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8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

http://www.wjgnet.com

ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 12193

Title: Pancreatic enzyme replacement therapy for pancreatic exocrine insufficiency in the 21st century

Reviewer code: 00058340

Science editor: Jin-Lei Wang

Date sent for review: 2014-06-26 13:36

Date reviewed: 2014-06-30 05:26

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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 type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

In this paper the authors reviewed pancreatic enzyme replacement therapy for pancreatic exocrine insufficiency, including the history of pancreatic enzyme therapy, current use of modern preparations, and approaches to overcoming unsatisfactory clinical responses. In my opinion this is a truly outstanding, fascinating and the state-of-the-art review paper. The paper is very well written, well focused and addresses clinically important and relevant issues. The senior and corresponding author Professor D.Y Graham is the world renowned academic gastroenterologist. I have only very minor comments. Minor Comments 1. The authors may briefly address, if they wish, whether and in which subset of patients pancreatic enzyme treatment relieves pain in chronic pancreatitis. 2. Page 9. "We performed experiments with patients with varying degrees of acid secretory capacity" - perhaps the authors may rephrase this sentence and use "studies" instead of "experiments". Same for other references to "experiments". 3. Page 16. "the remaining 4 patients with incomplete responses had higher gastric pH, suggesting that the poor responders may have released the enzymes in the stomach where they were subsequently inactivated. Is "higher gastric pH" correct? 4. Figure 2 legend. please explain abbreviation CFA, so the readers do not have go back to the text.



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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology

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Title: Pancreatic enzyme replacement therapy for pancreatic exocrine insufficiency in the 21st century

Reviewer code: 02903574

Science editor: Jin-Lei Wang

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existing	<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"/> No records	<input type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

This review aims at addressing, from both a historical and clinical point of view, the available evidence regarding the use of pancreatic enzyme replacement therapy in patients with exocrine pancreas insufficiency. The authors should be applauded for the effort in compiling an exhaustive review on this important topic. Overall, the manuscript is well written. However there are several drawbacks to this manuscript. General comments: First the manuscript is clearly too long and disorganised, with arguments coming back and forth (e.g. "more is not better" is discussed in several sections of the manuscript). The notion that gastric acid inactivates pancreatic enzymes is repeated a number of times. In its present form, I feel that the manuscript would better suit as a Book chapter, rather than a Journal article. If they wanted to see it published in the WJG, the authors would have to significantly shorten the manuscript, and go "straight to the point" (for instance, the last paragraphs of the review are very informative and of use to the reader). The role of narrative reviews like the current ones is increasingly been challenged in the scientific community, and I would be curious to know why did the authors not opt for a systematic review (+/- meta-analysis), which would have made their point stronger. The historical perspective (which again would suit more a book chapter) is not clearly delineated, and I find it difficult to understand which of the findings should be taken as "historical information for general medical interest" versus evidence (recent or not) which should be of scientific interest for the reader. The authors should give more attention to several randomized



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controlled trials which they have not discussed; evidence gathered from RCTs is often more informative than case-series: O'Keefe SJ, Cariem AK, Levy M. The exacerbation of pancreatic endocrine dysfunction by potent pancreatic exocrine supplements in patients with chronic pancreatitis. *Journal of Clinical Gastroenterology* 2001;32:319-23. Mossner J, Secknus R, Mayer J, Niedeau C, Adler G. Treatment of pain with pancreatic extracts in chronic pancreatitis: results of a prospective placebo-controlled multicenter trial. *Digestion* 1992;53:54-66. Malesci A, Gaia E, Fioretta A, Bocchia P, Dirauenga G, Cantor P, et al. No effect of long term treatment with pancreatic extract on recurrent abdominal pain in patients with chronic pancreatitis. *Scandinavian Journal of Gastroenterology* 1995;30(4):392-8. Delhaye M, Meuris S, Gohimont AC, Buedts K, Cremer M. Comparative evaluation of a high lipase pancreatic enzyme preparation and a standard pancreatic supplement for treating exocrine pancreatic insufficiency in chronic pancreatitis. *European Journal of Gastroenterology and Hepatology* 1996;8:699-703. Delhaye M, Meuris S, Gohimont AC, Buedts K, Cremer M. Comparative evaluation of a high lipase pancreatic enzyme preparation and a standard pancreatic supplement for treating exocrine pancreatic insufficiency in chronic pancreatitis. *European Journal of Gastroenterology and Hepatology* 1996;8:699-703. Lankisch PG, Lembcke B, Goke B, Creutzfeldt W. Therapy of pancreatogenic steatorrhea: does acid protection of pancreatic enzymes offer any advantage?. *Zeitschrift fur Gastroenterologie* 1986;24:753-7. Larwin M, McMahon MJ, Thomas WEG, Puntis MCA. Creon (enteric coated pancreatin microspheres) for the treatment of pain in chronic pancreatitis: a double blind randomized placebo-controlled cross-over study. *Gastroenterology* 1991;100:A283. I have concerns regarding the appropriateness of the (too) numerous figures: in fact, it is not pleasant for the reader to interpret so many different findings, drawn from different populations, comparing different interventions, with different outcome measures. Thus, this important number of figures is a limitation rather than a strength of this article. This does not mean that the view of the author



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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology

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<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
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<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

Authors aim to concentrate their attention on efforts that can explain the use of pancreatic enzyme replacement therapy in patients with exocrine pancreas insufficiency. overall it is a very long paper, which required tremendous amount of work. however, my major problem with the manuscript is as follow: 1. needs to be polished out with a more focus writing 2. too many figures and in fact authors should try to either combine some of them or use it in the sup. section which might help in re-organizing the work. overall it is a very interesting work and with a bit more work i believe it has a great potential for a highly cited publication.