Author's response to reviews

Title: Drug Interaction: Omeprazole and Phenprocoumon

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PDF covering letter
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Dear Dr. Veitch,

Re.: BMC MS
Enderle et al., ‘Drug interaction: Omeprazole and Phenprocoumon’

We refer to your communications of March 7th, 20th and 23rd (Fiona Godlee) 2001 and appreciate that Dr. Godlee does not insist that we provide written patient consents in this instance.

In response to Christopher Kohl’s comments, we have re-written large parts of the Discussion section. In particular:

1. We have removed our statement concerning the bioavailability of phenprocoumon.

2. We have substantiated our statement regarding increased omeprazole levels in slow metabolisers (the area under the serum concentration vs. time curve is 10- to 20-times greater than in normal rate metabolisers) and included appropriate literature references (ref. 10,11). This should add some weight to our suggestion that in patients deficient in CYP2C19 omeprazole-phenprocoumon interaction involving CYP2C9 is possible.

3. We have done another Medline literature search using the following key words:
   - “omeprazole” AND “polymorphic” AND “CYP2C19”
   - “omeprazole” AND “slow” AND “metabolisers”
   - “omeprazole” AND “slow” AND “metabolizers”
   - “omeprazole” AND “poor” AND “metabolisers”
   - “omeprazole” AND “poor” AND “metabolizers”

Our search returned 55 hits but failed to reveal any additional literature evidence that could be interpreted to either support or reject our suggestion. So, regrettfully, we are unable to provide precisely the literature support that Dr. Kohl would have liked to see. However, we feel this should be no reason for rejecting our manuscript for publication. In Dr. Kohl’s own words, our suggested explanation “is certainly theoretically possible”. Thus, our explanation is consistent with the current scientific knowledge regarding omeprazole metabolism and the affinity of omeprazole for the isoenzymes implied here.
We also like to remind that case reports are retrospective by nature and thus the data on which to base discussion are often very limited. Our case report is primarily intended to inform the medical practitioner of individual drug interactions observed in routine practice.

That our idea cannot be further supported with currently published data would suggest to us that appropriate experimental work is needed to resolve the issue of interaction between omeprazole and coumarin derivatives in slow vs. normal rate metabolisers.

We hope that our amendments have improved our manuscript sufficiently to meet Dr. Kohl’s requirements and look forward to your reply to our revised Case Report (2nd revision) which we submitted today.

Yours faithfully

Ulrich Grass, MD, PhD