Reviewer's report

Title: Effects of oral adenosine 5'-triphosphate and adenosine in enteric-coated capsules on indomethacin-induced permeability changes in the human small intestine: a randomized cross-over study

Version: 1 Date: 14 February 2007

Reviewer: Marc Zuckerman

Reviewer's report:

General

This is an interesting and well-done study which adds to the scientific literature on NSAID-induced changes in small intestinal permeability as assessed by the lactulose/rhamnose disaccharide/monosaccharide test. The authors confirm that short-term administration of indomethacin causes an increase in the lactulose/rhamnose excretion ratio. The increase was due to increased urinary lactulose recovery. However, both ATP and adenosine administered via enteric-coated capsules did not reduce indomethacin-induced permeability changes in normal volunteers, contrary to expectations from a previous study not yet published in which ATP was administered via duodenal tube. The authors discuss possible explanations and conclude that the lack of efficacy of ATP administered via capsule may be related to delivery distal to the site of indomethacin-induced injury.

Methods are appropriate and well-described. Data are sound and well-controlled. The discussion is balanced. Mention is made of differences in baseline permeability data between this and the previous study. References are appropriate. It is well-written.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Comment should be made in the introduction regarding intestinal permeability in celiac disease, along with Crohn's disease, since celiac disease is then mentioned twice later (in exclusion criteria pg 7 and in results page 11).

Check spelling of dipyridamole.

Discretionary Revisions (which the author can choose to ignore)

1. Abstract - Conclusions include the expression "untimely opening" which has an ambiguous meaning which could be interpreted as premature opening.
2. Probabilities are often expressed as p=0.00, except for the discussion on pg 14 using pis less than 0.01, which is the more usual term.
3. Introduction - Clarify that paracellular pathway is being used as a synonym for intercellular pathway.
4. Methods - The comments on pg 8 protocol on alcohol and drugs could be moved to pg 7 under exclusions based on drug use.
5. Discussion - Comments on pg 15 regarding ATP stability could be moved to results.

What next?: Accept after minor essential revisions

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests.