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COMMENTARY

A commentary on short-term efficacy of *N*-carbamylglutamate in a patient with *N*-acetylglutamate synthase deficiency

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N-acetylglutamate synthase (NAGS) deficiency is an autosomal recessive disorder of the urea cycle. Carbamylphophate synthase (CPS) 1, which acts in the first step of the urea cycle, has an absolute requirement for NAGS. NAGS deficiency is a very rare disease. Only 23 patients with NAGS deficiency were enrolled over 17 years in a phase III clinical trial study in Europe. In the USA, Batshaw *et al.*[1] reported the results of an analysis of 614 patients with urea cycle disorders. NAGS deficiency occurred in three patients, all with a late-onset form. There has been no case report of a patient with NAGS deficiency in Japan. Recently first Korean patient reported.[2] Some patients with NAGS deficiency may be misdiagnosed as having carbamylphosphate synthase 1 deficiency. Confirmation of NAGS deficiency or CPS1 deficiency requires mutation analysis or enzyme-activity assay of a liver biopsy when genetic diagnosis is inconclusive or rapid diagnosis is required. It is very difficult to measure NAGS enzyme activity. Genetic analysis is virtually the only method of diagnosing NAGS deficiency.

Carbamylglutamate was approved in Europe in 2003 and in the USA in 2010. A phase III clinical trial study has now been developed in Japan. Many papers have reported that this drug has good effects for the treatment of NAGS deficiency patients. NAGS deficiency patients treated with *N*-carbamylglutamate do not require protein restriction or other medications, except during metabolic crises.[3]

Guidelines for the diagnosis and management of urea cycle disorders in Europe[4] recommend monotherapy with *N*-carbamylglutamate as the treatment of choice in NAGS deficiency. The Guidelines recommend that *N*-carbamylglutamate should be considered in severe hyperammonemic decompensations of unknown etiology in the neonatal period as well. When *N*-carbamylglutamate will be approved in Japan, it will be necessary to administer this drug for the differential diagnosis of NAGS versus CPS1 deficiency.

Kido *et al.*[5] recently reported an improvement in the prognosis of patients with urea cycle disorders in Japan. This new drug may improve the prognosis of these patients. To achieve more improvement, it is important to develop a rapid diagnostic system for urea cycle disorders, especially for genetic diagnosis.

CONFLICT OF INTEREST

The author declares no conflict of interest.

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