

Ketoconazole in Cushing's Disease Management

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BACKGROUND:

Transphenoidal surgery is still the best initial therapy for Cushing's disease (CD), with a high probability of cure and few risks or complications. However, pharmacotherapy has a role as primary or adjunctive therapy: when surgery is delayed, in case of postoperative persistence or recurrence of hypercortisolism, or while waiting for radiotherapy effectiveness. Ketoconazole, a steroidogenesis inhibitor, is nowadays the main drug used to CD control by reducing cortisol levels, with potent antisecretory efficacy in majority of cases, and relatively rare major side effects (anaphylaxis and fulminant hepatitis), but its use remains controversial.

OBJECTIVE:

The present study aims to assess the efficacy and tolerance of ketoconazole in CD and evaluate the benefit/risk balance.

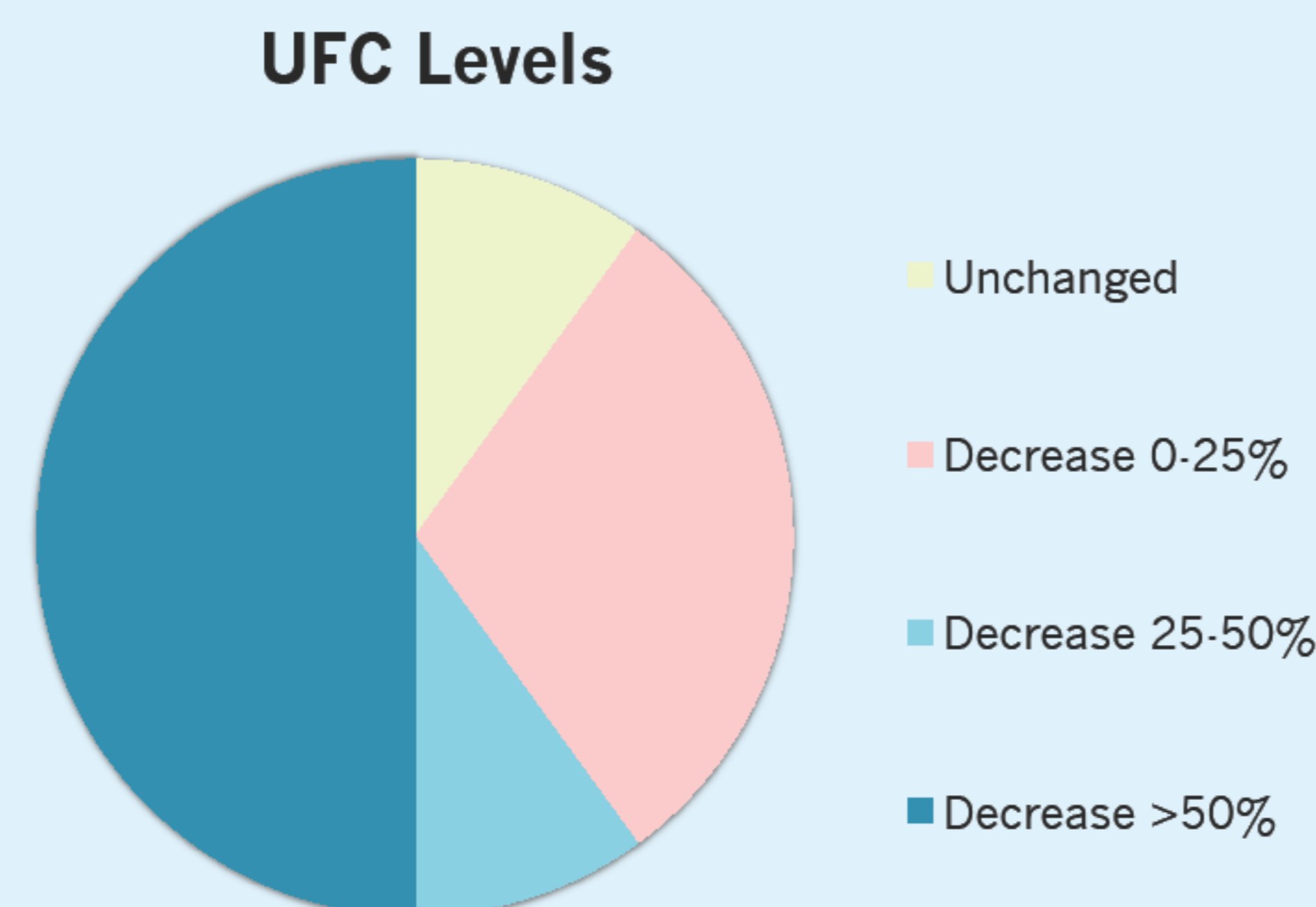
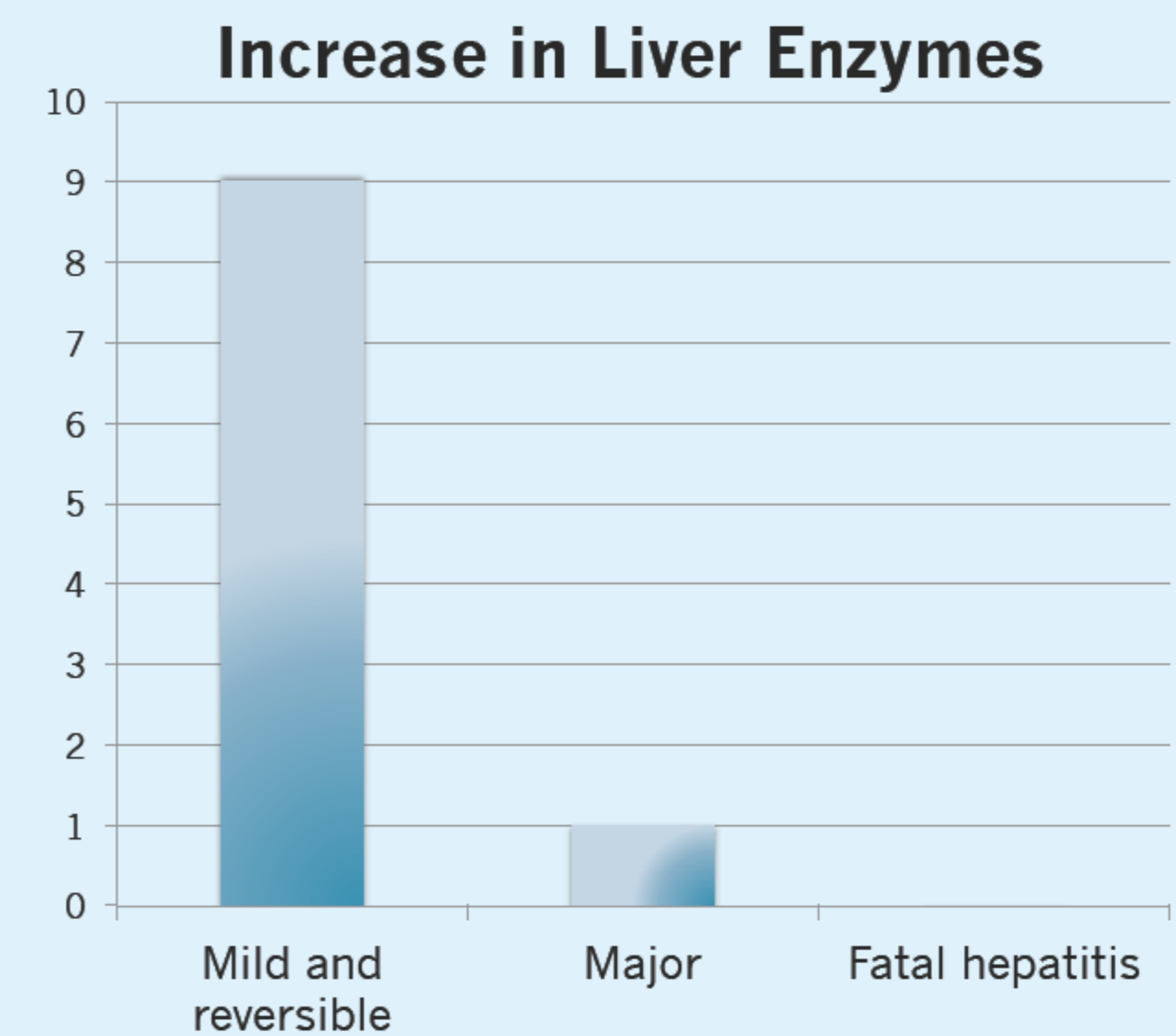
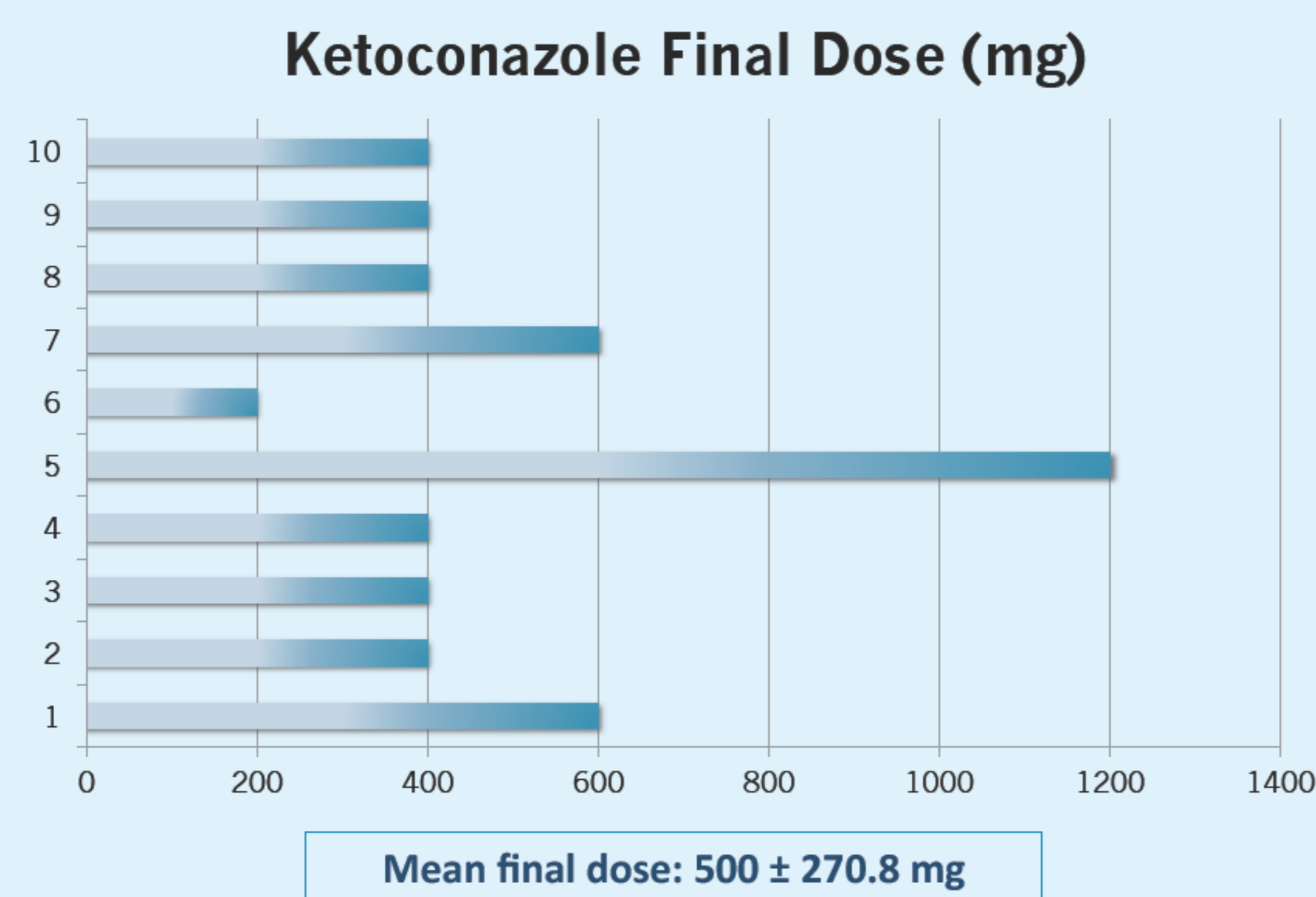
PATIENTS AND METHODS:

We reviewed 10 present cases of CD treated with ketoconazole in our center, with a mean follow-up of 16±15.3 months (0.25-40). Clinical assessment included age, gender distribution, BMI, blood pressure, levels of serum cortisol and ACTH, urinary free cortisol (UFC), hepatic function, lipid profile, glucose and Hb A1c levels, hypokalemia and GI tolerance.

RESULTS:

Baseline Characteristics	
Total of patients, n	10
Gender, n (%): Male	2 (20.0%)
Female	8 (80.0%)
Mean age, years	43.7±13.01
Mean BMI, Kg/m ²	29±6.2

Ketoconazole – Treatment duration	
9 patients	3-40 M
	1 suspended the drug after 3 M due to liver toxicity
	1 suspended the drug after 13 M due to an infectious intercurrent
1 patient	suspended the drug after 1week due to GI intolerance



No statistically significant difference was found on blood pressure, lipid profile, glucose and Hb A1c levels or hypokalemia.

CONCLUSION:

Ketoconazole is a safe and efficacious drug in CD, but has the potential hepatotoxicity that requires careful selection of patients and subsequent clinical and biochemical monitoring.