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LETTER TO THE EDITOR

Tramazoline turns asymptomatic into symptomatic hyper-CK-emia

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Sir,

Many drugs are myotoxic, manifesting as muscle aching, myalgias, cramps, weakness, rhabdomyolysis, elevated muscle enzymes, or malignant hyperthermia [1]. If there is a pre-existing asymptomatic or symptomatic primary myopathy myotoxic drugs may uncover the asymptomatic defect or even worsen the symptomatic disorder. Myalgias, muscle cramps, triggered by long-term misuse of tramazoline in a patient with asymptomatic hyper-CK-emia has not been reported.

A 26-year-old, HIV-negative, Caucasian male with a history of febrile seizures in childhood, reported exercise-induced myalgias since 2 years and occasional cramps of the pectoralis muscles. Also since 2 years CK was repeatedly elevated, initially being attributed to intensive sport activity (Table 1). Later on, metabolic myopathy was suspected but muscle biopsy revealed only mild myopathic features such as atrophic fibers, regenerating fibers, discrete fiber splitting, type-II-fiber predominance, one Ringbinde, utrophin-up-regulation, and disseminated endomysial and interstitial round cell infiltrates. Polymyositis and inclusion-body-myositis were excluded by the absence of HLA class 1 antigen-up-regulation and invasive CD8-positive T-lymphocytes. Re-evaluation in February 2006 revealed that he was addicted to a nasal spray, containing tramazoline, which he regularly used against nasal congestion since 6 years. He reported to use 1–1.5 bottles per week, corresponding to 12.7–19.0 mg/week. Clinical neurologic investigation was normal, CK elevated (Table 1) and needle electromyography of the right brachial biceps muscle non-specifically abnormal. He was told to withdraw from tramazoline and after 3 months of abstinence he noted complete suspension of the exercise-induced myalgias and muscle cramps, and why his complaints were attributed to the misuse of tramazoline. Electromyography 3 months after discontinuation of tramazoline was unchanged. His family history revealed hyper-CK-emia of his mother and his uncle.

Table 1 Muscle enzymes before and after discontinuation of tramazoline

Parameter	Normal values	8/04	8/05	8/05	2/06	3/06	5/06	5/06
CK	< 172 U/l	531	803	6130	1157	961	1476	1209
GOT	< 36 U/l	nd	nd	205	nd	56	64	nd
GPT	< 46 U/l	nd	56	105	nd	59	63	nd
LDH	< 249 U/l	nd	244	370	nd	208	261	nd
Aldolase	< 7.6 U/l	nd	nd	nd	nd	4.4	5.5	nd
Myoglobin	< 116 ng/ml	nd	nd	nd	nd	143	192	nd
Laktat	0.6–2.4 mmol/l	nd	nd	nd	1.4	nd	nd	1.2

CK, creatine-kinase; GOT, glutamate-oxalat transaminase; GPT, glutamate-pyruvat-transaminase; LDH, lactate dehydrogenase; nd, not done.

Tramazoline is an imidazoline, which acts as a pre-synaptic α2-sympathomimetic and results in vasoconstriction. Clinically, it is widely used against nasal congestion, which is achieved by debulging of the nasal mucosa. Contraindications for tramazoline use are narrow angle glaucoma and rhinopathia sicca. Manufacturer's recommendations restrict the use of tramazoline to a few weeks. Long-term use may result in chronic mucosal swelling and lastly mucosal atrophy [2]. Possible side-effects are rhinorrhoea, nausea, vertigo, headache, dysgeusia, burning mucosa, palpitations, or arterial hypertension. Muscular side-effects were not mentioned either in the manufacturer's instruction leaflet or found in the literature. None of the reported side-effects was found in the presented patient. Fluctuations of the CK-level were attributed to the patient's irregular sport activities and the fluctuations in the tramazoline dosages. Arguments for tramazoline as the cause of the described muscular symptoms are the prompt recovery after discontinuation of the drug, previous reports suggesting a myotoxic effect of other sympathomimetics [3,4], and the finding that catecholamines may play a pathogenetic role in the development of muscular dystrophy [5]. The persistence of hyper-CK-emia despite discontinuation of tramazoline and disappearance of the muscular symptoms and the family history suggest a primary, most likely metabolic myopathy underlying the transient secondary muscular abnormalities.

This case shows that long-term misuse of tramazoline may turn asymptomatic hyper-CK-emia into symptomatic hyper-CK-emia. Complete withdrawal of the substance may result in a prompt recovery of the muscular symptoms, but may not resolve hyper-CK-emia and the underlying subclinical metabolic myopathy.

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