

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 14848

**Title:** Association between polymorphism of beta-2 adrenergic receptor gene and response to propranolol in cirrhosis

**Reviewer's code:** 00050424

**Reviewer's country:** Greece

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2014-10-28 10:25

**Date reviewed:** 2014-12-15 23:53

| CLASSIFICATION   | LANGUAGE EVALUATION  | SCIENTIFIC MISCONDUCT                          | CONCLUSION   |
|--|--|--|--|
| <input type="checkbox"/> Grade A: Excellent            | <input checked="" type="checkbox"/> Grade A: Priority publishing     | PubMed Search:                                 | <input type="checkbox"/> Accept                        |
| <input checked="" type="checkbox"/> Grade B: Very good | <input type="checkbox"/> Grade B: Minor language polishing           | <input type="checkbox"/> The same title        | <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"/> Duplicate publication | <input type="checkbox"/> Rejection                     |
| <input type="checkbox"/> Grade D: Fair                 | <input type="checkbox"/> Grade D: Rejected                           | <input checked="" type="checkbox"/> Plagiarism | <input type="checkbox"/> Minor revision                |
| <input type="checkbox"/> Grade E: Poor                 |  | [Y] No   | <input type="checkbox"/> Major revision                |
|  |  | BPG Search:                                    |  |
|  |  | <input type="checkbox"/> The same title        |  |
|  |  | <input type="checkbox"/> Duplicate publication |  |
|  |  | <input type="checkbox"/> Plagiarism            |  |
|  |  | [Y] No   |  |

## COMMENTS TO AUTHORS

Comments : 1. The authors do not give data on the dose of propranolol that each patient was taking. Were there differences in the mean final propranolol dose in each group ;; 2. They do not describe how frequently they increased the dose. Every other day ;; 3. Were all patients receiving the best propranolol dose at 7 days or not ;; How reliable is the variceal pressure measurement ;; Is there a good correlation between variceal pressure (as it was measured) and portal pressure (HPVG) ;; 4. The authors although they describe how they classified esophageal varices, they do not provide data about the variceal size and other characteristics of the patients. 5. How long before the study somatostatin infusion was stopped ;; How many patients were under somatostatin infusion in each group ;; Could this medication have influenced the results ;;

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**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 14848

**Title:** Association between polymorphism of beta-2 adrenergic receptor gene and response to propranolol in cirrhosis

**Reviewer's code:** 01221192

**Reviewer's country:** Romania

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2014-10-28 10:25

**Date reviewed:** 2014-11-03 19:46

| CLASSIFICATION   | LANGUAGE EVALUATION   | SCIENTIFIC MISCONDUCT                          | CONCLUSION   |
|--|---|--|--|
| <input type="checkbox"/> Grade A: Excellent            | <input type="checkbox"/> Grade A: Priority publishing                 | PubMed Search:                                 | <input type="checkbox"/> Accept                        |
| <input checked="" type="checkbox"/> Grade B: Very good | <input checked="" type="checkbox"/> Grade B: Minor language polishing | <input type="checkbox"/> The same title        | <input type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C: Good                 |   | <input type="checkbox"/> Duplicate publication |  |
| <input type="checkbox"/> Grade D: Fair                 | <input type="checkbox"/> Grade C: A great deal of language polishing  | <input type="checkbox"/> Plagiarism            | <input type="checkbox"/> Rejection                     |
| <input type="checkbox"/> Grade E: Poor                 |   | <input checked="" type="checkbox"/> No         | <input checked="" type="checkbox"/> Minor revision     |
|  | <input type="checkbox"/> Grade D: Rejected                            | BPG Search:                                    | <input type="checkbox"/> Major revision                |
|  |   | <input type="checkbox"/> The same title        |  |
|  |   | <input type="checkbox"/> Duplicate publication |  |
|  |   | <input type="checkbox"/> Plagiarism            |  |
|  |   | <input checked="" type="checkbox"/> No         |  |

## COMMENTS TO AUTHORS

The paper evaluates the association between the effects of propranolol, variceal pressure and beta-2 adrenergic receptor ( $\beta$ 2-AR) gene polymorphism in a group of 64 non-related Chinese cirrhotic patients. The authors found that the variceal pressure response to propranolol was associated with  $\beta$ 2-AR gene polymorphisms, and that the patients with the Gly16-Glu/Gln27 haplotypes seem to benefit more from propranolol therapy. This is an interesting paper, with original data. However, it would be interesting to include in the Discussions a comment on the relation between non-responsivity at propranolol (in terms of portal pressure) and gene-expression profiles. It is well-structured paper, but the English need to be revised (see attached).

