Effect of Methionine restricted diet in Molybdenum Cofactor Deficiency in a resource limited setting

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Introduction: Molybdenum cofactor deficiency (MoCD) is a neurometabolic disorder characterized by severe congenital microcephaly, severe global developmental delay, intractable seizure disorder, and spastic quadriplegia. Brain MRI shows brain atrophy, delayed myelination and cystic leukomalacia. MoCD is caused by mutations in the *MOCS1*, *MOCS2*, *MOCS3* and *GPHN* genes. Substrate reduction therapy i.e. substitution of cyclic pyranopterin monophosphate (cPMP) is recommended for MoCD type A. No therapy is yet available for MoCD types B and C. However, methionine restricted diet has been attempted in a few reports with uneven results. We present herewith our results with effects of Methionine restricted diet in 2 patients.

Material & Method: This is a retrospective analysis of biochemical and clinical data in 2 patients with MoCD who were treated with methionine restricted diet. Biochemical data included Urinary levels of Sulfites, Xanthine, Hypoxanthine and Sulfocysteine along with serum levels of sulfocysteine, uric acid and Homocysteine. Genetic studies were done to confirm the diagnosis. Patient 1 was diagnosed to have MOCS2 and patient 2 was diagnosed to have MOCS1. Both patients tried methionine restriction of about 25-30 mg/kg/day. We herewith present the outcome data.

Case reports: We present herewith 2 cases of MoCD. Clinical features in both are mentioned below:

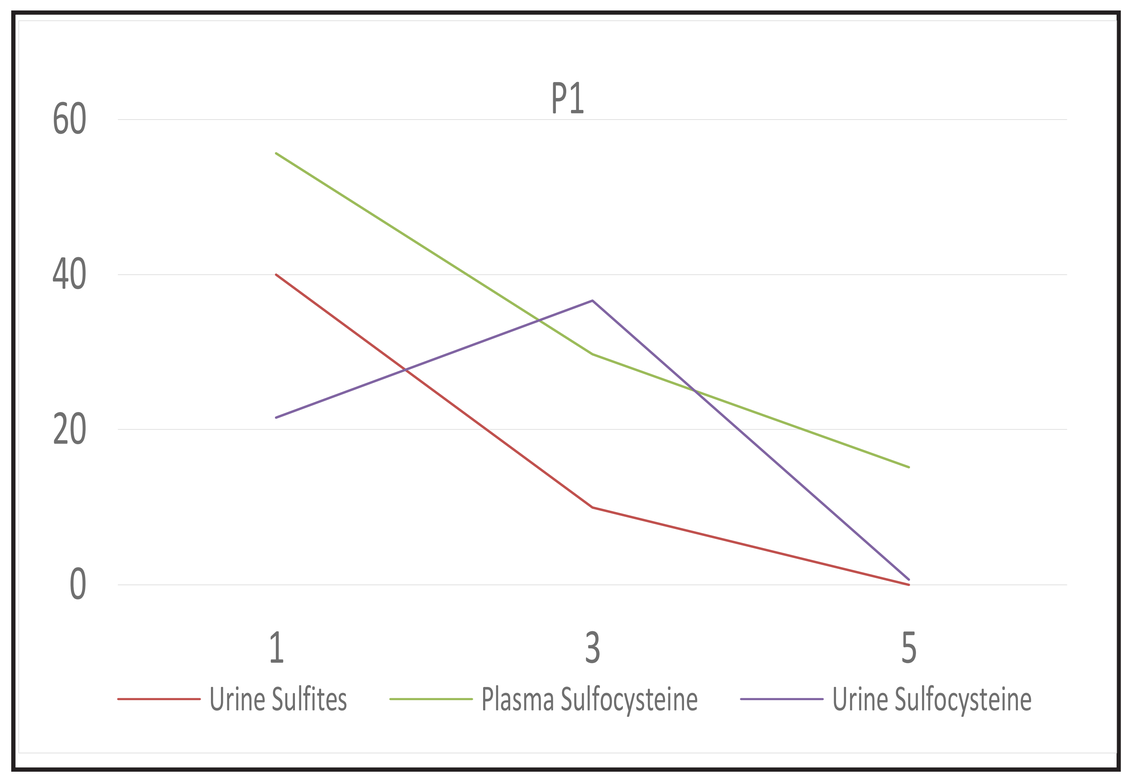
Parameter	Patient 1	Patient 2
Consanguinity	No	No
Birth history	Full term- LSCS	Full term- LSCS
Age at onset	5 months	3 months
Gender	Female	Female
Presenting symptoms	LRTI followed by up-rolling of eyeballs, seizures and loss of head control. Severe seizure disorder	Global developmental delay, seizures, cerebellar atrophy, regression, spasticity, axial hypotonia, dyskinetic movements
MRI	No cystic leukomalacia	Bilateral white matter hyperintensities with basal ganglia hypo intensities
Ectopia-lentis	No	No

