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Pancreatic Enzyme Eeplacement Therapy in paediatric care: Global insights and gaps in Bangladesh

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Abstract

Pancreatic Enzyme Replacement Therapy (PERT) remains the cornerstone of managing exocrine pancreatic insufficiency (EPI), especially in children with Cystic Fibrosis (CF). Globally, Pancrelipase a high-potency, enteric-coated pancreatic enzyme is widely recommended for effective symptom control and nutritional requirements. However, in Bangladesh, a critical gap exists in both the availability of Pancrelipase and awareness regarding its appropriate use. Clinicians often rely on low-potency, non-enteric-coated enzyme preparations, leading to suboptimal outcomes. This review summarizes current international recommendations on PERT and highlights the local challenges, including limited access to standard therapy and lack of clinical guidelines tailored for Bangladeshi children. Addressing these gaps is essential to improve nutritional status, reduce morbidity, and enhance the quality of life in children with pancreatic insufficiency. The article advocates for urgent policy-level interventions and increased clinician awareness to ensure equitable access to effective enzyme therapy.

Introduction

Pancrelipase is considered the most effective Pancreatic Enzyme Replacement Therapy (PERT) available worldwide. Unfortunately, Pancrelipase is not available at medicine market in Bangladesh. As a result, patients with conditions like exocrine pancreatic insufficiency, chronic pancreatitis, and cystic fibrosis are using local alternatives. In contrast, children in Bangladesh using local enzyme products often do not reach the same level of health and well-being.

While these local products offer some benefits, their effectiveness is noticeably lower compared to Pancrelipase of international market. Many patients, especially children, who use Pancrelipase in Western countries and even in neighboring India, show much better outcomes. Their digestion improves, and they achieve nearly normal nutritional status and quality of life.

Nutritional needs in children

Children require a balanced diet composed of carbohydrates, proteins, fats, vitamins, and minerals to support growth and development. In infancy and early childhood, nutrition typically includes breast milk or formula, transitioning to semisolid complimentary foods and then to a diverse diet containing cereals, fruits, vegetables, dairy, fish, eggs, and meats. In older children, this evolves into age-appropriate family meals with 3 main meals and 2-3 snacks per day.[1]

Physiology of digestion and impact of CF

Digestion of these foods requires coordinated enzymatic action. Carbohydrates are digested by salivary and pancreatic amylase, proteins by gastric pepsin and pancreatic proteases (trypsin, chymotrypsin), and fats by gastric and pancreatic lipases.[2] In children with cystic fibrosis (CF), pancreatic enzyme insufficiency impairs fat and protein digestion due to obstructed pancreatic ducts, leading to malabsorption, steatorrhea, poor growth, and fat-soluble vitamin deficiency.[3]

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Role of Pancreatic Enzyme Replacement Therapy (PERT)

To support optimal digestion, PERT with Pancrelipase is essential. Pancrelipase contains lipase, amylase, and protease to assist in food breakdown and nutrient absorption.[4] The enzyme dosing depends on the fat content and volume of meals, with the goal of mimicking physiological digestion as closely as possible.[5] Appropriate enzyme use improves nutritional outcomes, growth, and overall quality of life in children with CF.[6]

Diagnosis of pancreatic insufficiency (PI)

The best test to check for this is measuring faecal elastase in the stool. A low level of faecal elastase suggests pancreatic insufficiency. This test is reliable even if the child is already taking pancreatic enzyme supplements.[7] Stool samples should be sent to the Biochemistry lab for testing.

Monitoring pancreatic function

Faecal elastase levels:[8]

- Normal: >200 µg/g of stool (usually more than 500 µg/g)
- Mild to moderate PI: 100–200 µg/g
- Severe PI: <100 µg/g
- Typical CF with PI: <15 µg/g

In CF, most children with pancreatic problems have faecal elastase levels below 15 µg/g. In term babies, normal levels of faecal elastase are seen by day 3 of life, and by 2 weeks of age in preterm babies born before 28 weeks. So, this test should not be done earlier than these ages.[9]

Because faecal elastase test results may take time, checking for faecal fat globules under a microscope can help decide early if enzyme therapy is needed.[10]

Some babies with cystic fibrosis (CF) may have normal pancreatic function at birth, but around 90% develop pancreatic insufficiency (PI) within the first year of life.[11] If a child who was previously pancreatic sufficient (PS) shows signs like fatty stools or poor weight gain, it's important to check again for PI.[12]

For babies who are PS after newborn screening, the faecal elastase test should be repeated at 3 months, 6 months, and again at the 1-year review. If the levels fall in the borderline range (100-250 µg/g), or the child shows symptoms, the test should be done sooner. After the first year, it is only repeated if symptoms or concerns arise.[13]

Indications for enzyme therapy

The need for Pancreatic Enzyme Replacement Therapy (PERT) varies from child to child. It depends on the child's symptoms and food intake. Signs that PERT may not be working well include greasy, floating, pale/grey or yellow, and loose stools, as well as poor weight gain. If these are present, testing for faecal fat globules under a microscope can help guide treatment.[14]

Effect of CFTR modulators on pancreatic function

When a child starts CFTR modulators, their pancreatic function may improve, and PERT requirements might reduce. In such cases, faecal elastase should be tested again.[15]