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**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 14848

**Title:** Association between polymorphism of beta-2 adrenergic receptor gene and response to propranolol in cirrhosis

**Reviewer's code:** 00013649

**Reviewer's country:** Italy

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2014-10-28 10:25

**Date reviewed:** 2014-12-21 03:50

| CLASSIFICATION                              | LANGUAGE EVALUATION  | SCIENTIFIC MISCONDUCT                          | CONCLUSION   |
|---|--|--|--|
| <input type="checkbox"/> Grade A: Excellent | <input type="checkbox"/> Grade A: Priority publishing                | PubMed Search:                                 | <input type="checkbox"/> Accept                        |
| <input type="checkbox"/> Grade B: Very good | <input type="checkbox"/> Grade B: Minor language polishing           | <input type="checkbox"/> The same title        | <input type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C: Good      |  | <input type="checkbox"/> Duplicate publication |  |
| <input type="checkbox"/> Grade D: Fair      | <input type="checkbox"/> Grade C: A great deal of language polishing | <input type="checkbox"/> Plagiarism            | <input type="checkbox"/> Rejection                     |
| <input type="checkbox"/> Grade E: Poor      | <input type="checkbox"/> Grade D: Rejected                           | <input type="checkbox"/> No                    | <input type="checkbox"/> Minor revision                |
|   |  | BPG Search:                                    | <input type="checkbox"/> Major revision                |
|   |  | <input type="checkbox"/> The same title        |  |
|   |  | <input type="checkbox"/> Duplicate publication |  |
|   |  | <input type="checkbox"/> Plagiarism            |  |
|   |  | <input type="checkbox"/> No                    |  |

## COMMENTS TO AUTHORS

The study explores the influence of beta-2 receptor polymorphism and the response of esophageal variceal pressure to chronic treatment with propranolol. The originality is that authors associate the polymorphism to the measurement of variceal pressure and consider the response to chronic administration of propranolol. The topic is of interest, however some criticism may be moved as following detailed: MAJOR POINTS 1-authors should describe the dose of propranolol in each polymorphism group (genotype homozygous for Arg16-Gln27, homozygous for Gly16-Glu/Gln27 or compound heterozygous) since the dose can influence the final response of the hemodynamic parameters considered in the analysis. Moreover the influence of the polymorphism on variceal pressure and the other hemodynamic parameters should be adjusted for those clinical variables non uniformly distributed between groups of polymorphism. 2- Patients homozygous for Gly16-Glu/Gln27 haplotype should be those with the highest response to beta-blockade since this polymorphism is that associated with the highest response to the adrenergic stimulation in physiologic conditions. By contrary, in their series, authors found the lowest response to the

beta-blockade in association with this polymorphism. This contradictory result is not opportunely commented and deserves some cautionary note for the final interpretation of the report. 3-The dose titration of propranolol was achieved in one week for all patients included in the study. This is the most critical point. In real life there is not a fixed period to get the maximum tolerated dose of NSBB. I wonder if further increase of the dose after the one-week period of dose titration would have allowed patients to achieve a higher decrease of variceal pressure. 4-It would be desirable associating the results of the polymorphism to the clinical outcome. This would be extremely original and would give a highest score of interest to the manuscript MINOR POINTS The manuscript should be extensively revised for the language. Several typos mistakes can be detected and some sentences are very confusing and should be rephrased.

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**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 14848

**Title:** Association between polymorphism of beta-2 adrenergic receptor gene and response to propranolol in cirrhosis

**Reviewer's code:** 00053417

**Reviewer's country:** China

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2014-10-28 10:25

**Date reviewed:** 2014-12-07 17:24

| CLASSIFICATION   | LANGUAGE EVALUATION   | SCIENTIFIC MISCONDUCT                          | CONCLUSION   |
|--|---|--|--|
| <input type="checkbox"/> Grade A: Excellent            | <input type="checkbox"/> Grade A: Priority publishing                           | PubMed Search:                                 | <input type="checkbox"/> Accept                        |
| <input checked="" type="checkbox"/> Grade B: Very good | <input type="checkbox"/> Grade B: Minor language polishing                      | <input type="checkbox"/> The same title        | <input type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C: Good                 |   | <input type="checkbox"/> Duplicate publication |  |
| <input type="checkbox"/> Grade D: Fair                 | <input checked="" type="checkbox"/> Grade C: A great deal of language polishing | <input type="checkbox"/> Plagiarism            | <input type="checkbox"/> Rejection                     |
| <input type="checkbox"/> Grade E: Poor                 |   | <input checked="" type="checkbox"/> No         | <input type="checkbox"/> Minor revision                |
|  | <input type="checkbox"/> Grade D: Rejected                                      | BPG Search:                                    | <input checked="" type="checkbox"/> Major revision     |
|  |   | <input type="checkbox"/> The same title        |  |
|  |   | <input type="checkbox"/> Duplicate publication |  |
|  |   | <input type="checkbox"/> Plagiarism            |  |
|  |   | <input checked="" type="checkbox"/> No         |  |

## COMMENTS TO AUTHORS

The effect of single nucleotide polymorphisms (SNPs) in the  $\beta$ 2-adrenergic receptor (ADRB2) gene on the risk of COPD and lung function, and on clinical response to drugs in asthmatic patients has been documented. In this manuscript the authors investigated its effect on cirrhotic patients responded to propranolol, which is innovative. There are some reservations about the study, which needs revision: 1 The term "haplotype" is used as a key word in the manuscript. A haplotype is a set of SNPs at a single chromosome or a chromosome pair which are statistically associated. However, there is no description of relevant data in the whole paper. Whether or not the term "homozygote" should be used there? 2 It needs to explain the detail data about the diagnosis of cirrhosis, e.g. the number of patients diagnosed by liver biopsy, clinical data, imaging techniques or presence of the esophageal varices. 3 English needs polishing.