Biochemical features are mentioned below:

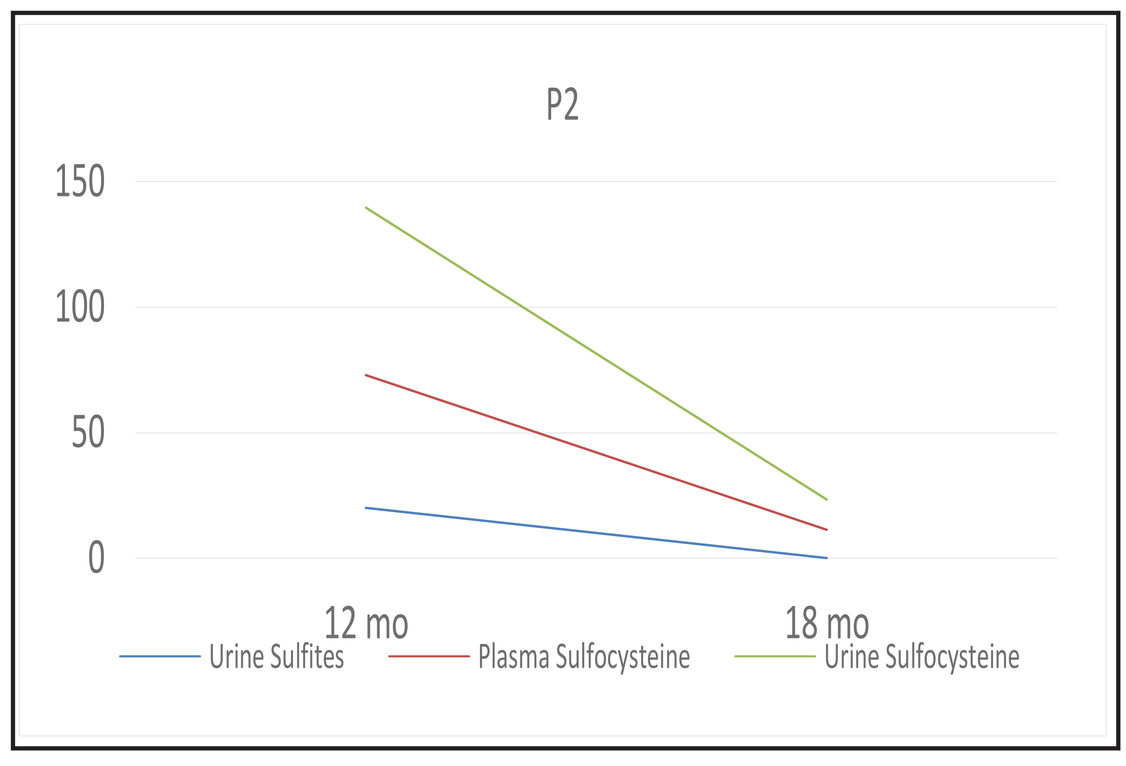
Parameter	Patient 1	Patient 2
Ur. Sulfites	40 mg/L	20 mg/L
Pl. Sulfo-cystine (0 – 5.39 µMol/L)	55.65 uMol/L	72.91 uMol/L
Ur. Sulfo-cysteine (0.26 – 20 µM/mM creat.)	21.61	139.65
Gene affected	*MOCS2*	*MOCS1*
Zygosity	Homozygous	Compound heterozygous
Mutation	Exon4: c.218T>C	Exon 6: c.656 T>G and Exon3: c.374 C>A

Both patients were given methionine restricted diet (2-2.5 g protein/kg/day and about 25-30 mgm methionine / kg / day. Changes in clinical and biochemical parameters were noted after 3 months.

Patient 1: Achieved partial head control, rolling over, sitting with support and reduced frequency of seizures. There was no further deterioration and loss of milestones. After this she was lost for follow up. Biochemical improvement was seen in all parameters.



Patient 2: Showed significant clinical improvement with reduction in seizure frequency, gaining of milestones, weight gain and reduction of spasticity. Biochemically all parameters improved post restriction.



Discussion: MoCD deficiency is a rare autosomal-recessive disorder leading to a combined deficiency of sulfite oxidase, xanthine dehydrogenase, and aldehyde oxidase. MoCD carries a poor prognosis. Therapy with IV cyclic Pyranopterin monophosphate has been shown to benefit MoCD type A only. This compound is ideally initiated at birth at a dose of 80 µgm/kg/d and increased to 240 µgm/kg/d. Neurocognitive outcome is markedly improved and lifelong therapy is recommended. However, this therapy is very expensive and the compound is not available in India. Hence, we tried methionine restricted diet in 2 of our patients. Both our patients have shown improvement in clinical as well as biochemical parameters.

Conclusion: In conclusion, we recommend the clinicians to consider a trial of methionine restriction in patients with mild forms of MoCD at least.

Conflict of Interest: None

References:

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