



## Highlight the caution use of gastrointestinal prokinetic antibiotics in patient with Henoch-Schönlein purpura

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Dear Editor,

We read the letter by Hu et al. (1) entitled "Erythromycin triggers intussusception in a pediatric patient with Henoch-Schönlein purpura" with great interest. They treated an 8-year-old girl diagnosed as having Henoch-Schönlein purpura (HSP) in combination with a mycoplasma pneumoniae infection using intravenous methylprednisolone (5 mg/kg/day) and erythromycin (30 mg/kg/day). After three days of treatment, the patient complained of having colicky abdominal pain and hematochezia. An intussusception was diagnosed by performing imaging; open appendectomy and manual reduction of the intussusception were performed. Finally, she was discharged with no specific complications.

The most important feature in the above case is that the intussusception occurred after 3 days of treatment; the authors speculate that erythromycin was the leading cause of the intussusception. We agree with the author's opinion. As they provided no further explanation, we present some evidence to support this view for the purpose of urging caution in the use of antibiotics having gastrointestinal motility stimulating effect.

In animal and human experiments, erythromycin is believed to act on the motilin receptor. A small dose of an oral or intravenous injection can promote gastric migrating motor complex contraction and improve gastric emptying (2,3). Though the mechanism of erythromycin on gastrointestinal motility has not been fully elucidated, animal experiments have shown that motilin receptor density has gradient distribution in different gastrointestinal parts. For instance, motilin

receptor distribution in the cat gastrointestinal tract is duodenum > jejunum > antrum of stomach > ileum > gastric body (2). The human gastrointestinal tract is also likely to have the gradient distribution. Therefore, when erythromycin is used in a patient with HSP, it may trigger gastrointestinal motility disorders, particularly in the presence of gastrointestinal edema. It is important to note that erythromycin is not the only antibiotic with the role of promoting gastrointestinal motility; the use of cephalosporin antibiotics such as cefazolin can improve gastric emptying more than the effect obtained using erythromycin (4).

We would like to thank and praise Hu et al. (1) for their efforts, and studies such as this are helpful to identify the optimal treatment method, which remains controversial for patients with HSP having an infection. More studies should be conducted in a manner that evaluates the promotion of the gastrointestinal motility effect of antibiotics for avoiding gastrointestinal motility disorders.

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## Author's Reply

### Erythromycin enhances gastrointestinal motor activity in a dose-dependent manner

To the Editor,

It is a great pleasure for us to reply to the letter by Zhang et al. (1) entitled "Highlight the caution use of gastrointestinal prokinetic antibiotics in patient with Henoch-Schönlein purpura." Erythromycin, a commonly used macrolide antibiotic, has been found to possess potent prokinetic properties. The exact mechanism by which erythromycin enhances gastrointestinal motor activity is not fully elucidated. Current evidence demonstrates that its prokinetic effects are mediated via the motilin pathway. Erythromycin serves as nonpeptide motilin agonist with high affinity for motilin receptors and mimics the biological effects of motilin on the proximal gastrointestinal tract. In addition, it is also known to promote the synthesis of endogenous motilin, and subsequently stimulate cholinergic nerves of the gut at both preganglionic and postganglionic levels, which leads to the release of calcium and contraction of smooth muscle cells (2).

The gastrointestinal motor activity of erythromycin is well documented in clinical applications, especially for the treatment of feeding intolerance in preterm infants. This condition is usually characterized by gastrointestinal hypomotility and a large residue of milk in the stomach at the next feed. A randomized controlled trial from Hong Kong Special Administrative Region, China showed that the median times taken to establish half, three quarters, and full enteral nutrition were 3.5, 8.5, and 13.5 days in preterm infants after receiving intermediate-dose oral erythromycin (12.5 mg/kg); nevertheless, the median times taken to achieve half and full enteral nutrition in the low-dose group (1~3 mg/kg) were almost twice as long (3). Therefore, the prokinetic effects of erythromycin seem to be dose dependent. The presence of two different types of motilin receptors may account for the discrepancy in responses to a low or intermediate dose of erythromycin. The neural motilin receptor on cholinergic neurons is principally stimulated by low dose erythromycin and can initiate phase III migrating motor complexes. In contrast, the smooth muscle motilin receptor responds to higher doses and results in sustained antral contractions and

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improved antroduodenal coordination, which effectively propels the gastric luminal contents distally towards the small and large intestines (4).

In our latest report (5), we encountered an 8-year-old girl who had Henoch-Schönlein purpura in combination with mycoplasma pneumoniae infection. Our patient was treated with intravenous methylprednisolone (5 mg/kg) plus erythromycin (30 mg/kg). Three days later, she complained of colicky abdominal pain and hematochezia, and an intussusception was diagnosed by performing imaging. Taking into account the gastrointestinal motor activity of erythromycin, we speculate that an antimicrobial dose of erythromycin may be a major trigger for the onset of intussusception, particularly under gastrointestinal edema.

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