

OVERDOSE OF METHIMAZOLE

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Objective

The acute toxicity of organic thiourea antithyroid drugs is considered as low. In contrast to reports about adverse effects due to therapeutic use (1) human poisoning cases were not known up to now. Firstly, the aim of the study was to evaluate the cases of acute overdose. Secondly, we present the lethal course of a chronic overdose.

Case Report

Patient: 84-year-old woman

Route of exposure and dose:

The patient was treated with methimazole 5 mg/d since two years. The daily dose was not changed despite of a chronic renal failure.

Time of admission:

3 weeks after onset of gastrointestinal symptoms

Clinical features:

➤ Initial symptoms:

Gastrointestinal discomfort with **nausea and sense of fullness in the abdomen** over some weeks.

➤ Symptoms at time of admission:

Grave general condition because of the reduced nutritional status.

Hypotension (RR 105/70 mmHg)

Atrial fibrillation (HR 110/min)

Anemia (Hb 7.14 mmol/L; normal 7.62 - 9.50)

Myoglobinemia (279.9 ng/mL; normal 25 - 58)

Renal failure (creatinine 775.5 μ mol/L; normal 44 - 80; uric acid 912.1 μ mol/L; normal < 340; BUN 34.2 mmol/L; normal <11.9)

Hyperkalemia (6.83 mmol/L; normal 3.6 - 5.5;)

Hyperglycemia (BG 9,3 mmol/L)

Thyroid status:

TSH: 46 mE/L (normal 0.27 - 4.20)

T3: 2.56 pmol/L (normal 3.90 - 6.70)

T4: 2,75 pmol/L (normal 12.0 - 22.0)

Treatment and course:

- Substitution of levothyroxine, insulin and hydrocortisone.
- Analgo-sedation; treatment for respiratory depression and cardiac failure; blood pressure couldn't be stabilized despite of increasing doses of catecholamines.
- Death following multiorgan failure one day after admission.

Mechanism of action

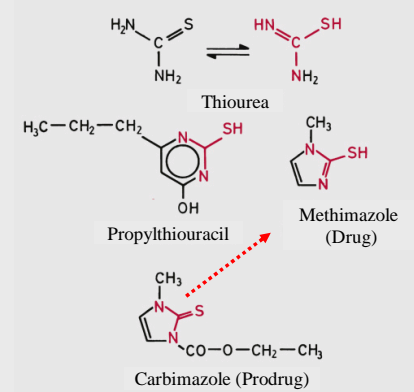
- ➔ Inhibitors of the thyroidal peroxidase:
Inhibition of incorporation of iodine in the tyrosine groups of thyroglobulin.

Consequences

- ➔ Onset of action with latency of 1 to 4 weeks.

(in case of poisoning 3 - 4 days ?)

- ➔ Iodine acts as a competitive inhibitor.

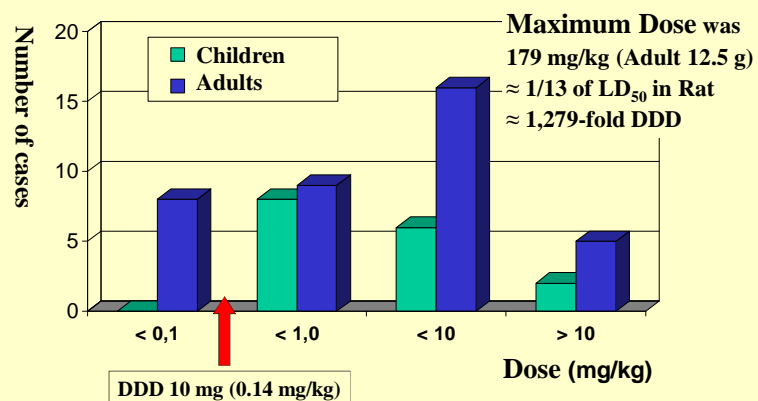


Toxicity of thiourea derivatives

Tabelle 130. Akut letale Dosen einiger Thioharnstoffe und Thiourazilderivate
Hauschild (1973) - Tab. 130

	LD ₅₀ oral	Species
Thiourea	1,8 g/kg	Rat
Allylthioharnstoff	0,85 g/kg	Rat
α -Phenylthioharnstoff	0,02 g/kg	Rat
α -Naphthylthioharnstoff	0,007 g/kg	Rat
Thiourazil	3,7 g/kg	Rat
Methylthiourazil	2,5 g/kg	Rabbit
Thiosemikarbazid	0,013 g/kg	Rat
Methimazole	2,25 g/kg	Rat (RTECS)

Methimazole - Poisoning cases 1994 to 2010



Conclusions

- No specific poisoning symptoms will be expected after single overdose of methimazole.
- It is unknown whether hormonal status will be changed when a very high dose was ingested. In such cases we recommend the control of thyroid-stimulating hormone and thyroid hormones few days after ingestion.
- In chronic overdose the hormone synthesis may be depressed dramatically resulting in a life-threatening hypothyroidism.

Literature

(1) Bartalena L, Bogazzi F, Martino E. Adverse effects of thyroid hormone preparations and antithyroid drugs. Drug Saf. 1996; 15:53-63.