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Maintenance therapy for Wilson disease with zinc: A comparison between zinc acetate and alternative zinc salts

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Background and aims: Our study evaluates treatment of Wilson Disease (WD) with zinc (Zn) acetate (FDA approved) and alternative Zn salts. Studies examining the effectiveness of Zn in WD are few and data on alternative Zn salts is limited. We describe one of the largest recent cohort studies of WD patients on Zn therapy and aim to improve our understanding of Zn as a treatment option.

Method: Single center retrospective review of 59 WD patients (age 6-88y, 32 females) treated with Zn (50-150mg) from 0.8 to 52 years (median 26y). Most patients (n = 39) were on prior chelation therapy. An online survey was used to explore patients' experience using different Zn salts. We contacted 56 subjects; 31 completed the survey.

Results: Treatment response was evaluated using ALT and 24h urine Cu. Urine Cu excretion (µg/24h) was categorized as low < 25, target 25-100, or elevated > 100. Levels > 100 suggest medication or diet non-compliance, or treatment failure. Levels < 25 may indicate overtreatment. Target range was reached in 60% on Zn acetate, 65% on Zn gluconate and 50% on alternative Zn. Low urine Cu was not associated with a high ALT. Serum ALT was expressed as normal or a multiple (1-2, 2-3 or > 3 x) of the upper limit of normal (ULN). ALT was normal in 75% with target urine Cu but only in 16% with urine Cu > 100µg. ALT elevations were not significantly different between Zn Salts (34% Zn acetate, 21% Zn gluconate and 28% alternative Zn, Kruskal-Wallis, p = 0.26).

Our online survey showed the mean age at diagnosis to be 18 years (2-43y). The average age of starting Zn was 26.8 years (3.5-65y). Most were on Zn acetate (45%) followed by Zn gluconate (42%). The majority were taking non-prescription Zn. Prior to Zn treatment 45% were symptomatic (45% neuro, 25% liver and 20% psychiatric). The majority (80%) had no WD symptoms on Zn. Only one person took Zn incorrectly. Most (80%) had previously been on alternative WD treatment. Patients switched from a different Zn salt (38%) mainly due to GI side effects (Zn acetate n = 11, Zn gluconate n = 5, Zn sulfate n = 1). Most reported no side effects on current Zn therapy (67%). Gastric side effects were experienced in 32%.

		Zn Acetate (n = 26)			**Zn Gluconate (n = 19)**			**Alternative Zn (n = 7)**		
Urine Cu (mcg/24h)		< 25	25-100	> 100	< 25	25-100	> 100	< 25	25-100	> 100
ALT	Normal	2	15	0	2	12	1	2	3	0
	1-2xULN	0	5	0	0	2	0	0	1	1
	2-3xULN	0	1	1	0	0	0	0	0	0
	3-4x ULN	0	0	2	0	1	1	0	0	0

Conclusion: Effective treatment with Zn preparations is possible in many WD patients. The potential for treatment failure in some suggests close monitoring is paramount for individuals on zinc therapy without both a normal ALT and an appropriate urine Cu excretion. More clearly defined parameters determining treatment success or failure will inform our clinical decision making for continuation of Zn treatment or a timely change to alternative therapy.