

P1-12 Trientine® Treatment Mimicking Severe Hyperandrogenism

¹ Gerhard Binder, ¹ Karin Weber, ² Stefan A. Wudy, ³ Paul-Martin Holterhus, ¹ Steffen Hartleif

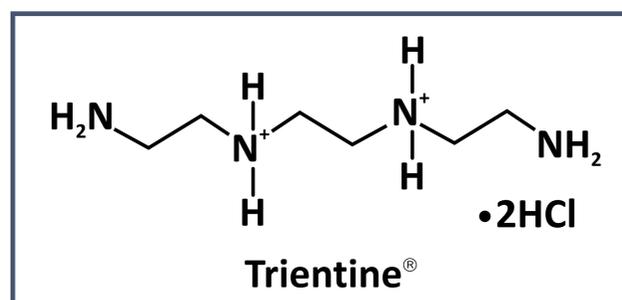
¹ University Children's Hospital, Pediatric Endocrinology and Gastroenterology, Tübingen, Germany

² Center of Child and Adolescent Medicine, Division of Pediatric Endocrinology & Diabetology, University of Giessen, Germany

³ Department of Pediatrics, Division of Pediatric Endocrinology and Diabetes, University of Kiel, Germany

Introduction

Drugs can interfere with immunoassays causing false measurements. This is the first report of an interference of Trientine® with two chemiluminescence assays causing falsely high measurements of testosterone and androstendione. Trientine® (triethylene tetramine dihydrochloride) is a chelator of copper and is used in the treatment of patients with Wilson's disease as alternative for penicillamine. Trientine® mainly increases urinary copper excretion leading to a negative copper balance. Serum concentrations of Trientine® under treatment are not known.



Case Report

A 16 year old German girl with recently diagnosed Wilson's disease treated with 750 mg Trientine® daily presented with post-pill oligomenorrhea. She was mildly overweight (BMI 24.9 kg/m²), but had no hirsutism or other signs of hyperandrogenism.

In her serum extremely high levels of androgens were measured by Immulite chemiluminescence assays. This was unexpected and not confirmed by LC-MS/MS (Table 1). In addition, 24h-urine collection contained normal amounts of androgen metabolites as determined by GC-MS.

Table 1 Different androgen serum concentrations measured by chemiluminescence or by LC-MS/MS

		Chemiluminescence assay	LC-MS/MS	Reference
Testosterone	ng/dl	384	57	<45
Androstendione	ng/dl	720	116	<157

After a drug pause for two days the patient had normal testosterone (43 ng/dl) and androstendione (195 ng/dl) serum concentrations in chemiluminescence assays.

Hypothesis

The false-high measurement of androgens is caused by interference of Trientine® with the luminescence reaction of the assay, which includes alkaline phosphatase and dioxetane phosphate.

In general, the chemiluminescence signal is inversely correlated to the read of the assays. In agreement with our hypothesis after spiking of human serum with pure substance of triethylene tetramine dihydrochloride serum probes showed increasing testosterone concentration values (Table 2).

Table 2 Increase of serum testosterone reads after spiking with triethylene tetramine dihydrochloride

Spiked with triethylene tetramine dihydrochloride reaching a concentration of [mg/ml]	Testosterone [ng/dl]			
	Probe 1	Probe 2	Probe 3	Probe 4
0	<15	35	143	264
10	<15	55	not done	336
20	26	50	not done	340
33.3	21	57	278	460
100	28	71	268	432

Conclusions

The drug Trientine® very likely interferes with two chemiluminescence assays causing false high measurements. Therefore, chemiluminescence assay results have to be interpreted with caution in patients treated with Trientine® and should be confirmed by MS if values are unexpected.