Composition and forms of pancrelipase

The most commonly used PERT brand is Pancrelipase, which contains 3 digestive enzymes: lipase (breaks down fat), protease (breaks down protein), and amylase (breaks down carbohydrates). Pancrelipase is available in different forms, including:

Pancrelipase Micro (tiny enteric-coated beads)

Capsules with 10,000 or 25,000 units of enzyme activity.[16]

Timing and administration of pancrelipase

Children with cystic fibrosis (CF) should take pancreatic enzymes every time they eat meals, snacks, or drink anything that contains fat or protein.[17] These enzymes help the body digest food properly when the pancreas is not working well. A dietitian teaches families how much Pancrelipase (enzyme supplement) to take with different types of food.[18]

Foods not requiring enzyme supplementation

Some foods do not need enzyme supplements. These are foods made only of sugars or carbohydrates, and they include[19]:

- Fruits and vegetables (except avocado, which is high in fat)
- Sugar, jam, honey, and syrup
- Fruit juice, fizzy drinks, and squash
- Sorbet or fruit lolleis
- Jelly and boiled sweets
- Juice-based nutritional supplements

These foods are digested easily without help from enzymes because they don't contain fat or protein.[20]

Special considerations in infants and toddlers

Babies and young children under 3 years old usually start enzyme treatment with Pancrelipase Micro, which contains tiny, enteric-coated granules.[21] Each scoop of commercially available Pancrelipase has 5,000 IU of lipase, one of the enzymes that helps break down fat.[22] These enzymes are made from porcine (pig) sources.[23]

The granules should be given on a spoon with a small amount of apple puree just enough to hold the granules together at the beginning of a feed. They should not be mixed into bottle feeds or full meals. This is because enzymes may become active too early, especially in theacidic stomach, and will not work properly when they reach the small intestine where digestion takes place.[24]

Also, the granules should never be chewed, as they may taste unpleasant, damage the mouth and gums, and discourage children from eating.[25]

Switching to capsules and swallowing techniques

At around 1 year of age, parents may be offered a switch to Pancrelipase 10,000 IU capsules for easier handling. The capsules can be opened and the granules sprinkled onto apple puree. One capsule equal about two scoops of Pancrelipase Micro.[26]

Between the ages of 2 to 5 years, children should be gently taught how to swallow enzyme capsules whole.[27] These are usually taken at the start of a meal. Though many studies have looked into the best time to take pancreatic enzyme replacement therapy (PERT), there is no clear answer yet.[28]

Enzyme dosing and administration

Enzymes can be taken at the beginning, middle, or end of a meal.[29] However, after swallowing the enzymes, they work best for about 20-30 minutes. So, if possible, meals should be completed during this time for the enzymes to help with digestion properly.[30]

Since this timing may not always work for every child, one helpful method is to split the enzyme dose giving half with the main meal and the other half with dessert or pudding. This can help the enzymes match better with how the child eats and improve digestion.[31]

Dosing strategies for pancrelipase

There are no strict rules for the exact dose of pancreatic enzymes (Pancrelipase), but doctors usually start with general guidelines and then adjust the dose individually. The goal is to stop signs of poor digestion (like oily stools or weight loss) and help the child grow well.[32]

Usual starting doses:

- **Babies**: Start with $^{1}/_{3}$ to $^{1}/_{2}$ scoop of Pancrelipase Micro per breastfeed or 120 ml formula. This may increase to 1-2 scoops as needed. A rough guide is 1 scoop for every 4 grams of fat, 120 ml milk contained 4 to 6 grams fat.
- **Toddlers**: Usually take 2 Pancrelipase 10,000 IU capsules with meals and 1 capsule with snacks.
- **Pre-schoolers**: May need 2-3 capsules with meals and 1-2 with snacks.
- **School-aged children**: Usually need 4-6 capsules with meals and 2-3 with snacks.
- **Teenagers**: Often require 5-8 capsules with meals and 2-3 with snacks, depending on their weight and food intake.[33]

Some babies may get constipated when starting Pancrelipase. In that case, they might need a small laxative daily to help soften their stools until the right enzyme dose is found.[34]

Experts recommend that children should not take more than 10,000 IU of lipase per kilogram of body weight per day.[35] But in real life, some infants and children may need higher doses to manage signs of poor digestion, especially during times when they are growing fast like infancy and teenage years.[36]

Use of Pancrelipase in tube-fed children

For children who are tube-fed, Pancrelipase Micro can be given through the feeding tube. The tube should be flushed well with water to stop it from getting blocked or damaged.[37] Only large tubes (14FR or bigger) should be used because the enzyme granules are too big to pass through smaller tubes.

If needed, Pancrelipase Micro can be mixed with water and/or sodium bicarbonate, but this must be first discussed with a doctor and pharmacist.[38]

Other options include Pancrelipase powder (measured with a special scoop) or the contents of Pancrelipase capsules, which can be opened and the powder inside used for feeding.[39]

Conclusion

PERT is crucial for children suffering from exocrine pancreatic insufficiency, especially in conditions like cystic fibrosis. Global use of Pancrelipase has shown significantly better health outcomes, yet its low practice in Bangladesh because of less availability. To bridge this gap, improving availability of PERT and updated knowledge are vital for ensuring better growth and nutritional health in affected children.

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