

## FULL ABSTRACT

Impaired Exocrine Pancreatic Function in Children with Persistent Diarrhea and Malnutrition, and Effects of Pancreatic Enzyme Supplementation on Persistent Diarrhea

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Persistent diarrhea is a serious health problem and is closely related to malnutrition. Prolonged mucosal injury in diarrhea is thought to cause reduced secretin and cholecystokinin (CCK) secretion, which decreases stimulation to the pancreas and further aggravate persistent diarrhea and malnutrition.

This research aims to study pancreatic exocrine function in children with persistent diarrhea and children with malnutrition, to obtain reference values of fecal elastase-1 (FE-1) in Indonesian children, and to assess the ability of stool analysis and steatocrit in detecting exocrine pancreatic insufficiency. Cross-sectional study was done to obtain FE-1 distribution in healthy children, to study FE-1 levels in children with persistent diarrhea and children with malnutrition, and to study the sensitivity, specificity, and discriminative capacity of stool analysis and steatocrit in detecting exocrine pancreatic insufficiency. A randomized, double-blind, parallel group, placebo-controlled clinical trial was conducted to evaluate the effects of 8371 USP units of pancreatic enzyme replacement therapy (PERT) 3 times daily for 1 month in children with persistent diarrhea. This study involved children age 6–60 months in 5 hospitals in Jakarta from January 2015 to July 2016.

As much as 182 children 6–60 months of age consisting of 31 children with persistent diarrhea, 31 children with malnutrition, and 120 healthy children were recruited as subjects. Cut-off point of FE-1 in this study was 307 mcg/g faeces. Significant difference of FE-1 was found between children with persistent diarrhea and healthy children. The FE-1 difference between subjects with malnutrition and healthy children was not significant. Duration of diarrhea was 7 days significantly shorter in the PERT group. Changes of FE-1 and prealbumin values between baseline and endpoint in placebo and treatment group were found to be statistically insignificant. The diagnostic value of each stool analysis component and steatocrit test showed that the sensitivity was within range of 5–32%, specificity 73–98%, positive predictive value 1–43% and negative predictive value 87–89%. The AUC values of stool analysis and steatocrit were 0.664 (95% CI 0.539–0.788) and 0.501 (95% CI 0.372–0.629), respectively, and the combined AUC 0,671.

In conclusion, exocrine pancreatic insufficiency was observed in children with persistent diarrhea, and PERT has been proven to significantly shorten the duration of diarrhea by 1 week. Stool analysis and/or steatocrit has low sensitivity, high specificity, and low discrimination capacity.

Keywords: children, exocrine pancreatic function, malnutrition, pancreatic enzyme supplementation, persistent diarrhea