

ACUTE POISONING WITH TRICHOLOMA EQUESTRE AS CONSEQUENCE OF SIMVASTATIN-MUSHROOM INTERACTION

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Objective

The incidence of myopathy and/or rhabdomyolysis is less than 0.1 % among patients treated with simvastatin. On the other hand, rhabdomyolysis was described as a life-threatening consequence after repeated ingestion of *Tricholoma equestre* in 12 patients in France (1) and in two patients in Poland (2). We report a case after consumption of these mushrooms under simvastatin treatment.

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Patient: 71-year-old man

Anamnesis:

- diabetes mellitus type II, hypothyroidism, arterial hypertension, chronic ischaemic heart disease

Exposure:

- simvastatin for treatment of hyperlipidaemia in the last six months, occasionally muscular pain under this treatment
- every year he had eaten *T. equestre* in large quantities without problems
- ingestion of mushroom meals twice daily on six consecutive days

Admission: one week after the last meal

Clinical feature:

- myalgia
- fatigue
- muscle weakness
- profuse sweating

Laboratory findings (one day after admission):

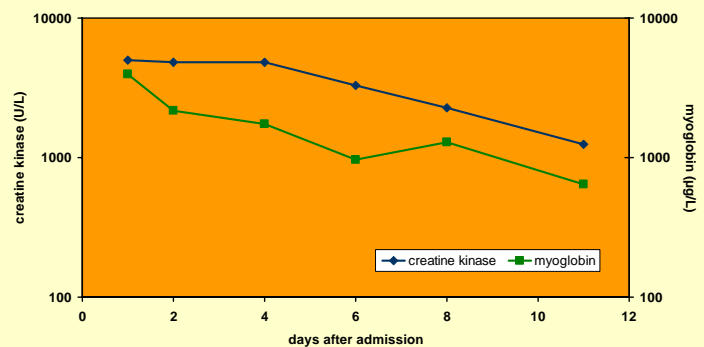
- creatinine kinase 4,986 U/L (reference range < 189 U/L)
- myoglobin 3,976 µg/L (reference range 23-72 µg/L)
- aspartate aminotransferase 336 U/L (reference range < 38 U/L)
- alanine aminotransferase 213 U/L (reference range < 41 U/L)

Treatment and course:

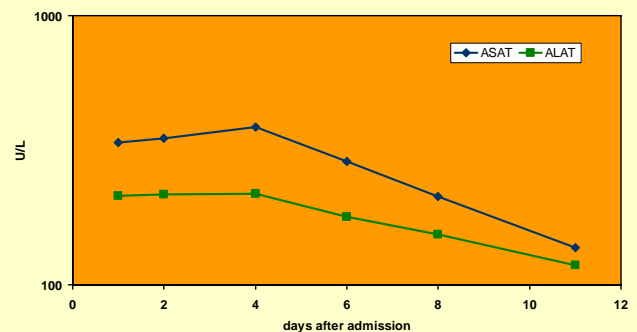
- Simvastatin treatment was discontinued immediately.
- Alkaline diuresis was administered to prevent myoglobin precipitation in renal tubules.
- Under this therapy the symptoms disappeared. Pathological laboratory findings decreased but not fully normalized within ten days.



Time course of creatine kinase and myoglobin in serum



Time course of transaminases in serum



Conclusion:

- The mechanism of the toxic interaction is still unknown.
- Cause of rhabdomyolysis may be simvastatin alone, *T. equestre* alone or the combination of both, respectively
- Increased simvastatin plasma level may be the result of increased absorption and/or inhibition of cytochrome P450 3A4-mediated metabolism (e.g. the combination with grapefruit or erythromycin).
- A combined cytotoxic effect on muscle fibres and liver cells is possible.
- Although a recent study could not demonstrate toxic effects in patients treated with different statins and fibrates consuming large quantities of *T. equestre* (between 300 g and 1200 g for four consecutive days) simultaneously (3), we discourage from ingestion of *T. equestre* in patients receiving HMG-CoA-reductase inhibitors.

References:

- Bedry R, Baudrimont I, Deffieux G, Creppy EE, Pomies JP, Ragnaud JM, Dupon M, Neau D, Gabinski C, De Witte S, Chapalain JC, Godeau P, Beylot J. Wild-mushroom intoxication as a cause of rhabdomyolysis. *N Engl J Med* 2001;345(11):798-802.
- Chodorowski Z, Waldman W, Sein Anand J. Acute poisoning with *Tricholoma equestre*. *Przegl Lek* 2002;59(4-5):386-387.
- Chodorowski Z, Sein Anand J, Madalinski M, Rutkowski B, Cylkowska B, Rutkowski P, Wisniewski M, Hajduk A. Enzymatic examination of potential interaction between statins or fibrates and consumed *Tricholoma equestre*. *Przegl Lek* 2005;62(6):468-470.