Stem Cells for Neonatal Lung Disease Caused by SP-B Deficiency?
Stammzellen bei neonatalen Lungenerkrankungen verursacht durch SP-B Mangel?

Ludwig Gortner

Recent reports confirm the serious consequences of partial surfactant protein B (SP-B) deficiency in a heterozygous SP-B121ins2 mutation [1], the homozygous form of this specific mutation initially had been described by the group of Nogee and co-workers in a term neonate with intractable respiratory failure about 20 years ago [13]. Before this substantial contribute to our understanding of genetic pulmonary disorders with neonatal onset, the clinical entity was described as idiopathic pulmonary alveolar proteinosis [12]. The disorder was characterized by an uniform lethal course [12]. Medical and physical approaches to improve the course of the disease included among others administration of surfactant, corticosteroids and other immunosuppressants, repeated lung lavage and ultimately lung transplantation. Medical attempts were not successful at long-term and lung transplants in neonates and young infants, if available, were reported to be overall accompanied by a high rate complications [8–10]. Thus, also a recent report confirms that SP-B deficiency is a devastating diagnosis in neonates with irreversible respiratory failure [18]. A recently published observational study conducted between 2006 and 2011 from the UK showed that out of 427 cases with unclear severe neonatal respiratory failure, 25 cases could be identified to suffer from surfactant dysfunction disorders, i.e. about 6% overall. SP-B dysfunction could be confirmed in 8 cases and furthermore, 3 affected individuals with SP-B deficiency following prenatal diagnostic were reported. All aforementioned neonates with disorders in the surfactant B system died from intractable respiratory failure [15]. Recent reports on experimentally induced chronic neonatal lung disorder [6]. Furthermore, reports on experimentally induced acute respiratory distress syndrome in adult animals by various noxious stimuli to the lung have been published previously [4]. Most transplants were given as allogeneic mesenchymal stem cells, some other groups also used cell xenotransplants obtained from human preterm neonates [11]. Homing of stem cells in the lungs at a variable extent and transformation of mesenchymal and hematopoietic stem cells into type II alveolar cells have been reported nearly uniformly [16].

A first clinical phase I study using allogeneic mesenchymal stem cells in very preterm neonates with threatening BPD has been published recently by a Korean group [2]. Thus, there is now a high degree of experimental evidence that stem cell administration is effective in experimentally induced respiratory failure in neonates as well as in adults and as a consequence, the Korean group started a clinical study based on several experimental studies. Given these fact SP-B deficiency may be considered as a further field for research on regenerative therapy i.e. stem cell administration in models of postnatal SP-B deficiency. If the findings of these experiments will be positive, this distinct disorder could be considered a further candidate for stem cell administration during the neonatal period. Due to the unique fatal course of SP-B deficiency in neonates, they might be excellent candidates for regenerative therapies. Before coming into clinical reality however, a number of experimental data on safety and efficacy needs to be worked out further. Long-term outcome of the preterm neonates, who were enrolled in the above mentioned phase I trial from Korea using allogeneic mesenchymal stem cells in threatening bronchopulmonary dysplasia should be considered as one key issue [2]. If successful in SP-B deficiency, other disorders in surfactant homeostasis, e.g. ABCA3-defects may be addressed further [17].

Bibliography
DOI http://dx.doi.org/10.1055/s-0034-1395697
Klin Padiatr 2015; 227: 1–2
© Georg Thieme Verlag KG
Stuttgart · New York
ISSN 0300-8630

Correspondence
Prof. Dr. Ludwig Gortner
Clinics for Paediatrics and Adolescent Medicine
University Hospital of the Saarland
Building 9
66421 Homburg
Germany
ludwig.gortner@uksh.de

References


