Srinagarind Hosp Med J 1991; 5(4) : 285-288

Successful treatment of Wilson's disease with zinc acetate solution

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Abstract

A case of Wilson's disease, presented with neurological disorders, was reported. Her symptoms were deteriorated during D-penicillamine therapy and recovered with zinc acetate solution treatment.

Key words : Wilson's disease, zinc acetate solution.

ผลการรักษาโรค Wilson ด้วยสารละลาย zinc acetate

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โรงพยาบาลศรีนครินทร์ คณะแพทยศาสตร์
มหาวิทยาลัยขอนแก่น จังหวัดขอนแก่น

รายงานผู้ป่วยโรค Wilson 1 ราย ที่มีอาการผิดปกติทางระบบประสาทซึ่งมีอาการเลวลงหลังจากได้รับยา D-penicillamine และกลับมีอาการดีขึ้นเมื่อได้กินยาสารละลาย zinc acetate ที่เตรียมขึ้นเองในโรงพยาบาลศรีนครินทร์ ซึ่งมีราคาถูกมาก

INTRODUCTION

Wilson's disease (WD) is an autosomal recessive disorder of copper metabolism. WD is clinically characterized predominately in the liver and/or brain, secondary to excessive accumulation of copper in these organs. Successful therapy depends on producing a negative copper balance. The standard decoppering therapy is treatment with D-penicillamine. However, 10-20% of the patient[1,2], the neurologic syndromes become worse with this drug treatment and never recover to their pre-

penicillamine baseline. Zinc, a known antagonist of copper, has been introduced as an alternative therapy for WD[3]. We herein report a case of WD. Her neurological symptoms became worse during penicillamine therapy and improved after zinc acetate solution treatment. This solution is prepared in Srinagarind hospital which is very cheaper than commercial zinc tablet and D-penicillamine.

Case report

A 25-year-old woman was admitted to our hospital with progressive speech disturbance for 1 year. For about 3 months prior to admission she experienced dystonicity in her arms and legs. From familial history revealed that her brother died at age of 14 years from liver disease.

General examination showed normal findings. Neurological examination revealed an alert woman with marked dysarthria. Her speech was incomprehensible. There were rigidity of all extremities, gait disturbance, persistent retraction of upper lip (figure 1a) and Kayser-Fleischer (K-F) rings in the cornea.

Routine hematological and biochemical tests were within normal limits.

WD was diagnosed and treated with D-penicillamine, started with 250 mg/d for 1 week then stepped up to 500 mg/d. Her speech was improved with decreasing of muscle tone within two weeks. Then she was discharged with 750 mg/d of D-penicillamine for maintenance. Two weeks later, she became worsen with dysarthria and severe ataxia. So we switched to zinc acetate solution (zinc acetate 50 mg/5ml) 150 mg/d, devided in 3 times per day and penicillamine was discontinued. Later on, her symptoms gradually improved within one month. Unfortunately she lost to follow-up. Five months later she developed progressive neurological symptoms as resting and action coarse tremor of trunk and extremities. She could not walk by herself. Retreatment with zinc acetate solution, 150 mg/d improved the symptoms again. On follow-up for 1 year she could close her mouth properly (Figure 1b) and walk without assistance. There was still mild resting tremor of both hands.

Discussion

For about 40% of patients with WD, the first clinical manifestation is neurologic symptoms. Age of onset occurred between 6[4] and 46 year-old[5]. Although excess copper is ubiquitous in the whole brain, the neurologic disturbances are almost completely limited to the motor system. The most common neurologic findings are dysarthria, dystonia, rigidity, gait and postural abnormalities and tremor (resting, action). Chorea and dementia are rare[1].

Apart from clinical manifestations and K-F rings, other criteria for diagnosis includes, serum ceruloplasmin <20 mg/dl, 24-hour urinary copper > 100 mcg and hepatic copper concentration > 250 mcg/gdw. However all of these laboratory studies are not available at Srinagarind hospital.

