

Format for ANSWERING REVIEWERS



June 6, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 3330-review.doc).

Title: Berberine behind the thriller of symptomatic marked bradycardia.

Author: Margherita Cannillo, Simone Frea, Cristina Fornengo, Elisabetta Toso, Giancarlo Mercurio, Stefania Battista, and Fiorenzo Gaita.

Name of Journal: *World Journal of Cardiology*

ESPS Manuscript NO: 3330

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

- (1) processing was done by entrusting the language service American Journal Experts
- (2) we have discuss the possible mechanism that have caused the onset o the symptoms after the patient started berberine: the loss of AV synchronization during the onset of competitive junctional rhythm, and the reduction of chronotropic competence on stress.
- (3) we have reported information on drug half-life and excretion, and an overdose of berberine was ruled out because the patient consumed the correct daily dose.
- (4) We have underlined that this is the first report this side effect.
- (5) We do not know whether the bradycardic and antiarrhythmic properties of berberine are vagally mediated by the activation of muscarinic receptors, or are not vagally mediated. However, it is possible that in hypervagotonic people with marked sinus bradycardia, berberine's bradycardic effect can induce the onset of competitive junctional rhythm, causing a loss of atrioventricular synchronisation, and can reduce chronotropic competence with the onset of symptoms upon exertion.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Cardiology*.

Sincerely yours,
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