REPLY

Reply to 'Some More Comments on Folate Deficiency in Chronic Pancreatitis'

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Dear Sir,

Dr Wagner's erudite comments in the present issue of JOP. J Pancreas (Online) [1] further illuminate the complex interactions between micronutrient deficiency, electrophilic stress, and disrupted methionine homeostasis, that together seem to precipitate chronic pancreatitis by impairing the exocytosis of zymogen granules from pancreatic acinar cells [2, 3].

Dr Wagner's studies and arguments [1] underline the essentiality of methyl moieties for exocytosis. They act directly (by carboxymethylating small G proteins in the apical membrane), and indirectly by incorporation into phosphatidylcholine for granule membrane-apical membrane fusion during the exocytosis process. Dietary methionine is the main source of methyl groups, delivered via its first metabolite S-adenosylmethionine (SAM). Dietary folic acid - in concert with vitamin B_{12} and ascorbic acid (bioactive fraction of vitamin C) - facilitates methionine regeneration from homocysteine. Dietary betaine and choline provide pre-formed methyl groups.

The ancillary methyl sources (folic acid, betaine, choline) could determine whether or not exocytosis can proceed when methionine intake falls short of need, as it does (along with insufficiency of vitamin C) in chronic pancreatitis wherein demand increases due to cytochrome P450 induction [4], with increased release of reactive oxygen and xenobiotic species [2]. The vulnerability to the ensuing electrophilic stress of enzymes such as that which catalyses the conversion of methionine to SAM [5] rationalizes both the surge in circulating level of methionine and SAM in an acute exacerbation of chronic pancreatitis [6, 7], and evidence that the methionine metabolic pathway remains fractured thereafter [8]. A supplement of methionine (or SAM) plus vitamin C curbs attacks, and additional choline (theoretically betaine alternatively [1]) is helpful when treatment fails [2]. All these observations indicate the clinical relevance of methionine plus/minus choline-deficient dietary models of pancreatic injury [9, 10, 11].

Received September 9th, 2010

Key words Ascorbic Acid, Exocytosis; Folic Acid; Methionine

Abbreviations SAM: S-adenosylmethionine

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URL http://www.serena.unina.it/index.php/jop/article/view/3420/3721

Conflict of interest None

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