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CORRESPONDENCE

Pregnancy in patients with Alpha 1 Antitrypsin (AAT) deficiency and the role of intravenous AAT therapy. Authors' reply

We would like to thank Dr. Hernandez Perez and colleagues for their comments on our article concerning pregnancy in patients with Alpha 1 Antitrypsin Deficiency (AATD),[1] and for engaging in an interesting discussion surrounding the critical issue of Alpha 1 Antitrypsin (AAT) replacement therapy in non-standard indications, such as individuals with *Pi**SZ genotype and/or diseases other than pulmonary emphysema.[2] We certainly agree that the case presented is very complex; therefore, we will attempt to clarify some points.

The first point by Hernandez Perez and colleagues is that we prescribed augmentation therapy to a patient with *Pi**SZ genotype, despite the ERS statement not supporting this indication.[3] When making this decision, we nevertheless considered that an unknown proportion of *Pi**SZ individuals may have an increased risk for lung and liver diseases, especially if they suffer from frequent inflammatory respiratory exacerbations, which is the case for our patient.[4] As an indirect confirmation of this, approximately 8% of patients carrying the *Pi**SZ genotype receive AAT therapy in Italy and Spain.[5] In support of our decision, it is important to note that at the time augmentation therapy was initiated (week 18 of pregnancy), our patient had serum AAT levels largely below the theoretical "protective threshold" (38 mg•dL^{-1}).

A second point notes that we treated a patient suffering from severe asthma, despite the fact that AAT therapy is only approved for subjects with pulmonary emphysema. The effective contribution of AATD to asthma severity is unclear; however, the potential pathophysiological implications of low levels of AAT suggest an association with an increased risk of bronchial remodelling and fixed obstruction. Recently, we retrospectively investigated a group of 143 patients with severe asthma, showing that AATD was present in 10 out of 143 patients (6.99%). At the 12-month follow-up, forced expiratory volume in 1 second (FEV_1; litres), FEV_1 % predicted, and forced vital capacity (FVC) decline expressed as variation vs. baseline were significantly greater in individuals with abnormal AAT levels compared to those with normal values (>110 mg•dL^{-1}).[6] Considering this and the significant drop in FEV_1 recorded at week 18 of pregnancy, we considered that AAT therapy might be effective in reducing the rate of lung volume decline and improving asthma control in our patient.

Finally, Hernandez Perez and colleagues note that we treated a pregnant woman despite a lack of studies on the effect of augmentation therapy in pregnancy. However, when making this choice we believed that our patient was at increased risk of pregnancy-related complications, due to the combined effect of low AAT levels and recurrent asthma exacerbations,[7] and concluded that AAT therapy might reduce both the maternal and foetal risk.

In summary, although we agree that AAT augmentation therapy for non-standard indications requires further study to investigate its safety and efficacy, we believe that it is probably time to move on from its original prescriptive placing to broader scenarios.

Conflicts of interest

AV received research grants from CSL Behring. The other Authors have no conflicts of interest to declare.

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