

KETOCONAZOLE: MEDICAL TREATMENT OF CUSHING'S SYNDROME

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Background

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In Cushing's syndrome (CS), when surgery is unsuccessful or contraindicated, ketoconazole is the drug most frequently used to treat hypercortisolism.

On July 2013, European Medicines Agency (EMA) announced their negative risk-benefit assessment for oral ketoconazole as treatment of fungal infections, because it can cause liver injuries and drug interactions by cytochrome P450 inhibition.

Ketoconazole was suspended as antifungal in European Union, but **compassionate use is authorized for CS.**

Purpose

Analysis of hormonal effects and tolerance of ketoconazole in CS on last year.

Material and methods

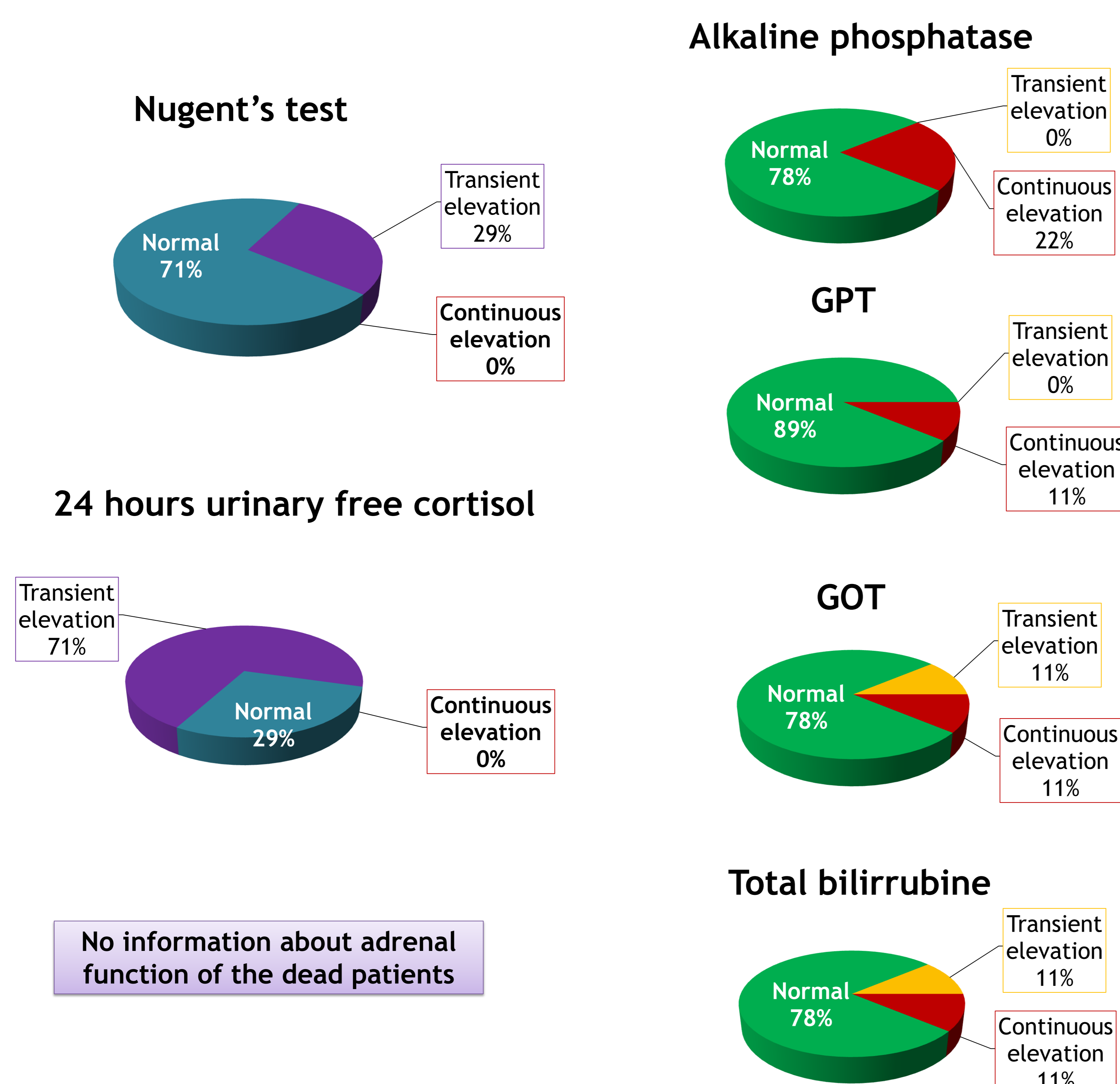
• **9 patients** [32-83 years-old] were treated at hospital. All patients were retrospectively studied with a follow-up of 26 months, whose treatment had lasted from 12 days-25 years. One patient had ectopic ACTH production, two had pituitary adenoma, and six had adrenal neoplasia. Four patients had previous surgery, but it was not effective in two cases. Ketoconazole dose was between 200-1200 mg/day.

