

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Endoscopy

ESPS manuscript NO: 28948

Title: Does serotonin reuptake inhibitor therapy increase the risk of post-sphincterotomy bleeding in patients undergoing ERCP? A cohort study

Reviewer's code: 03479389

Reviewer's country: Japan

Science editor: Jing Yu

Date sent for review: 2016-07-25 12:01

Date reviewed: 2016-09-13 12:03

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	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"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input checked="" 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 checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
		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 authors described that the use of SRIs was not associated with an increased risk of EST bleeding. Please describe the mechanism of SRI's on bleeding in discussion deeply. Please show the flow chart including the exclusion cases. Is the SRI dose associated with EST bleeding? How did you perform EST? Is it small to middle incision in the Endocut mode? What kind of sphincterotome is it?

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Title: Does serotonin reuptake inhibitor therapy increase the risk of post-sphincterotomy bleeding in patients undergoing ERCP? A cohort study

Reviewer's code: 03027027

Reviewer's country: France

Science editor: Jing Yu

Date sent for review: 2016-07-25 12:01

Date reviewed: 2016-09-27 14:23

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" 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 checked="" 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 type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

Dear author, Thank you for giving me the opportunity to read your paper. It is very clear, and easy to read. The interest of the subject can be discussed, but you are right it is important to know. I have several comments about your text You enrolled 447 patients during 9 years. It is not a lot for a tertiary centre. Would you mind giving us the number of ERCP you perform during the 9 years before exclusion. You have 219/447 patients who have SRI therapy. I do not know the frequency of this therapy in the population. Do you know it? Would you mind precising it? Table 8: I do not understand abdominal pain as an indication for ERCP. It is difficult to understand the difference between LFT (We suppose it is liver function test) and jaundice. It is difficult to say that only 8 patients had a dilation of the bile duct. I think you should distinguish benign and malignant stenosis or causes. In your benign stenosis you have stones, post surgical complications....In your malignant stenosis: pancreatic cancer, cholangiocarcinoma... Table 9: That is a major point of discussion. To have a significant statistically result you took in account all your bleedings. I think you have to discuss if bleeding without endoscopic treatment in your table (Probably you just wait it stop bleeding), is a



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real complication. You should present your results of bleeding with endoscopic procedure or blood transfusion separately even it is not significant. Besides could you tell us end discuss your bleeding management. Do you only perform epinephrine injection? Can you use covered metallic stents? or something else? Do you wait the patient needs transfusion of 4 units before performing new endoscopic procedure? I hope I was enough clear in my comments. Congratulation for your work. Sincerely yours, Your reviewer

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Name of journal: World Journal of Gastrointestinal Endoscopy

ESPS manuscript NO: 28948

Title: Does serotonin reuptake inhibitor therapy increase the risk of post-sphincterotomy bleeding in patients undergoing ERCP? A cohort study

Reviewer's code: 03666794

Reviewer's country: Czech Republic

Science editor: Jing Yu

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
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<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 checked="" 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 type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
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		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This manuscript contributes to discussion about serotonin reuptake inhibitor (SRI) therapy and its association with gastrointestinal tract (GIT) bleeding. This concrete study evaluates influence of SRI therapy on post-sphincterotomy bleeding. As authors claim, this study is the first one to assess the SRI's impact on post-sphincterotomy bleeding. That might be valuable concerning publishing the manuscript. Hypothesis is clearly defined, authors suggested that SRIs therapy would increase the risk of post-sphincterotomy bleeding. What is not fully explained is how the authors came to that suggestion. There are some studies cited in the manuscript that assess the association between SRIs and risk of upper GIT bleeding, those studies are more aimed at the role of NSAIDs and aspirin eventually their combination with SRIs in GIT bleeding. Solely the association between percutaneous endoscopic gastronomy (PEG) and SRI's bleeding is mentioned. Also the suggested mechanism of possible increase in post-sphincterotomy bleeding in patients on SRIs therapy is not much explained. Authors mention association of SRIs and increased gastric acidity that might influence upper GIT bleeding, but this doesn't have any association with post-sphincterotomy bleeding or it might be

better explained. More possible mechanism as authors suggest is that SRIs influent the function of presynaptic neurons and impair the hemostasis function. Although the exact mechanism of how SRIs lead to increased risk of bleeding is unknown I would expect for the purpose of this study more attention to the explanation concerning post-sphincterotomy bleeding. Also more citations to the matter of mechanisms how SRIs lead to increased risk of GIT bleeding would be appreciated. Authors tried to exclude possible confounding factors. From my point of view missing information is how many patients underwent ERCP in the study period of January 2006 to September 2015 in total and how many were excluded. Concerning ERCP procedure itself there is no information how many endoscopists did all the examinations involved in the study. One must consider that one of the confounding factors may be the diversity of experts proceeding ERCP, that is not mentioned in the manuscript. In general overall structure of the manuscript is complete. Hypothesis is clearly defined, proposal of the study is adequate to the suggested aim of the study. Number of patients involved in the study cohort is sufficient. Methods including statistic assessment are clearly described. Use of tables to present complications of sphincterotomy, bleeding grading system, exclusion criteria and some preliminary data helps reader to understand presented probematic. Results are clearly arranged in tables and one figure. Authors answered proposed question. SRIs has been widely prescribed in patients with depression and discussion about their safety profile is considered to be very important. This study contribute to this discussion and is the first one to asses the SRI's impact on post-sphincterotomy bleeding. As mentioned above that is valuable concerning publishing the manuscript.