

Acute Kidney Injury Due to Interaction of Methyl-1-testosterone with Ciclosporin Metabolism in a Patient with Severe Atopic Dermatitis

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ABSTRACT

Ciclosporin is widely used in a number of inflammatory disorders and has the potential for drug interactions. We report here a case of acute kidney injury due to the interaction of ciclosporin with methyl-1-testosterone. This has not been previously reported and it is relevant as methyl-1-testosterone can be purchased online. Physicians should be aware

of any over the counter or online purchased “supplements” and consider possible drug interactions.

Keywords: Acute kidney Injury; Ciclosporin; Dermatitis; Dermatology; Drug interaction; Methyl-1-testosterone

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INTRODUCTION

Ciclosporin is widely used in a number of inflammatory disorders and has the potential for drug interactions [1]. We report here a case of acute kidney injury due to the interaction of ciclosporin with methyl-1-testosterone. This has not been previously reported and it is relevant as methyl-1-testosterone can be purchased online.

CASE REPORT

A 29-year-old male patient with longstanding atopic dermatitis was referred to the dermatology outpatient department (Dermatology Department, York Hospital, UK) with a history of rapid deterioration of his condition despite optimal topical therapy. Due

to the severity of the symptoms and condition, he was started on systemic ciclosporin (3.0 mg/kg, twice daily). His ultimate ciclosporin dose was 4.0 mg/kg which was gradually increased from the initial dose of 3.0 mg/kg. The patient's baseline findings are presented in Table 1. Good clinical response was achieved whilst on ciclosporin and he was maintained on it for 4 months (the later 3 months on the maximum dose) with stable serial blood tests.

During routine follow-up, he was found to be in acute renal impairment with urea of 17 $\mu\text{mol/L}$, creatinine of 266 $\mu\text{mol/L}$ and deranged liver function tests with bilirubin 37 $\mu\text{mol/L}$, alanine transaminase 304 U/L and aspartate transaminase 48 IU/L. Investigations included a urine dipstick and renal ultrasound which were both normal. The ciclosporin level during routine follow-up was elevated (trough level 622 $\mu\text{mol/L}$) despite consistency with the dose over 3 months and two stable previous blood tests.

On direct questioning, the patient admitted that he had been recently taking a "supplement". The patient had purchased this

over the Internet from an online shop and this was dispatched along with some written information. Subsequently, the "supplement" was found to be oral methyl-1-testosterone (systematic name: 17 alpha methyl-17beta-hydroxy-androst-1-ene-3-one). The patient discontinued both ciclosporin and methyl-1-testosterone and his renal function and liver function tests returned to normal within 1 week. The patient had been administered irregular amounts of methyl-1-testosterone with no regular pattern. Atopic dermatitis gradually flared up over 3 months and was treated with ultraviolet B phototherapy as he was reluctant to restart ciclosporin treatment.

Informed consent was obtained from the patient for being included in the study. This article does not contain any studies with human subjects performed by any of the authors.

DISCUSSION

A detailed review of pharmacokinetics and metabolism of ciclosporin and sex steroids revealed the likely cause of his acute kidney injury. Ciclosporin is produced as a metabolite by the fungus species *Beauveria nivea* and is extensively metabolized by hepatic cytochrome P-450 enzymes [1]. It is an immunosuppressive agent with a narrow therapeutic index [2]. Since ciclosporin is primarily metabolized by the cytochrome P-450 enzymes in the liver and hepatic function plays an important role in its metabolism [1, 2], concurrent administration of other drugs that are metabolized by the hepatic P-450 enzyme system (e.g., ketoconazole) may alter ciclosporin concentrations in the blood [1, 2].

Methyl-1-testosterone is an orally active derivative of the potent anabolic/androgenic

Table 1 The baseline findings for the patient

Test (units)	Patient	Normal range
Blood pressure (mmHg)	125/70	–
Renal function test		
Urea ($\mu\text{mol/L}$)	6.3	2.8–7.2
Creatinine ($\mu\text{mol/L}$)	93	59–104
Liver function test		
Aspartate transaminase (IU/L)	48	30–120
Alanine transaminase (IU/L)	31	0–45
Bilirubin ($\mu\text{mol/L}$)	12	1–25

IU international unit

steroid 1-testosterone [3]. Methyl-1-testosterone is an illegal, unlicensed drug and finds its way into Internet commerce through lack of regulations. Due to its structure, it is entirely metabolized by the liver and has high hepatotoxicity compared to other anabolic steroids [4, 5].

Methyl-1-testosterone could compete with ciclosporin for metabolism by microsomal cytochrome P-450, the major recognized metabolic pathway for both drugs in the liver [6, 7]. Cholestasis is a well-recognized side effect of methyl-1-testosterone and, as ciclosporin is eliminated through biliary excretion, reduced biliary flow can result in increased ciclosporin levels leading to nephrotoxicity [3]. The peak ciclosporin levels in our patient correlated with the commencement of methyl-1-testosterone administration and returned to normal within a week of discontinuing it. Furthermore, the blood tests were normal on two separate occasions prior to the commencement of methyl-1-testosterone administration despite continuing on the same ciclosporin dose.

Testosterones are not listed in British National Formulary as interacting with ciclosporin [8]. In our patient, although it is possible that the rise in creatinine could have been due to an increase in the muscle bulk, the trough ciclosporin level of 622 $\mu\text{mol/L}$ is very high, suggesting impaired metabolism. It is recommended that in patients treated with ciclosporin, renal and liver function tests should be routinely monitored every 2 weeks during the initial 3 months of therapy and then monthly if the results are stable.

CONCLUSION

Prior to starting a patient on ciclosporin, a careful drug history should include enquiries

about over-the-counter medications and supplements purchased via the Internet. Our case highlights the dangers of so-called “supplements” purchased online that can have detrimental effects due to drug interactions. To our knowledge, the interaction of methyl-1-testosterone with ciclosporin has not been reported in the literature.

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Conflict of interest. Dr. Al-Niaimi and Dr. Lyon declare no conflict of interest.

Compliance with ethics guidelines. Informed consent was obtained from the patient for being included in the study. This article does not contain any studies with human subjects performed by any of the authors.

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