• **Hepatic measures** were controlled transaminases, total bilirrubine and alkaline phosphatase.

• **Hormonal control** was observed with Nugent's test and 24 hours urinary free cortisol.

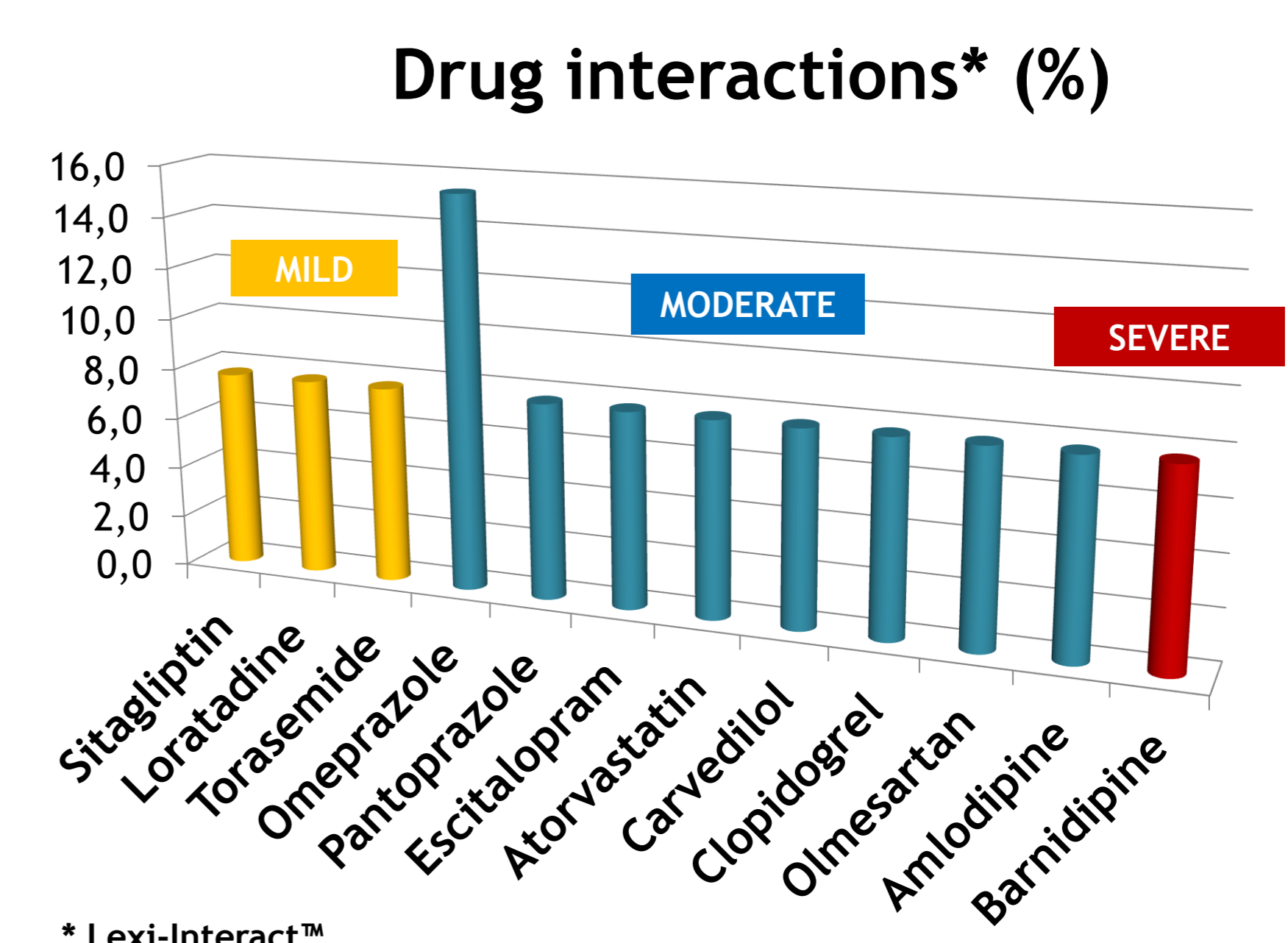
• **Current therapy** of patients was collected to detect **drug interactions.**

Results



No information about adrenal function of the dead patients

77.8% of the patients had some possible drug interaction



5/9 patients stopped ketoconazole

1	a potential drug interaction with calcium antagonism
2	dead for metastatic cancer
2	adrenal surgery

Conclusions

Ketoconazole seems to be a safe and efficacious treatment in CS. But it requires periodic monitoring of adrenal and liver functions and to control drugs interactions.

However, it would be necessary performing a study with more patients to get significant conclusions.