A MORE EFFECTIVE APPROACH TO TREATING EoE

DESIGNING A NEW MEDICATION DELIVERY METHOD TO THE ESOPHAGUS

Although eosinophilic esophagitis (EoE) is rare, hospitals across the country, including Children’s Mercy Kansas City, have seen an increase in prevalence in the past 20 years. When this allergic response strikes younger children they respond by vomiting and refusing to eat, which leads to poor weight gain and nutritional deficiencies. Older children experience painful swallowing and can develop scar tissue in their esophagus, requiring surgical intervention. Rachel Chevalier, MD, pediatric gastroenterologist at Children’s Mercy, is leading an effort to change that by developing a new method of delivering medication to the esophagus.

CURRENT TREATMENT OPTIONS LESS THAN EFFECTIVE

Two approaches to treatment are common today: medication and an elimination diet. Neither works perfectly and both come with side effects. The medication used most commonly, budesonide, is used in the form developed for treating asthma via nebulizer. When used to treat EoE, however, the liquid medication must be mixed with something to thicken it to a viscous slurry before the child is asked to swallow it. The taste and texture are highly unpleasant, making adherence difficult for small children and families. More importantly, after it is swallowed, the medication can be quickly washed away from the tissue where it is needed.

As for elimination diets, it can be challenging to identify the right food or food group that is causing the reaction. Often, children who are already at risk for growth failure are asked to remove multiple food groups from their diet, severely limiting their nutrition options and affecting their social interactions around food at home and at school. In addition, repeated endoscopies with anesthesia are required along the way. Meanwhile, the inflammation worsens, creating a vicious cycle.

RETHINKING THE DELIVERY METHOD

In her study, Dr. Chevalier is learning the answers to these questions:

• What makes medications stick in the esophagus?
• What increases the likelihood that esophagus tissue will take up the medication?

Dr. Chevalier began her project with the understanding that uptake is improved dramatically the longer the medication remains on the walls of the esophagus. The challenge is that the esophagus is designed to quickly propel ingested contents to the stomach and its cells are not designed to take up medication. To date, providers have increased the viscosity of the delivery solution in an attempt to prolong its residence time and increase the amount of medication the cells pick up.

Dr. Chevalier began developing a two-pronged approach to ensure the medication remains in the esophagus longer. It is based on a polymer that’s known to be sticky to these cells and a shape that will help the medication resist the flow of saliva and peristalsis.
STEP ONE: IDENTIFY AN APPROPRIATELY STICKY SUBSTANCE

First, Dr. Chevalier selected the polymer sodium alginate, which is FDA-approved for use in a variety of medications and food items. It is sticky to certain types of mucus and cells, including cells lining the esophagus, making it an ideal candidate for study. Dr. Chevalier then developed a method to embed the medication into the polymer.

STEP TWO: CREATE A SHAPE THAT STAYS IN PLACE

Second, Dr. Chevalier fabricates coin-shaped discs that would not be easily dislodged from the walls of the esophagus. She is creating the small discs out of the medication-embedded polymer. Each disc is minuscule, at 300 micrometers across and only a few micrometers tall. A single dose of the medication is made up of thousands of the discs. Dr. Chevalier uses microfabrication techniques, including photolithography, to fabricate the discs.

These discs are being designed to slowly release the medication as they dissolve. The goal is for the combination of stickiness and shape to keep the medication in place much longer on the cells that line the esophagus.

TESTING THE NEW DESIGN IN AN ANIMAL MODEL

Finally, Dr. Chevalier tests the new delivery method using a pig esophagus model, which is similar to the human esophagus. She built a machine to match the temperature and humidity typically found in the esophagus. She then simulates the flow of saliva over the walls of the esophagus. With this model she is able to test different slurries of medication to see how much remains in place and is absorbed into the tissue – including the medication released from the polymer discs.

THE FUTURE OF THE PROJECT

Although this study is still in the early laboratory phase, Dr. Chevalier hopes to be able to prove that the new design is beneficial to the uptake of the medication. The next phase will be an animal study using diseased tissue – important because tissue reacts to medication differently when it is inflamed. If those results are promising, she hopes to proceed to a clinical trial in patients.