

DRUG POINTS

High doses of deferiprone may be associated with cerebellar syndrome

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We report two cases of cerebellar syndrome after treatment with deferiprone, a metal chelator used to treat iron overload in thalassaemia major.

Case 1—A 9 year old boy was treated for two years with 119 mg/kg/day deferiprone, but this dose was not sufficiently effective (increased ferritin and hepatic cytolysis were noted) and was increased to 238 mg/kg/day. Sixteen months later, the patient developed cerebellar syndrome (dizziness, axial hypotonia, nystagmus, diplopia) and obsessive compulsive disorder. Magnetic resonance imaging, electroencephalogram, and cerebrospinal fluid findings were normal. No infection, inflammation, or immunological disorder was present. Three weeks after deferiprone had been stopped, the neurological problems began to resolve and disappeared within one year.

Case 2—A 7 year old girl was treated with deferiprone for two years, with poor compliance. After two months of regularly taking 232 mg/kg/day, she developed cerebellar syndrome (inability to walk in a straight line, impaired motor coordination, nystagmus, and dystonia). Results of C reactive protein testing and magnetic resonance imaging were normal. The symptoms disappeared one month after deferiprone had been stopped.

The development of cerebellar syndrome soon after the dose of deferiprone had been increased and resolution of these problems after the drug was stopped suggests that the drug was responsible for these symptoms. This effect seemed to be related to the high doses—the patients were given doses greater than

the recommended maximum of 100 mg/kg/day—and no other cause was found.

We found no previous reports of an association between deferiprone and neurological disorders. However, this drug has shown great ability to cross the blood-brain barrier, and five patients treated with the usual dose for six months developed subclinical impairments of hearing and vision.^{1,2} In our cases, the high dose may have had a direct toxic effect, or it might have caused excessive loss of other metals chelated by deferiprone (copper, zinc, aluminium, gallium) that are potentially important co-factors for enzyme activity.³

These cases have led to the inclusion of neurological side effects in deferiprone's summary of product characteristics, and confirm that doses greater than 100 mg/kg/day should not be used.

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