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PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Pathophysiology

Manuscript NO: 52378

Title: Fecal lactoferrin accurately reflects mucosal inflammation in inflammatory bowel disease

Reviewer's code: 00074323
Position: Editorial Board
Academic degree: MD, PhD
Professional title: Assistant Professor, Medical Assistant, Senior Scientist
Reviewer's country: Italy
Author's country: United States
Reviewer chosen by: Artificial Intelligence Technique
Reviewer accepted review: 2019-10-30 15:36
Reviewer performed review: 2019-11-04 22:42
Review time: 5 Days and 7 Hours

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[ ] Grade E: Do not publish		[ ] Rejection	[ ] Advanced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

SPECIFIC COMMENTS TO AUTHORS

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In this single center retrospective cohort study the Authors aim at investigating the correlation between fecal lactoferrin (FL) levels and the degree of mucosal inflammation, disease location and disease extension. To be included in the study, patients had to have an endoscopy performed within 30 days of FL measurement. The degree of mucosal inflammation was assessed by validated endoscopic scores, disease extension and disease location were assessed with colonoscopy plus imaging in CD patients. Observation reported in the result section are: 1. A significantly different median FL level between specific levels of disease activity as assessed by endoscopic scores. 2. A slighlty stronger correlation, expressed as Spearman score, between FL and endoscopic disease activity compared to CRP in patients with CD but not in patients with UC. 3. Higher median FL levels in patients with more than one inflamed colonic segment. 4. FL levels obtained before colonoscopy had a better correlation with SES-CD and DAI than levels measured after the colonoscopy in patients given steroids and biologics in between marker determination and the procedure. Based on this observation the Author conclude that: 1. FL is able to separate different levels of disease activity 2. There is a positive, significant correlation of FL with SES-CD and DAI and such correlation is not seen for WBC and is weaker for CRP 3. FL increase with the number of colonic segments involved and it might be an accurate indicator of the total disease burden. 4. FL variation in response to an immunomodulating drug is faster than mucosal macroscopic change thus FL is a more timely indicator of disease activity than endoscopy. Major issues: 1. A measure of test accuracy should be provided to be able to draw this conclusion. 2. The statement contradicts the results presented in Table 2. 3. This conclusion cannot be drawn based on the results. Authors provide median FL levels according to disease extension in the colon. However, no p-value is provided nor a measure of test accuracy. 4. This conclusion cannot be drawn based on this observation. To be able to state so, an endoscopy should have been repeated at the time

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of FL collection. In patients with UC, MH can be achieved as early as week 6 after the introduction of an anti-TNF thus mucosal changes reasonably start occurring within days after an effective immunomodulating therapy is introduced.

INITIAL REVIEW OF THE MANUSCRIPT

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Pathophysiology

Manuscript NO: 52378

Title: Fecal lactoferrin accurately reflects mucosal inflammation in inflammatory bowel disease

Reviewer's code: 01047558
Position: Editorial Board
Academic degree: PhD

Professional title: Doctor, Professor

Reviewer's country: Tunisia

Author's country: United States

Reviewer chosen by: Artificial Intelligence Technique

Reviewer accepted review: 2019-10-30 05:10

Reviewer performed review: 2019-11-05 07:07

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

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The manuscript "Fecal lactoferrin accurately reflects severity and extent of mucosal inflammation in inflammatory bowel disease" is a retrospective study which evaluates the fecal lactoferrin in IBD. The results of this study were already published as an abstract in: American Journal of Gastroenterology: October 2018 - Volume 113 - Issue - p S402 and in Gastroenterology April 2017 Volume 152, Issue 5, Supplement 1, Page S777 The results are from 2016 and are not innovative.

INITIAL REVIEW OF THE MANUSCRIPT

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Pathophysiology

Manuscript NO: 52378

Title: Fecal lactoferrin accurately reflects mucosal inflammation in inflammatory bowel disease

Reviewer's code: 03249854
Position: Peer Reviewer
Academic degree: MD

Professional title: Chief Doctor, Professor, Surgeon

Reviewer's country: China

Author's country: United States

Reviewer chosen by: Artificial Intelligence Technique

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Reviewer performed review: 2019-11-10 11:08

