

LETTER TO THE EDITOR

(Es)omeprazole and Discoloration of Regurgitated Gastric Contents in Infants: Worrying for Care-Takers and a Sign of a Reduced Bioavailability

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Gastro-esophageal reflux is usually self-limiting and without complications.^{1,2} When reflux is associated with symptoms such as poor weight gain, esophagitis, or respiratory problems it is known as gastro-esophageal reflux disease (GERD).¹ When pharmacological treatment of GERD is deemed necessary, the proton pump inhibitors (PPIs) omeprazole and its S-enantiomer esomeprazole can be prescribed. Omeprazole is licensed for children aged 1 year and older and with weights above 10 kg with severe reflux esophagitis or GERD.³ Esomeprazole is licensed for the treatment of erosive reflux esophagitis or GERD for all children.⁴ The experience of treatment with esomeprazole in children of <1 year is limited, and esomeprazole treatment in this group is not recommended.⁴ The stability of both esomeprazole and omeprazole (i.e., (es)omeprazole) is pH dependent. Therefore, omeprazole and esomeprazole tablets or capsules contain enteric-coated granules that can be dispersed in slightly acid liquid (e.g., applesauce) for use in infants.⁵

In this letter we describe 6 cases of purple/red gastric juice discoloration associated with the use of (es)omeprazole for gastro-esophageal reflux that were reported to the Netherlands Pharmacovigilance Centre Lareb. Four children had discoloration of regurgitated gastric juices associated with the use of omeprazole and 2 had discoloration with esomeprazole (see the Table). In 4 cases red or purple granules were also present in the regurgitated stomach contents. In all

children on omeprazole a dosage of 10 mg daily was prescribed; 1 child received 5 mg esomeprazole once and another received 5 mg twice daily. None of the children were using concomitant medication during treatment with (es)omeprazole. In case E initially it was thought that there was blood in the regurgitated gastric contents. The outcome was reported in 4 cases: cessation led to the disappearance of the discoloration of gastric juices.

The enteric coating of (es)omeprazole prevents the release of the drug before it reaches the intestine. Below a pH value of 4 omeprazole rapidly degrades to a dark purple compound.⁶ It seems that dispersion in water or insertion of (es)omeprazole-coated particles in the buccal space can lead to degradation of the coating.^{7,8} Tuleu et al⁷ have previously reported on dark purple-colored 'poppy seed'-like structures found in the aspirated stomach contents and feces of infants treated with omeprazole, comprising of undissolved omeprazole and its degradation products. Beers et al⁸ found that adding omeprazole particles from capsules to a slightly alkaline solution of pH 8 in a laboratory setting lead to degradation of the coating and visible turbidity of the solution. The enteric coating, methylacrylic acid-ethyl acrylate co-polymer, that is used in omeprazole capsules and omeprazole tablets dissolves at pH levels greater than 5.5. When omeprazole is given with water, after sufficient contact with the stomach contents of pH 3 to 4, the permeability of the enteric coating can in-

Table. Case Descriptions of Discoloration of Regurgitated Gastric Juices in 6 Infants Using (Es)omeprazole for GERD

Case	Age at Time of Reaction (mo)	Sex	Drug (Formulation)	Dose	Mode of Administration	Description of Adverse Reaction	First Occurrence, Outcome
A*	3.5	M	Omeprazole (tablets)	10 mg qd	Tablets were dissolved in water prior to administration	Spit out red granules	7 hr after first dose, resolved after discontinuation
B*	3.5	M	Omeprazole (tablets)	10 mg qd	Tablets were dissolved in water prior to administration	Spit out red granules	7 hr after first dose, resolved after discontinuation
C	6	M	Omeprazole (capsules)	10 mg qd	Capsules were opened, coated particles inserted in the buccal space	Purple color of gastric juices/vomit	After 45 days of treatment, resolved after discontinuation
D	3.5	M	Omeprazole capsules	10 mg qd	Unknown	Spit out purple granules	After 40 days of treatment, outcome unknown
E	1	F	Esomeprazole granulate	5 mg qd	Granulate dissolved in water and administered orally using a syringe	Vomit contained red granules	After 13 days of treatment, resolved after discontinuation
F†	3	F	Esomeprazole granulate	5 mg BID	Granulate dissolved in water and administered orally using a syringe	Purple color of gastric juices and vomit	After 2 days of treatment, therapy continued and dose unchanged; at the time of reporting the reaction had not resolved

BID, twice daily; F, female; GERD, gastro-esophageal reflux disease; M, male; qd, once daily

* Twin brothers

† Born prematurely at 31 wk

crease. Acid-induced degradation of omeprazole leads to dark purple discoloration of the drug.^{7,8} Using tap-water to dissolve the PPI when treating infants may therefore add to a reduced efficacy.

In conclusion, our findings illustrate that clinicians should be aware of the possibility of gastric content discoloration and related reduced bioavailability of (es)omeprazole when administering the drug off label to infants of <1 year using a liquid dispersion of solid dosage forms or buccal administration. Although the red/purple discoloration itself will not be harmful, it can cause a scare for the infant's care-takers, and it is a sign of decreased effectiveness of the treatment.

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