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READER'S FORUM

ACTA PÆDIATRICA NURTURING THE CHILD WILEY

Reply to risk factors for pulmonary interstitial emphysema in the preterm infant: Still more challenges than answers

Dear Editor,

We thank for the opportunity to respond to the letter of Dr Al-Abdi [1] concerning our manuscript "Preeclampsia was a risk factor for pulmonary interstitial emphysema (PIE) in preterm infants born ≤32 weeks of gestational age".[2] We like to comment on the chronology and scientific facts. The case report by Al-Abdi et al is within a series of PIE in infants on non-invasive ventilation (NIV), and we added two additional cases.[3,4] These observations permit the conclusion that PIE can occur during NIV what is contradictory to the long-lasting assumption that PIE is caused by high ventilation pressures or tidal volumes. Pre-eclampsia/HELLP accounts for about 20% of preterm births and poses a tremendous risk to the immature lung.[5] But the identification as risk factor for PIE cannot be validly deducted from the summary of three out of five PIE cases in the context of pre-eclampsia/HELLP. Our two and further published cases with negative history for pre-eclampsia/HELLP demonstrate the shakiness of this assumption. In the case of Al-Abdi et al, the high plasma level of magnesium needs to be acknowledged as key predisposing factor for PIE; therefore, citation of its association to PIE is not justified.[6] The lack of scientific knowledge is substantiated by other authors that propose lung immaturity, retention of lung fluid or infection as risk factors. These different hypotheses indicate the need to decipher the origins of PIE. Our retrospective matched-pairs study used univariable conditional logistic regression, not in favour of a hypothesis or any of the items studied.[2] Known risk factors for PIE as low birth weight and impaired gas exchange after birth were confirmed assuring a representative study cohort. Surprisingly, PIE was identified as the sole maternal risk factor while amongst others antenatal steroids, amniotic infection and diabetes during pregnancy were not. The sample size of n = 179 cases was still underpowered to assess the strength of association and confirmation in independent cohorts is pending. Coming back to the reports of Al-Abdi and others, our study underlines the previous assumption that PIE aetiology can be ascribed to lung immaturity and not ventilation strategies: (a) the occurrence of PIE was closely associated with severe respiratory distress after birth, (b) about half of the infants in our cohort developed PIE on NIV and (c) we were able to define an upper birth weight cut-off. Lung development constitutes a highly orchestrated process that requires the interplay between alveolar and vascular growth factor signalling.[7] The previously described association of pre-eclampsia/HELLP with distorted vascular growth factor signalling suggests a mechanistic link to lung immaturity and PIE.[5] This remains to be proven on a molecular level. Whether this pathophysiology can be applied to the majority of PIE cases without a history of pre-eclampsia/HELLP needs to be developed. In neither case, we may expect citation of our hypothesis. Lastly, the discussion about risk factors for PIE should not distract the focus from the urgent clinical need to establish preventive measures to the occurrence of PIE.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

Judith Behnke[1,2]
Anita Windhorst[3]
Frank Oehmke[4]
Lars Daniel Berthold[5]
Klaus-Peter Zimmer[1]
Markus Waitz[1]
Harald Ehrhardt[1,2]

[1]*Department of General Pediatrics & Neonatology, Justus Liebig University and Universities of Giessen and Marburg Lung Center (UGMLC), Giessen, Germany*
[2]*Member of the German Center for Lung Research (DZL), Giessen, Germany*
[3]*Department of Medical Statistics, Justus Liebig University of Giessen, Giessen, Germany*
[4]*Department of Gynecology and Obstetrics, Justus Liebig University of Giessen, Giessen, Germany*
[5]*Department of Pediatric Radiology, Institute for Diagnostic and Interventional Radiology, Justus Liebig University of Giessen, Giessen, Germany*

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Correspondence
Harald Ehrhardt, Department of General Pediatrics and Neonatology, Justus Liebig University, Feulgenstrasse 12, 35392 Giessen, Germany.
Email: Harald.Ehrhardt@paediat.med.uni-giessen.de

ORCID

Judith Behnke https://orcid.org/0000-0003-4307-8759

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