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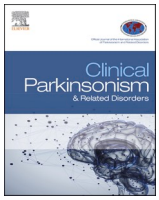

Case Reports

Zinc gluconate for Wilson disease

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ABSTRACT

Due to financial constraints, a patient with Wilson disease required transitioning his maintenance pharmacotherapy from zinc acetate to zinc gluconate. Herein, we report the clinical and laboratory outcomes of this switch and review the relevant literature on the treatment of Wilson disease with zinc. Zinc gluconate can be a viable treatment option for patients with Wilson disease and may be associated with fewer gastrointestinal side effects than zinc acetate and, accordingly, improved long-term compliance and improved clinical outcomes.

1. Introduction

The majority of textbooks, medical websites (e.g., https://www.mayoclinic.org/diseases-conditions/wilsons-disease/diagnosis-treatment/), and review articles indicate that zinc acetate is an accepted therapeutic option for the treatment of Wilson disease [1–3]. Zinc acetate is marketed under the brand name Galzin in the United States and Wilzin in Europe. For uninsured patients, Galzin is quite expensive (50 mg PO TID x 30 days > $350, 18AUG2024, https://www.goodrx.com). For insured patients, co-payments can also be burdensome. As such, patients may explore alternative options such as zinc gluconate, zinc citrate, zinc glycerol, zinc picolinate, or zinc monomethionine. These "alternative" forms of zinc can be purchased through a variety of online distributors. For example, a search of the https://www.amazon.com website on 18AUG2024 with the term "zinc citrate" generated 115 results, "zinc acetate" generated 29 results, "zinc monomethionine" generated 21 results and "zinc picolinate" generated 138 results. In the United States, Good Manufacturing Practice (GMP) requirements of the the Federal Drug Agency (FDA) are less stringent and more flexible for supplements than prescription drugs. For example, supplements do not require an expiration date or associated stability testing (Code of Federal Regulations, Title 21; https://www.ecfr.gov/current/title-21). Patients and their treating physicians may be concerned and confused regarding the most appropriate zinc formulation to use. Here we report a patient no longer able to afford Galzin therapy and successful transition to zinc gluconate.

2. Case report

The male patient was diagnosed with Huntington disease at 33 years of age. He presented with an asymmetric action tremor of the upper extremities and mild dysarthria. Kayser-Fleisher rings were present on initial clinical examation. Diagnostic findings included mild cirrhosis, splenomegaly, mild portal venous hypertension, and slight elevation of liver enzymes (aspartate transaminase [AST]: 42 IU/L, 0 – 40 IU/L; alanine transaminase [ALT]: 73 IU/L, 0 – 55 IU/L). His initial treatment was zinc acetate and he was prescribed zinc acetate 50 mg capsules (Galzin, Teva Pharmaceuticals, Tel Aviv-Yafo, Israel; 50 mg elemental zinc) one PO TID for over 15 years. His neurological examination nearly normalized within one year of zinc therapy. His liver function testing and imaging studies of cirrhosis also improved. With zinc acetate, he experienced intermittent gastrointestinal cramping, upper gastrointestional pain, and occasional nausea, particularly with his first morning dosage. He would typically take zinc acetate with food that included protein to limit gastrointestinal side effects. Yet, he was intermittently non-compliant with TID dosing due to residual side effects. In 2022 his insurance plan would no longer cover Galzin. After discussion of therapeutic options, the patient was switched to zinc gluconate 50 mg tablet (Rugby® Laboratories, Livonia, Michigan, USA; 50 mg elemental zinc; $7.93 for 100 capsules on 17AUG2024) one PO TID. He has had virtually no gastrointestinal side effects with zinc gluconate and his 24 hr urine copper results showed quantitative improvement (Table 1). In addition, his 24 hr zinc levels increased. As seen in the Table 1, 24 hr urine copper levels have been inversely correlated with 24 hr zinc levels. His neurological and hepatological conditions have remained stable on zinc

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Table 1
Serial Laboratory Testing.

Date	Therapy	24 hr urine copper	24 hr urine zinc	24 hr urine creatinine	Serum creatinine	Urine creatinine
06FEB2024	zinc gluconate	74 μg/24hr (9–71 ug/24hr)	3759 μg/24hr	*NA	NA	NA
21APR2023	zinc gluconate	99 μg/24 hr (9–71 μg/24hr)	3165 μg/24hr	1.69 g/24hr (0.98 – 2.20 g/24hr)	1.31 mg/dl (0.67 – 1.17 mg/dl)	77.9 mg/dl
15JUL2021	zinc acetate	140 μg/24 hr (9–71 ug/24hr)	2832 μg/24hr	NA	1.34 mg/dl (0.67–1.17)	74.0 mg/dl
23DEC2020	zinc acetate	180 μg/24 hr (9–71 μg/24hr)	NA	2.43 g/24hr (0.98 – 2.20 g/24hr)	1.36 mg/dl (0.67–1.17 mg/dl)	NA
04APR2019	zinc acetate	173 μg/24 hr (3 – 35 μg/24 h)	2756 μg/24 hr	2.026 g /24 hr (1.0 – 2.0 g/24hr)	NA	64.4 mg/dl

*NA, not acquired.

gluconate. His most recent ALT and AST were 52 U/L (range: 0–41 U/L) and 38 U/L (0 – 40 U/L), respectively.

3. Discussion

Zinc may be used as first-line therapy for patients with Wilson disease, particularly in asymptomatic or minimally symptomatic patients [4]. Zinc is commonly used for maintenance therapy. In the context of Wilson disease, zinc works by inducing synthesis of metallothionein in enterocytes and inhibiting the absorption of copper [5]. Recent guidelines do not address potential differences in side effects among the various zinc salts [4]. Moreover, clinicians should be aware that the bioaccessibility of zinc in dietary supplements may show significant variability [6]. The Wilson Disease Association (https://www.wilsondisease.org) reports that zinc gluconate is "friendlier on the stomach" and provides a link to Gluzin™ (50 mg zinc gluconate, $27.99/60 capsules, 18AUG2024). Compliance with zinc therapy is critical and the potential for reduced side effects with zinc gluconate should be expected to improve long-term outcomes. Long-term prospective controlled studies comparing the efficacy and tolerability of zinc acetate and zinc gluconate have not been completed. A randomized intervention study showed that zinc gluconate was non-inferior to zinc acetate in reducing hepatic copper content after 4 weeks of therapy [7].

In summary, zinc gluconate is a viable treatment option for patients with Wilson disease and, like zinc acetate, should be dosed TID [7]. Brewer and colleages have shown that the minimum effective dosage of zinc is 25 mg administered TID [1]. Once daily dosing is significantly less effective than BID dosing and TID dosing is commonly used to provide a margin of safety for noncompliance [8]. Along with serial neurological examinations and laboratory testing of liver function, urine copper and zinc levels should be monitored during the course of zinc therapy and within a few months of switching zinc formulations. In this regard, there is no guarantee that product bioaccessibility for supplements will remain consistent over time.

4. Financial disclosures

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5. Ethics statement

The subject of this case report provided written informed consent for publication of his clinical history, radiographic images, and video.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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