

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 43461

Title: Triggers of histologically suspected drug-induced colitis

Reviewer's code: 00058340

Reviewer's country: United States

Science editor: Ruo-Yu Ma

Date sent for review: 2018-11-27

Date reviewed: 2018-12-02

Review time: 16 Hours, 5 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

In this RETROSPECTIVE COHORT STUDY, CASE CONTROL STUDY, the authors aimed to investigate drugs that are potential triggers for drug-induced colitis (DIC). The assessment was mainly based on histopathological findings. Comments: 1. There are no specific, commonly agreed upon histopathologic features of DIC and different drugs



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may induce different histopathologic changes. Given the common absence of strictly specific histopathological features, the diagnosis of DiC often relies upon thorough clinicopathological correlation, but in clinical practice it is difficult to establish the correlation between a certain medication and a particular pattern of injury. For example specific patterns – crypt epithelial cell apoptosis can be induced by fluorouracil, NSAIDs (diclofenac, mefenamic acid), cyclosporin, colchicine and ranitidine. With other drugs DiC may represents a diagnostic challenge (see below PDF) and may occur concomitantly with IBD. 2. Was histopathological reassessment performed by the same or different pathologist(s)? What was agreement rate between these different pathologists? 3. Histologic slides are not good quality and should be replaced with ones of better quality and specific changes should be labeled with arrows and/or asterisks 4. Some statements e.g. a)“Written, informed consent was obtained from all patients before specific examinations. Due to its retrospective character informed consent was neither practicable nor necessary” should be better clarified and rephrased e.g., Written, informed consents were obtained from all patients before specific examinations and procedures such as colonoscopy and biopsy. For this retrospective study informed consent was neither practicable nor necessary and was exempted byIRB? b) “Statistics were realized” should be rephrased [PDF] Drug-Induced colitis - IAP-AD

INITIAL REVIEW OF THE MANUSCRIPT

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 43461

Title: Triggers of histologically suspected drug-induced colitis

Reviewer's code: 01557050

Reviewer's country: Japan

Science editor: Ruo-Yu Ma

Date sent for review: 2018-11-27

Date reviewed: 2018-12-05

Review time: 9 Hours, 8 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Dr. Brechmann, et al. investigated 'Triggers of histologically suspected drug-induced colitis'. The manuscript is informative and well-presented. Comments 1. In Table 6-S, two titles of 'Drug-induced colitis without atherosclerosis' were seen. Please correct the titles.



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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 43461

Title: Triggers of histologically suspected drug-induced colitis

Reviewer's code: 02549032

Reviewer's country: Greece

Science editor: Ruo-Yu Ma

Date sent for review: 2018-11-27

Date reviewed: 2018-12-15

Review time: 16 Hours, 18 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
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SPECIFIC COMMENTS TO AUTHORS

This is an interesting retrospective cohort comparative single center study on drug induced colitis DiC. The authors concluded that DiCs although different entity from other colitides such as ischemic colitis, is related to more drug categories that we knew, and is related to atherosclerosis and microcirculatory disturbances. The study is



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well-written and conducted and suitable for publication. Some major issues: 1. In tables 6S and 9S 1st and 2nd column is the same? DiC without atherosclerosis? Probably column 2nd is <<DiC with atherosclerosis>>> 2. The study is based on histological examination of colorectal biopsies. More specific definition of histological diagnosis of DiC and differential diagnosis from ischemic colitis is necessary. Please give in details, which are the histological features specific for DiC and which are the histological features of both groups. 3. In patients with atherosclerosis and multiple anti-atherosclerotic medications, it is not easy to prove etiologically the connection of specific drug category to DiC. A comment is necessary. 4. A major conclusion is that: <<In univariate analysis, DiC was associated with diuretics, dihydropyridines, glycosides, ASS, platelet aggregation inhibitors, NSAIDs, statins and fibrates.>> However, the majority of these drugs are also used in atherosclerotic patients, who are also candidates for ischemic colitis. So it is difficult to prove the DiC. The definition of DiC should exclude atherosclerosis. 5. It is very important to differentiate ischemic colitis from drug-induced colitis histologically. <<...DiC patients with atherosclerosis exhibited histological features from both other groups..>> Did the patients have two etiologies for colitis? DiC plus ischemic? This is a little confusing.

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