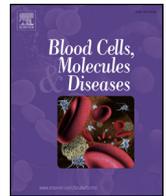




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The additive effect on the antiepileptic treatment of ambroxol in type 3 Gaucher patient. The early observation

Lukasz Pawlinski, Maciej T Malecki, Beata Kiec-Wilk *

Department of Metabolic Diseases University Hospital, Krakow, Poland

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Dear Editors,

It is a pleasure to present our preliminary research that supports recent data of positive effect of ambroxol on patient with Gaucher Disease (GD). An introduction of the drug decreased the frequency of seizures in our patient.

Gaucher Disease is an autosomal recessive, lysosomal storage disease in which a deficiency of glucocerebrosidase enzyme occurs, causing the glucocerebroside to accumulate in specific tissues. The clinical manifestation varies from early-onset to late-onset disease according to a residual activity of the enzyme and the rate of metabolic products accumulation. The most represented type 1 GD is connected with haematopoietic impairment, hepatosplenomegaly or bone involvement which may produce acute and chronic pain. In addition, in type 3 GD the neurological symptoms occur like ataxia, oculomotorus apraxia, or epilepsy [1]. In 1991 enzyme-replacement therapy (ERT) was introduced, although its known benefit in type 1 GD, the effect on neurological deficits in type 3 GD is nugatory [1]. Therefore finding a potential drug to manage those symptoms is substantial.

Ambroxol is a mucolytic drug used in clinical practice for many years to cope with airways and GI tract production of mucus in such diseases as pneumonia or cystic fibrosis. In addition it was proven that this particle can bind to mutant, misfolded glucocerebrosidase helping in proper folding thus amending its function [2]. Ambroxol can cross the blood–brain barrier; therefore, it has emerged as a promising therapy for type 3 GD [3].

Our 34-year old patient was diagnosed with Gaucher Disease type 3 in the second year of life, upon histological analysis of removed spleen. She was qualified to ERT administration when she was 19 years old. Amelioration of hepatomegaly, haematological manifestations and normalization of liver size occurred in a first year of therapy. Nevertheless,

after a year on therapy a first episode of epilepsy occurred. Initially seizure were presented every day. The introduction of antiepilepsy drugs reduced the frequency of epileptic fits in a very regular manner. On a given day seizures in bursts of 4–5 fits were noted followed by 5–11 days break. Seizures persisted despite changes in the therapy and so drug resistant epilepsy was diagnosed. For the next 15 years the situation stayed stable. For over a year now the therapy has been fixed and based upon 3 drugs: topiramatum, levetiracetam and valproic acid. Those epilepsy fits were decreasing the well-being of the patient and caregiving family.

Based on the previous clinical observations we introduced the ambroxol to our Gaucher patient, upon informed consent, starting from a dose of 150 mg/d (2×75 mg, patient body weight = 38 kg, dose: 4 mg/kg/day) [4]. Drug tolerance was good. Only the slight reduction of strength of the epileptic attacks, referred by the patient and her family, was observed. In the 6th month of the ambroxol therapy the neurological drug topiramatum had been changed to lacosamide, for this time the significant reduction of epileptic fits frequency has been observed.

In 2016 a pilot study involving ambroxol chaperone therapy in few patients with GD showed improvement in the neurological manifestation of the disease [5]. Encouraged by these findings, after 15 months of ambroxol therapy, we doubled the dose to 2×150 mg (8 mg/kg/day). No side effects were observed. During the time of observation no significant changes of such parameters as platelets or haemoglobin level were noted, although the patient for many years maintained proper haematological parameters, so no further improvement was expected.

After increasing the daily dose of chaperone therapy the epileptic fit frequency diminished remarkably to one series per 3–4 weeks, consisting of 1–2 fits at most.

In compare to the observation made by Aya Narita's team we reduced the rate of increasing the dose of ambroxol. Our obtained results however imply the additive effect of ambroxol to the neurological treatment of our patient. The authors are aware that it is a pilot study and further studies must be conducted to confirm the acquired effect.

Given paper is based on subjective data from the patient.

This preliminary report reveals probable efficacy in mitigating important complication of GA.

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* Corresponding author at: Department of Metabolic Diseases University Hospital, Kopernika 15, 31-501 Krakow, Poland.

E-mail address: mbkiec@gmail.com (B. Kiec-Wilk).

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