Editorial
Korean J Pediatr 2019;62(11):410-411
https://doi.org/10.3345/kjp.2019.00570
pISSN 1738-1061 • eISSN 2092-7258

Korean J Pediatr

Controversy in the diagnosis and treatment of hemodynamically significant patent ductus arteriosus in preterm infants

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Lee[1] reported an excellent review article on the management of preterm patent ductus arteriosus (PDA) in a recent issue of the Korean Journal of Pediatrics. PDA in premature infants may be the most controversial topic in neonatology. The main reason for the controversy is the difficulty in detangling the consequences of hemodynamically significant (HS) PDA from that of prematurity per se because HS PDA is associated with both prematurity and poor neonatal morbidities.[2] Furthermore, although we reject the null hypothesis and agree to actively treat PDA to induce its closure, the current methodology and measures have limited ability to determine the hemodynamic significance of PDA and accordingly select high-risk patients who require pharmacological treatment or a more invasive surgical ligation with potentially detrimental effects. The clinical symptoms and signs of PDA are often obscure in extremely preterm infants, and the absence of classical physical signs does not exclude a large left-to-right shunt.[3] The single index of ductal diameter measurement by echocardiography revealed a weak correlation with other various echocardiographic markers of shunt volume.[4] Therefore, as Lee mentioned, the combination of clinical and echocardiographic staging systems with or without biological markers, including NT-proB-type natriuretic peptide, is considered the best diagnostic tool to date for predicting the hemodynamic significance of PDA.[5] Moreover, near-infrared spectroscopy may be more desirable because it demonstrates the systemic impact of PDA rather than ductal characteristics.[6] A recent study by Dagle et al.[7] showed that single-nucleotide polymorphisms in several genes were associated with HS PDA that required surgical ligation, suggesting the genetic predisposition of HS PDA. Future studies to assess the hemodynamic significance of PDA through genetic, echocardiographic, and biologic tools will provide a more precise staging system for risk stratification.

The effect of active treatment for HS PDA is also controversial. Whether prolonged exposure to a moderate-to-large ductal shunt is detrimental and whether active treatment to reduce the duration of exposure to ductal shunt will decrease the incidence of neonatal morbidities remain to be determined. Well-designed randomized clinical trials will address these questions in the future. Since publication of the review article by Lee, the PDA-TOLERATE trial was published.[8,9] The study included infants <28-week gestational age and compared the rates of surgical ligation, presence of PDA at hospital discharge, and various neonatal morbidities between the early routine and conservative treatment groups. In the study, early treatment did not reduce the frequency of PDA ligation or presence of PDA at discharge; however, it increased the incidence of sepsis and death in infants ≥26-week gestation. However, the study has some limitations. Twenty-one percent of the eligible infants were not enrolled owing to unwillingness of the medical team. Sixty-three infants in the conservative treatment group eventually received rescue pharmacological treatment. Therefore, the study could be considered a comparison between early and late rescue treatments rather than between early and conservative treatments. The effect of active treatment compared with that of nonintervention

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Received: 22 May, 2019
Accepted: 17 June, 2019

See the article "Practice for preterm patent ductus arteriosus; focusing on the hemodynamic significance and the impact on the neonatal outcomes" in Volume 62 on page 245.

for preterm PDA may remain unclear. The wide variation among units in practice for HS PDA implies the urgency of establishing treatment guidelines for HS PDA in preterm infants.

Conflicts of interest

No potential conflict of interest relevant to this article was reported.

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