The goal of treatment is producing a negative copper balance. D-penicillamine, a chelating agent, is effective for removal of copper from the affected organs. However some cases still have deterioration of symptoms while copper removal is adequate. Brewer[2] found that 14/26 case were worse during therapy, usually occurred within one month, and 7/14 cases never recovered to their prepenicillamine baseline. He found from his case that there were new brain lesions, detected by MRI scan, while copper removal was adequate. He proposed that while penicillamine was initially mobilizing the very large storage of hepatic copper, the blood and brain levels of copper still kept rising up for some period of time.

Zinc is an alternative agent for treatment of WD[3]. It blocks the intestinal

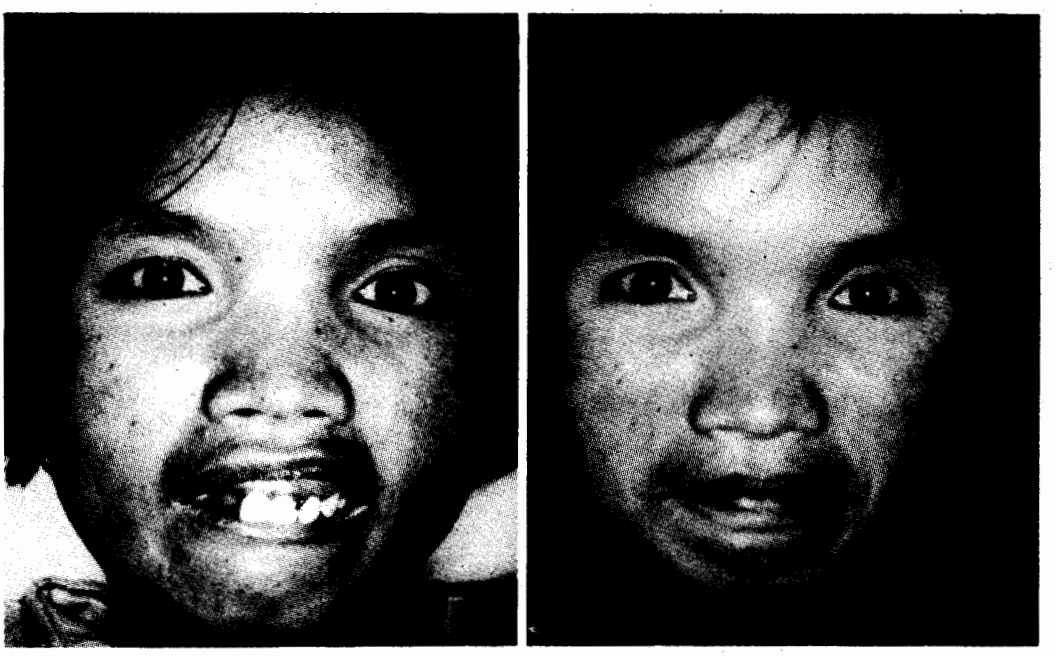
uptake of copper, including the reabsorption of copper secreted in salivary, gastric and certain other alimentary juices, resulting in high fecal excretion of copper. Thus, the dynamics of zinc action involves a "pulling" of copper from the blood, rather than "pushing" of copper into the blood for excretion in the urine, as is the case with penicillamine. Adverse effect of zinc overdose is anemia[6].

Zinc are usually prepared in vitamin tablets which are expensive and in form of zinc sulphate that commonly irritates the stomach. Thus we use zinc acetate solution, prepared in our hospital, which is less gastric irritation, much more cheaper (Table 1) and effective.

According to our case, zinc acetate solution is an alternative therapy of WD, especially for low socio-economic patients.

Table 1 Comparison of the cost between D-penicillamine, zinc tablet and zinc acetate solution

drug	daily dose	cost (baht)/m
D-penicillamine (250 mg)	1-2 g	1074-2148
Z-bec (Zn 22.5 mg)	Zn 45 mg	176.50
สารละลาย zinc acetate (Zn 14.9 mg/5 ml)	Zn 45 mg	25.00



(a) (b)

Figure 1 a. Pre-treatment : persistent retraction of upper lip
b. Post-treatment : the patient can close her mouth

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