

ESPS Peer-review Report

Name of Journal: World Journal of Gastrointestinal Pharmacology and Therapeutics

ESPS Manuscript NO: 9960

Title: Rhabdomyolysis after midazolam in cirrhotic patient treated with statins

Reviewer code: 00506397

Science editor: Wen, Ling-Ling

Date sent for review: 2014-03-06 22:59

Date reviewed: 2014-03-15 03:39

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

In this Case Report Gigante et al., contend that rhabdomyolysis was related to administration of atorvastatin and midazolam in the setting of alcoholic liver disease. The case for this is not convincing since rhabdomyolysis occurred the day after atorvastatin was discontinued. Although both atorvastatin and midazolam are metabolized by CYP3A4 (a P450 enzyme not isoenzyme) there are no reports of midazolam affecting atorvastatin, rather a minor interaction in the other direction (see attached). Although it is certainly plausible that underlying liver disease might have predisposed to myopathy with atorvastatin this is difficult to prove. Based on the laboratory data, the primary underlying process was hepatic failure manifested by progressive elevation in bilirubin and prolonged INR. Again in this context the risk of rhabdomyolysis may have been higher even with discontinuation of atorvastatin. Literature references supporting this contention are not provided however.

With regard to English many terms and phrases used are not understandable. The Case Report needs to be edited to improve communication in English better. Some examples are listed below: 1. Introduction-The concomitant use of other drugs that are metabolic substrates of the same isoenzymes (say Cytochrome P-450 etc) to be more specific 2.The most important side effects consist of increased transaminase levels, abdominal pain or muscle weakness, associated with increased levels of creatine kinase and even rhabdomyolysis. 3.The Chest X-ray and brain computed tomography (CT) scans were performed and were negative. 4. Therefore markers for hepatitis were sought and found to be negative, and thus the patient was diagnosed with alcoholic liver cirrhosis. 5. "Although measurement of the atorvastatin and midazolam serum levels couldn't check, it is well known that the concomitant use of drugs that are substrates of the same



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isoenzymes, as midazolam and atorvastatin, can increase statin concentration in the blood and consequently the risk of myopathy." Do the authors mean: Although serum levels of atorvastatin and midazolam were not checked, we hypothesized that the concomitant use of drugs that are substrates of the same Cyp isoenzymes, as midazolam and atorvastatin, can increase statin concentration in the blood and consequently the risk of myopathy. 6. The author should include a more recent literature review (Needham and Mastaglia *Neuromuscular Disorders* 24:4-15, 2014) in addition to their Reference #1 (2009)



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Title: Rhabdomyolysis after midazolam in cirrhotic patient treated with statins

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

It was a nicely written case report. Some suggestions for consideration: 1. Please provide the dosage of midazolam used. 2. Please offer recommendation on the way to use midazolam in patients taking