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AMIFAMPRIDINE AND PYRIDOSTIGMINE HARD CAPSULES FOR TREATMENT OF CONGENITAL MYASTHENIC SYNDROMES : A CASE REPORT

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OBJECTIVE

Congenital myasthenic syndromes (CMS) are a group of inherited neuromuscular disorders caused by defects at the neuromuscular junction. Mutations in the choline acetyltransferase gene (CHAT) on chromosome 10q11 causes a type of presynaptic CMS characterised by hypotonia, paralysis of cranial and limb muscles and apnea at birth. Diagnosis is based on genetic testing and electromyography.

OBJECTIVE: to describe the efficacy and safety of combined treatment with amifampridine and pyridostigmine in childhood presynaptic CMS.

CONCLUSIONS

- ❖ The recommended treatment for presynaptic CMS is acetylcholinesterase inhibitor (pyridostigmine or neostigmine). Amifampridine has been presented as an effective treatment only for some postsynaptic types of CMS. In this case, however, amifampridine was useful for symptom management and it allowed punctual acetylcholinesterase inhibitor dose reduction.
- ❖ Pharmaceutical compounding is frequently indispensable to obtain the exact paediatric dosages.

METHODS

- ❖ A four-day-old newborn male with generalized hypotonia and respiratory failure requiring mechanical ventilation was taken to our hospital. Physicians performed intravenous neostigmine diagnostic test showing improvement of muscle strength and ability to move.
- ❖ Two CHAT gene heterozygous mutations (c.1249 G>A and c.1505 T>C) were detected through genetic testing four months later. The first one is already linked to presynaptic CMS [Schara U. et al, *Long-term follow-up in patients with congenital myasthenic syndrome due to CHAT mutations*. Eur J Paediatr Neurol. 2010 Jul;14(4):326-33]

RESULTS

- After performing a neostigmine diagnostic test, his physicians established treatment with oral pyridostigmine 4 mg/4h. The hospital Pharmacy Department compounded 4 mg hard capsules starting from pyridostigmine 60 mg tablets and maltodextrin as excipient. Dose had to be reduced due to anticholinergic toxicity (oliguria and heavy sweating) several months later, consequently physicians added oral amifampridine 2 mg/6h to previous treatment.
- The hospital approved this “off-label” use of amifampridine, and our department made compounded amifampridine capsules using raw material because of the greater cost of amifampridine 10 mg tablets. Both drugs are being administered by gavage using a stomach tube due to difficult swallowing.
- Combination therapy seemed to facilitate eye opening and limb movement. Amifampridine was better tolerated than pyridostigmine by the patient. He received medical discharge three weeks after starting the new treatment.
- Since then, it was possible to manage the disease at home. However, he required two hospital admissions during the following six months for a respiratory tract infection and an acute respiratory failure. At extrahospitalary level, our department has continued to supply amifampridine capsules upon outpatient prescription, whereas the other compound has been dispensed at community pharmacy.

