unnecessary use of broad–spectrum antibiotics is associated with increased antimicrobial resistance We aimed to

describe 10–year trends in use of antibiotics and regional variations among very preterm infants in Norway.

Methods: All liveborn very preterm infants (gestational age <32 weeks) admitted to any neonatal unit in Norway and reported to the Norwegian Neonatal Network database during 2009–2018 were included. Main outcomes are antibiotic consumption expressed as days of antibiotic therapy (DOT) per 1000 patient days (PD), regional variations in use across four health regions, rates of sepsis and sepsis–subtypes and trends of antibiotic use during the study period.

Results: We included 5296 infants; 3646 (69%) born at 28–31 weeks and 1650 (31%) born before 28 weeks gestation. The median GA and birthweight were 29 weeks and 1.2 kg, similar across the four health regions. CRIB scores, sex distribution and proportion of growth restricted infants were also similar across regions, indicating little case mix variation, but there were some differences in rates of Caesarean delivery. Overall, 80% of the included infants received antibiotic therapy. There were considerable regional differences in antibiotic consumption (Table); greatest variation found in the consumption of vancomycin, broad–spectrum antibiotics and first–generation cephalosporins. The most prescribed antibiotics were the combination of narrow–spectrum beta–lactams and aminoglycosides for suspected early–onset sepsis, but between 2009 and 2018 we have observed more than 50 % reduction in their use from 100 to 40 DOT per 1000 PD ($p< 0.001$). In contrast, consumption of broad–spectrum antibiotics remained unchanged ($p=0.308$) in all health regions. There were only marginal differences in rates of sepsis and no differences in sepsis–attributable mortality across regions.

Conclusion: There was a great variance both in overall antibiotic consumption and types of antibiotics used across the four health regions in Norway, with no clear correlation to sepsis subtypes or sepsis–attributable mortality. Our results highlight the need for antibiotic stewardship strategies.

DOT per 1000 PD	All n=5296	South-East n=2919	West n= 1217	Mid n=730	North n=430	p-value
All antibiotic treatment ^	149	159	141	161	122	0.012*
Narrow-spectrum antibiotics	108	103	109	108	70	<0.001†
Broad-spectrum antibiotics	34	42	24	31	17	<0.001~
Aminoglycosides	102	100	108	108	91	0.038*
First-generation cephalosporins	3	1	1	1	25	<0.001†
Vancomycin	27	36	18	22	8	<0.001†

DOT per 1000 PD; days of antibiotic therapy per 1000 patient days
^ when calculated "all antibiotics", one day with combination therapy is counted as one day
*Significant differences between North and Mid, North and South-East, West and South-East
† Significant differences between North and all other regions
~ Significant differences between South-East and all other regions
* Significant differences between North and South-East, North and West

None Declared

ID 729. Metabolic shift of Bifidobacterium longum subsp. infantis in response to acid stress is associated with failure to prevent sepsis in preterm infants

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Background: Early alterations of the gut microbiome are considered as drivers of sepsis risk in preterm infants. Bifidobacterium longum (B. longum) containing probiotics are frequently supplemented to preterm infants with the aim to restore early microbiome distortions and to prevent adverse outcome. However, the effect of the probiotics on sepsis prevention is inconclusive, and we herein hypothesized that their metabolic features are key modulators of sepsis risk.

Methods: We conducted a prospective longitudinal study in preterm infants during the period of highest vulnerability for late-onset sepsis (LOS; fecal sampling: days 7, 14, and 21 of life). 108 infants received routine supplementation with B. longum subspecies infantis plus Lactobacillus acidophilus and were compared to 126 infants who did not receive probiotics. Following metagenomic sequencing and determination of metabolic profiles via nuclear magnetic resonance (NMR) spectroscopy, we assessed microbial community function using metabolic network modelling.

Results: Administration of probiotics led to an early colonization of the probiotic bacteria in the preterm infant gut in line with an increase of fecal concentrations of most metabolites. In our cohort, 70/234 preterm infants developed LOS and had

distinct microbiome features preceding sepsis: (i) increased abundance of Staphylococcus epidermidis and reduced prevalence of Veillonella sp., especially in co-occurrence with B. longum, and (ii) increased rates of branched-chain and aromatic amino acids along with decreased rates of acetate and lactate in infants supplemented with probiotics. Our data suggest that B. longum switches metabolism as a response to acid stress (low pH) which may be a crucial determinant for the failure to prevent sepsis. These specific features are associated with impaired ecological succession and reduced establishment of secondary fermenting microorganisms.

Conclusions: Further studies are needed to identify the targets for metabolic shifts prior to LOS development in order to optimize probiotic interventions and to facilitate multi-site collaborative efforts to define the patient groups that benefit most.

None declared