Evaluation of Early-Onset Very Preterm Neonatal Sepsis in Australia and New Zealand, 2007-2018

Husharn Duggan[1], Sharon Chow[2], Nicola Austin[3], Prakesh Shah[4], Kei Lui[2] and Kenneth Tan[1], on behalf of the Australian and New Zealand Neonatal Network (ANZNN)

[1]Department of Paediatrics, Monash University, Clayton, Victoria, Australia, [2]School of Women's and Children's Health, University of New South Wales, Sydney, New South Wales, Australia, [3]Department of Paediatrics, University of Otago, Christchurch, New Zealand; [4]Department of Pediatrics, University of Toronto, Toronto, Ontario, Canada

Background

Neonatal sepsis is characterised as an invasive bloodstream infection that occurs within the first 28 days of life, and notably contributes to worldwide morbidity and mortality rates.[1] Epidemiological research has found Group B *Streptococcus* (*GBS*) to be the leading causative microorganism of early-onset sepsis (EOS).[2] This discovery has led to the implementation of innovative preventative strategies, such as intrapartum antibiotic prophylaxis,[3] to reduce the global burden of this pervasive disease. However, recent studies have found *Escherichia coli* (*E. coli)* to be an emerging pathogen,[4] especially in very preterm (VPT) populations.

Since VPT neonates are at significant risk of mortality due to EOS, there is a low threshold for antibiotic administration in this cohort. This inappropriately exposes certain neonates that would be at a lower risk of acquiring EOS to antibiotics during a period of vulnerability and crucial development. Studies have shown that this can increase their risk of developing necrotizing enterocolitis and late-onset sepsis.[5] Socioeconomic issues also stem from excessive antimicrobial use, including early separation from the mother after birth, global antimicrobial resistance and resource overconsumption.

Aim

To evaluate the epidemiology, population trends and predictive factors for EOS in VPT neonates admitted to neonatal intensive care units (NICU) in Australia and New Zealand.

Methods

The Australian and New Zealand Neonatal Network provided data for neonates born at <32 weeks' gestation and then admitted to one of 29 Australian or New Zealand NICUs between 1 January 2007 and 31 December 2018. We performed a retrospective cohort study on this data, which included linear regression analyses to create temporal trends and multivariate backwards logistic regression analysis for analysing predictive factors.

Results

Over the 12-year period, 614 EOS cases from 43,178 VPT admissions (14.2/1000 admissions) were identified. The trends of EOS incidence remained stable, varying between 9.8-19.4/1000 admissions (linear trend, *P*=.56). The leading causative organisms were *E. coli* (33.7%) followed by *GBS* (16.1%). The incidence of *E. coli* increased between 2007 (3.2/1000 admissions) and 2018 (8.3/1000 admissions; *P*=0.02). Neonates with *E. coli* had higher odds of mortality compared to those with *GBS* (OR=1.9, 95%CI 1.1-3.5, *P*=0.03). Mortality due to *GBS* EOS decreased over the same period (2007: 0.6/1000 admissions, 2018: 0.0/1000 admissions; *P*=0.01). The most significant predictors for early-onset infection included prolonged rupture of membranes >18 hours (OR 2.5; 95%CI 2.1–3.0, *P*<0.001), fetal distress (OR 1.8; 95%CI 1.5–2.1, *P*<0.001) and preterm labour (OR 1.5; 95%CI 1.2–1.8, *P*<0.001). Protective maternal factors included hypertension in pregnancy (OR 0.4; 95%CI 0.3–0.7, *P*<0.001) and non-singleton pregnancy (OR 0.4; 95%CI 0.3–0.5, *P*<0.001).

Conclusion

The trends of EOS among VPT neonates have remained low and stable in Australia and New Zealand. Furthermore, *E. coli* is a dominant microorganism of VPT EOS and the rates of *E. coli* have been

increasing in recent years. The regression model created in this study can form the basis of a tool that predicts the likelihood of EOS in VPT neonates, which will require validation using prospective data.

References

1. Hug L, Alexander M, You D, Alkema L. National, regional, and global levels and trends in neonatal mortality between 1990 and 2017, with scenario-based projections to 2030: a systematic analysis. The Lancet Global Health. 2019;7(6):e710-e20.
2. Singh T, Barnes EH, Isaacs D. Early-onset neonatal infections in Australia and New Zealand, 2002–2012. Archives of Disease in Childhood - Fetal and Neonatal Edition. 2019;104(3):F248-F52.
3. Russell NJ, Seale AC, O'Sullivan C, Le Doare K, Heath PT, Lawn JE, et al. Risk of Early-Onset Neonatal Group B Streptococcal Disease With Maternal Colonization Worldwide: Systematic Review and Meta-analyses. Clinical Infectious Diseases. 2017;65(suppl_2):S152-S9.
4. Sgro M, Campbell DM, Mellor KL, Hollamby K, Bodani J, Shah PS. Early-onset neonatal sepsis: Organism patterns between 2009 and 2014. Paediatrics & Child Health. 2020;25(7):425-31.
5. Shah P, Nathan E, Doherty D, Patole S. Prolonged exposure to antibiotics and its associations in extremely preterm neonates - the Western Australian experience. The Journal of Maternal-Fetal & Neonatal Medicine. 2013;26(17):1710-4.