Methionine supplementation for multi-organ dysfunction in MetRS-related pulmonary alveolar proteinosis

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Shareable abstract (@ERSpublications)
Pulmonary alveolar proteinosis related to mutations in *MARS1* is a rare and severe lung disease with early onset and no curative treatment to date. In four affected children we showed that methionine supplementation is an effective treatment. https://bit.ly/2WlbcOz

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Abstract

Introduction Pulmonary alveolar proteinosis related to mutations in the methionine tRNA synthetase (*MARS1*) gene is a severe, early-onset disease that results in death before the age of 2 years in one-third of patients. It is associated with a liver disease, growth failure and systemic inflammation. As methionine supplementation in yeast models restored normal enzymatic activity of the synthetase, we studied the tolerance, safety and efficacy of daily oral methionine supplementation in patients with severe and early disease.

Methods Four patients received methionine supplementation and were followed for respiratory, hepatic, growth and inflammation-related outcomes. Their course was compared to those of historical controls. Reactive oxygen species production by patient monocytes before and after methionine supplementation was also studied.

Results Methionine supplementation was associated with respiratory improvement, clearance of the extracellular lipoproteinaceous material and discontinuation of whole-lung lavage in all patients. The three patients who required oxygen or noninvasive ventilation could be weaned off within 60 days. In addition, liver dysfunction, inflammation and growth delay improved or resolved. At a cellular level, methionine supplementation normalised the production of reactive oxygen species by peripheral monocytes.

Conclusion Methionine supplementation was associated with important improvements in children with pulmonary alveolar proteinosis related to mutations in the *MARS1* gene. This study paves the way for similar strategies for other tRNA synthetase deficiencies.