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Adverse reactions increase in children with use of common reflux aids: study

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Proton Pump Inhibitors (PPIs)—such as Prilosec, Protonix and Nexium, have long been one of the most prescribed medications in the country to aid in the reduction of stomach acid.

The use of these medicines among children is on the rise and so are potential side effects, which is sparking concern according to a recent study published in *Pediatrics*.

"CYP2C19 Phenotype and Risk of Proton Pump Inhibitor-Associated Infections," a retrospective, biorepository, cohort study led by Sara Van Driest, MD, Ph.D., assistant professor of Pediatrics at Monroe Carell Jr. Children's Hospital at Vanderbilt, examined DNA from patients ages 0 to 3 years old at the time of PPI exposure.

"PPIs are commonly used in children to treat gastrointestinal disorders, and we are seeing an increase in the number of adverse infection events associated with their use," said Van Driest, the principal investigator of the study.

"Because these medications are available over the counter for adults, they are thought to be a safe option for children. These medicines are seen as very low risk with few downsides. But what we have found is that PPIs aren't without risk," she stressed.

According to Van Driest, there is a specific enzyme in the body, CYP2C19, that helps break down these medications. The enzyme works

differently in each person—from slow, normal, fast and sometimes not at all—impacting the ability of the medication to be safely metabolized.

Because CYP2C19 inactivates PPIs, genetic variants that decrease the enzyme's function may increase the medicine levels in the body leading to more infection events. Stomach acid naturally protects the body from dangerous organisms that can be found in water and food. Reducing stomach acid may increase an infant's risk of these kinds of infections.

The study included PPI-exposed infants, both healthy and those with chronic health conditions, with varying levels of enzyme function. In all, 670 individuals were included using BioVU samples, Vanderbilt's biorepository of DNA extracted from discarded blood collected during routine clinical testing.

The team hopes its findings will help clinicians make the best decisions on prescribing PPIs in children.

"The fact that children who have been characterized as normal CYP2C19 metabolizers actually had more infection events than the fast metabolizers tells us that being exposed to these drug levels actually puts the child at risk for having an extra infection event," said Van Driest.

"We were able to highlight that these medicines do have side effects, and as clinicians we need to think very carefully about the benefits and the risks. We can consider doing a genetic test to identify if a patient is a slow, normal or fast metabolizer."

Genetic testing can be a useful tool to determine if a patient requires a lower or higher dose of the drug.

At Vanderbilt, the PREDICT (Pharmacogenomic Resource for Enhanced Decisions in Care and Treatment) genetic test is available to

predict patient responses to drugs. Some people metabolize drugs abnormally, to the point of deriving no benefit from a particular drug or responding dangerously to a normal dose. These different drug responses increasingly are associated with different common genetic variants.

The study findings add to the growing evidence that CYP2C19's impact on PPIs warrants extra consideration when prescribing.

"We are hoping that pediatricians will pause before starting PPIs knowing that there is an increased risk of infections while their patients are on this drug," said Van Driest. "If there is a need to start the drug, they can consider genetic testing to find out their patient's CYP2C19 status."

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