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CORRESPONDENCE

Comment on "Pancreatic Enzyme Replacement Therapy in Pancreatic Exocrine Insufficiency—Real-World's Dosing and Effectiveness: A Systematic Review"

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Abstract

Pancreatic enzyme replacement therapy (PERT) is vital for managing pancreatic exocrine insufficiency (PEI), yet real-world use often deviates from guideline-recommended dosing. In response to the recent review by Kadaj-Lipka et al., we highlight several overlooked but critical factors influencing PERT effectiveness. While the review identifies underdosing trends, it does not address patient adherence or the timing of enzyme intake, both essential for therapeutic success. Clinical applicability was further limited by the inconsistent measurement of important nutritional outcomes like weight gain, fat absorption, and fat-soluble vitamin levels. Even though dosing requirements differ by cause, the review does not stratify findings by PEI etiology. Cost implications and high-dose safety concerns, particularly in pediatric or long-term use, were also not thoroughly investigated. We commend the authors' contribution but emphasize the importance of incorporating adherence, standardized outcomes, etiology-specific dosing, safety, and cost-effectiveness in future analyses to improve PERT delivery and patient outcomes.

To the Editor,

We read with keen interest the article by **Kadaj-Lipka et al.**, "Pancreatic Enzyme Replacement Therapy in Pancreatic Exocrine Insufficiency—Real-World's Dosing and Effectiveness: A Systematic Review", recently published in *Digestive Diseases and Sciences* [1]. The authors systematically reviewed real-world practices of pancreatic enzyme replacement therapy (PERT) in patients with pancreatic exocrine insufficiency (PEI), highlighting that nearly 40% of studied cohorts received suboptimal dosing (< 40,000–50,000 lipase units per meal). Their synthesis offers important insights into current clinical gaps between recommended and actual PERT use. Although, this is useful but there are a few points that need more discussion.

If patients take enzymes irregularly or late with meals—factors that are critical to PERT efficacy—reported dose per meal does not guarantee optimal therapy [2, 3]. It is unclear if the real-world studies that were included addressed patient education, adherence, or the timing of administration—all of which have a significant impact on results.

Although improvements in diarrhea were frequently reported, nutritional status was only consistently improved by regimens that adhered to guidelines. Important outcomes such as fat absorption (e.g., coefficient of fat absorption), weight gain, and levels of fat-soluble vitamins were not consistently measured [1]. These metrics are recommended as essential by PEI core outcome sets [4]. Higher enzyme dosage is advised by guidelines for etiologies like cancer or post-pancreatic surgery [5]. The review does not stratify results by PEI cause, but it does report average dosing. PERT customization by clinicians would be better guided by etiology-specific analyses.

High-dose PERT, particularly in pediatrics or with long-term use, has been linked to fibrosing colonopathy [6]. The authors do not discuss safety monitoring for high-dose regimens, which is important given their advocacy for guideline-level dosing. Increasing daily enzyme doses significantly raises costs. Considering the modest benefit on nutritional outcomes, a cost–benefit assessment, especially in resource-constrained contexts, would add practical value to the recommendations.

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Despite these points, Kadaj-Lipka et al. have provided a compelling evaluation of real-world PERT dosing. For future analyses, deeper attention to adherence, standardized nutritional outcomes, etiology-specific dosing, safety monitoring, and cost-effectiveness will optimize PERT delivery and patient benefit.

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Data Availability No datasets were generated or analysed during the current study.

Declarations

Competing interests The authors declare no competing interests.

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