C03 – Diuretics
5PSQ-016

TOLVAPTAN ASSOCIATED CREATINE KINASE ELEVATION IN TWO PATIENTS WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE

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BACKGROUND AND IMPORTANCE

Autosomal dominant polycystic kidney disease (ADPKD) is a genetic disorder that causes kidney damage. The treatment goal is to postpone renal failure; however, there were not specific treatments for ADPKD until tolvaptan (Jinarc®, Otsuka Pharmaceutical) was approved. Tolvaptan is an arginine-vasopressin-receptor antagonist that is taken by oral route, 45mg in the morning and 15mg in the evening.

AIM AND OBJECTIVES

To present two cases of tolvaptan-associated-toxicity

MATERIALS AND METHODS

The two cases reported were diagnosed and monitored by a specialized nephrologist in outpatient visits in our center. Tolvaptan was dispensed in the outpatient pharmacy, and laboratory test were performed to evaluate patients' evolution. When there was a suspiction of tolvaptan-associated-toxicity the clinical team reviewed electronic clinical records and laboratory tests.

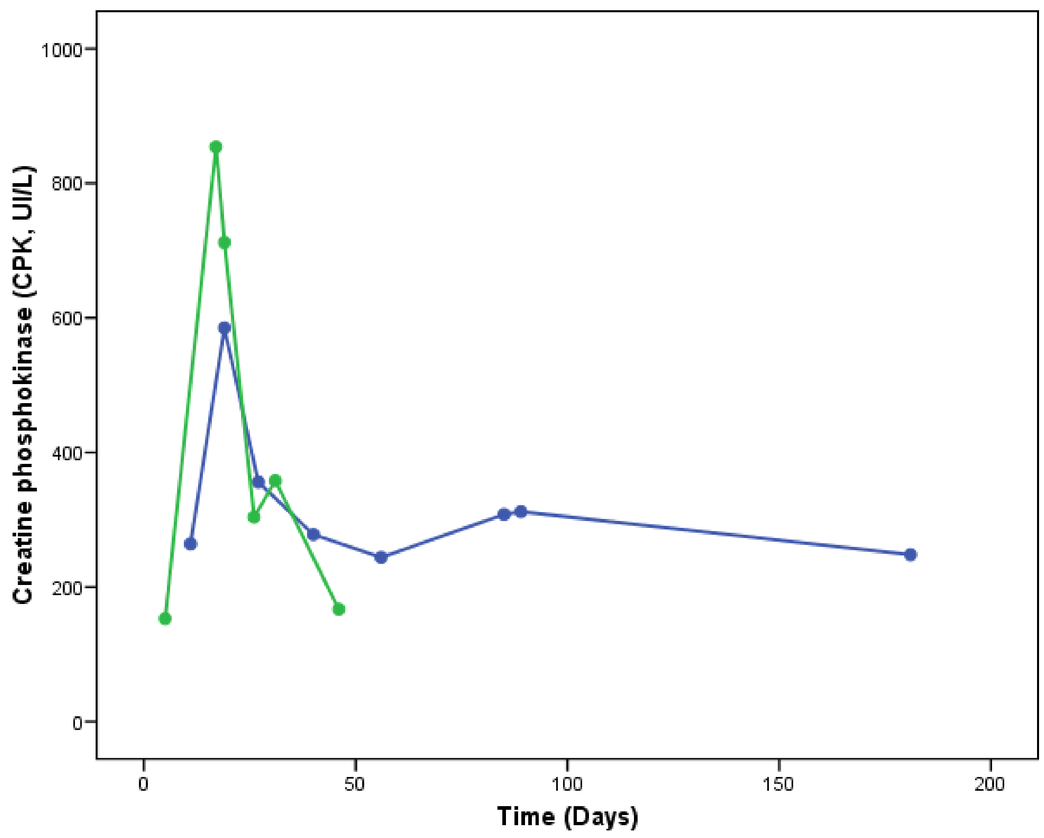
CASE 1

A 43-year-old man with ADPKD, whose mother had ADPKD, had been using losartan, carbonate calcic, manidipine, valsartan and hydrochlorothiazide for symptoms control. He started tolvaptan at the lowest dose and it was well tolerated; weeks after, an increase of creatine phosphokinase (CPK) plasma levels were detected. Tolvaptan was stopped. The patient reported he felt better after treatment discontinuation.

CASE 2

A 41-year-old man with ADPKD, whose mother and siblings were also affected, was treated with enalapril, amlodipine and allopurinol. He initiated tolvaptan at the lowest dose with good tolerance. An increase of CPK was detected, treatment was stopped (all other treatments continued) and CPK plasma levels were reduced.

	Date	Days of treatment *Days after treatment cessation	CPK (UI/L) [55-171 UI/L]	Creatinine (mg/dL)
CASE1	11/12/2018	11	264	1.73
	19/12/2019	19	585	1.74
	27/12/2018	*7	356	1.72
	09/01/2019	*20	278	1.8
	15/02/2019	*36	244	1.64
	13/03/2019	*65	308	1.88
	17/03/2019	*69	312	1.82
	29/05/2019	*161	248	1.82
CASE2	10/05/2019	5	153	1.62
	22/05/2019	17	854	1.65
	24/05/2019	*1	712	1.55
	30/05/2019	*8	304	1.76
	05/06/2019	*13	358	1.72
	30/06/2019	*28	167	1.58



Neither patient 1 nor patient 2 showed clinical symptoms or liver enzymes (alanine and aspartate transaminase) elevation. They reported that they had not taken other treatments and had occasionally performed moderate exercise, as usual. In the absence of other justification, according to the *Naranjo*-causality-assessment, it is probable (6 points) that tolvaptan caused hyperCKemia.

CONCLUSIONS AND RELEVANCE

These are the first cases of tolvaptan-induced-hyperCPKemia reported. HyperCPKemia could be common in ADPKD patients taking tolvaptan and might be underestimated; therefore, it is advisable to monitor CPK serum concentration in these patients.

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