Review time: 9 Days and 8 Hours

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

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This is a retrospective cohort study in a IBD center in Roanoke, VA, USA, including 131 CD and 57 UC patients. In general, the language quality (style, grammar, and spelling) of this paper is good. The article also showed complete and well-constructed logicality. However, there are some questions that might need the authors to illuminate: 1. This study depicted the known conclusion among IBD patients that FL showed a close correlation with the involved mucosal surface and with disease extent and was more closely correlated to endoscopy. But this article didn't point out the exact FL level that can accurately reflect the endoscopic assessment, and didn't answer that if FL could be the substitution of endoscopy for diagnosis and monitoring of IBD. 2. Methods: authors didn't point out the time of this retrospective study and why? 3. The number of CD patients in the abstract was inconsistent with that in the results. 4. One of the results showed that FL showed a higher correlation to SES-CD and DAI when it had been tested before the procedure compared to when it had been tested after the procedure in patients given effective fast acting medications (steroids and biologics). And authors gave the explanation: FL is a more timely indicator of disease activity than endoscopy. But why only in patients given steroids and biologics? Does it common in patients given other medications such as immunosuppressants (AZA)? The medications of these patients were not showed in the patients baseline characteristics.

INITIAL REVIEW OF THE MANUSCRIPT

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Pathophysiology

Manuscript NO: 52378

Title: Fecal lactoferrin accurately reflects mucosal inflammation in inflammatory bowel disease

Reviewer's code: 02529364
Position: Editorial Board
Academic degree: MD, PhD
Professional title: Senior Lecturer
Reviewer's country: Australia
Author's country: United States
Reviewer chosen by: Artificial Intelligence Technique
Reviewer accepted review: 2019-10-30 04:36
Reviewer performed review: 2019-11-11 23:46
Review time: 12 Days and 19 Hours

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

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This manuscript reports the findings from a retrospective study conducted by the authors in which they found that fecal lactoferrin accurately reflects severity and extent of mucosal inflammation in inflammatory bowel disease (IBD). The findings reported in this study are interesting, suggesting that fecal lactoferrin is a potential non-invasive biomarker for monitoring mucosal inflammation in IBD. Overall, the manuscript is clearly written. However, the followings should be corrected: 1. Page 3. Abbreviations for Crohn's disease and ulcerative colitis were already used in the first paragraph of the Introduction. However, in the second paragraph, the full names were still used. Please change them to abbreviations. 2. Page 4. CRP and WBC: please provide full name when first mentioned in the manuscript. 3. Page 5: Biomarker testing: FL is from fecal sample, CRP and WBC are from blood samples. Please include this information in the manuscript. 4. Table 2: Please include P values in Table 2. 5. Figure legends: in the figure legends, please include the statistical analysis method used. The patient numbers in each group should also be included. The current Figure legends particularly Figure 1 and Figure 2 are just titles/subtitles.

INITIAL REVIEW OF THE MANUSCRIPT

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[ ] Plagiarism

[Y] No

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Pathophysiology

Manuscript NO: 52378

Title: Fecal lactoferrin accurately reflects mucosal inflammation in inflammatory bowel disease

Reviewer's code: 00503883
Position: Peer Reviewer
Academic degree: MD

Professional title: Doctor

Reviewer's country: Brazil

Author's country: United States

Reviewer chosen by: Artificial Intelligence Technique

Reviewer accepted review: 2019-11-06 18:02

Reviewer performed review: 2019-11-18 00:38

Review time: 11 Days and 6 Hours

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

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I think that endoscopic parameters of SES-CD and endoscopic component of the Mayo score for UC could be more descriptive. For example: Endoscopic findings of UC: 0 - normal mucosa or inactive disease; 1 - Mild activity: erythema decreased vascular pattern, mild friability; 2- Moderate activity: marked erythema, lack of vascular pattern, friability, erosions; 3 - Severe activity: spontaneous bleeding, large ulcerations. More complete description could help readers that are not familiar to endoscopic scoring in IBD. SES-CD already includes surface involved by disease and surface involved by ulcerations. I really don't feel necessary to further include an analysis with a simple score system providing one point for each colonic segment. This analysis could add more bias. The cutoff reference value of "normal" fecal lactoferrin (TECHLAB, Blacksburg, VA) could interest for better comprehension. The number of patients with CD described in abstract is different from table 1: 92 patients versus 131 patients. Of note most of the patients had severe activity for both UC and CD. No patient with ulcerative colitis was in remission. This is not unusual at IBD reference centers.

INITIAL REVIEW OF THE MANUSCRIPT

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[Y] No