Response to Letter by Temesvári

Response:

We thank Professor Temesvári for his comments regarding our recent article about the epidemiology of perinatal stroke (PS) in Estonia.\textsuperscript{1} The hypothesis of pneumothorax with subsequent air-embolism as a possible cause of neonatal ischemic stroke is interesting and has been demonstrated in piglet experimental model by professor Temesvári and his group.\textsuperscript{2} However, epidemiological studies of PS risk factors in term and near-term infants have not identified this association.\textsuperscript{3,4} Though intrapartum complications including the need for resuscitation and positive pressure ventilation are more common in infants with perinatal stroke,\textsuperscript{3} case-control studies have failed to identify these variables as independent risk factors for PS suggesting a different cause-result relationship.\textsuperscript{5} A recent case-control study on risk factors of PS in preterm infants failed to show any difference in the use of positive pressure ventilation between cases and controls.\textsuperscript{6} Actually, the time course of the events is likely to be vice versa: in infants with PS central nervous system injury often precedes respiratory problems, as was also documented in 3 of the 5 infants requiring positive pressure ventilation in our study population—1 was intubated at birth because of asphyxia and the other 2 because of seizure syndrome, reflecting already present brain injury at the age of 6 and 26 hours, respectively. Only 2 of the 5 patients needing respiratory support were ventilated for concomitant lung disease—meconium aspiration syndrome. All infants had at least 1 thoracic x-ray taken during the acute period with none having pneumothorax or any other air leak syndrome diagnosed.

Clinical cases of air embolism with or without ischemic stroke have been described in association with pulmonary air leak syndromes, most often pulmonary interstitial emphysema associated with positive pressure ventilation in preterm infants.\textsuperscript{7–9} Air leak syndromes are increasingly rare since the era of surfactant therapy and patient-synchronized ventilation. In contrast to the 30% to 50% suggested by Professor Temesvári in the Neonatal Intensive Care Unit of Tartu University Hospital, the incidence of air leak syndromes in ventilated neonates has varied between 5.7% to 7.5% over the last 8 years, with 80% occurring in preterm neonates. Other situations associated with documented air embolism in neonates include instrumental interventions like central venous catheters, ECMO and heart surgery with cardiopulmonary bypass. However, these presently identifiable risk factors for air embolism are rare in term or near-term neonates experiencing PS. We would consider air embolism rather a possibility, which cannot be ruled out in single cases, than a frequent cause of PS.

We quite agree that the proportion of infants with identifiable risk factors for perinatal stroke in our study is low although there are other series where no obvious precipitating cause has been identified in as many as 25% to 47% of cases owing probably to the still existing obscurities in the pathogenesis of perinatal stroke.\textsuperscript{10,11} Based on the design of our study, we could not identify new risk factors of PS but only describe the frequency of previously known risk factors in our study population. An important limitation of our study, rising from its largely retrospective nature, is that some of the most frequently suggested risk factors of PS like thrombophilias and cardiac disorders\textsuperscript{3,4} were not studied in all infants. In our study group, 17/38 infants were studied in detail for cardiac disorders and a complex screening for prothrombotic disorders was performed in 27/38, in many cases months to years after the acute event. Anticardiolipin antibodies, identified as the most common coagulation abnormality in the subgroup of the Canadian childhood stroke study may be transient.\textsuperscript{10,11} Thrombophilia screening in our study group did not include lipoprotein measurement, the most significantly acute ischemic stroke associated prothrombotic abnormality according to the case-control study by the German childhood stroke study.\textsuperscript{12} Thus, as has been pointed out in the discussion, we cannot claim to have identified the final prevalence of these possible risk factors in our study group.

In conclusion, we believe that air embolism as the causative mechanism of perinatal stroke may be considered in single cases but cannot be a predominant cause of perinatal stroke in term and near-term infants.

Disclosures

None.

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characteristics associated with perinatal arterial stroke in the infant. 


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