

Correspondence

The effects of probiotics on the treatment of *Helicobacter pylori* eradication in children

To the Editor

I read the study by Akcam et al,¹ and I have 2 comments on this interesting study.

First, Akcam et al¹ addressed that they found no evidence in terms of the eradication rate (ER) of *Helicobacter pylori* (*H. pylori*), or impact on adverse effects obtained after the addition of probiotics to the standard triple treatment (STT). Their observation could be confidently added to the conflicting results on that issue reported in the literature. The authors did well in partly attributing the different strains and doses of probiotics employed in the related studies reported in the literature as a possible explanation of the conflicting results.¹ However, I presume that the following 2 points might also be explanatory: 1. the resistance rate of *H. pylori* strains to the commonly used anti-*H. pylori* antibiotics used is increasingly reported worldwide as culture-based therapy is not always considered in the pediatric clinical settings; and 2. a review of the literature on that issue revealed that most of the conducted studies, including Akcam et al's study¹ employed the same methodology in terms of evaluating the regimen of concomitant probiotics with STT versus STT. Interestingly, an open label randomized observational clinical study was recently conducted on *H. pylori* infected cohort (age 12-80 years) to test 3 different regimens of *H. pylori* eradication treatment: STT with a concomitant probiotic added at the same time; starting the probiotic for 2 weeks before initiating STT along with the probiotic; and the third regimen consists of the probiotic given concomitantly to sequential treatment. The 3 regimens in the case group were compared to a control group of patients treated with the traditional STT. The study showed that the ER for the traditional STT was 68.9%, and adding the probiotic to STT led to a successful ER of 83% ($p < 0.001$). Pre-treatment with 2 weeks of probiotic before adding it to STT increased the success ER to 90.5%.² Similar improvement in ER was noted when the probiotic was added as an adjuvant to the sequential therapy leading to an ER of 90.8%.² I presume that employing a similar methodology on *H. pylori* infected pediatric patients in a large randomized controlled trial (RCT) is advocated, and improved *H. pylori* ER is solicited.

Second, yogurt is a traditional food worldwide. The nutritional aspects of yogurt for reducing the risk of chronic health conditions and improving nutrient status are well-emphasized. It is produced by bacterial fermentation of milk using a culture of *Lactobacillus delbrueckii subsp. bulgaricus* and *Streptococcus*

thermophilus bacteria. In addition, other lactobacilli and bifidobacteria are also sometimes added during, or after yogurt culture.³ Interestingly, the probiotics-containing yogurt has been found to offer benefits to restore *Bifidobacterium spp./Escherichia coli* (*E. coli*) ratio in children, and suppress the *H. pylori* load with increment of serum IgA, but with reduction in IL-6 in *H. pylori*-infected children.⁴ Reviewing the literature revealed only one study⁵ evaluating the potential activity of the probiotic food (yogurt) as an adjuvant to STT for eradication of *H. pylori* infection in children. Although the study demonstrated no adjuvant effect,⁵ determining the efficacious effect of adding commercial yogurt to the STT of *H. pylori* infection in children still need to be extensively investigated. If that regimen proved to be efficacious in large clinical trials, I presume that its advantages would be manifold for *H. pylori* infected pediatric patients in terms of higher ER, better compliance, reduced cost, improved tolerability, and less therapy-related side effects, particularly diarrhea.

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Reply from the Author

We are grateful to Prof. Al-Mendalawi for his interest in our study and commenting on our article,¹ and providing additional information from the clinical study by Dajani et al.²

First, it should be clarified that children differ from adults with respect to *H. pylori* infection in terms of the prevalence of infection, complication rate, age-specific problems with diagnostic tests and drugs, and a higher rate of antibiotic resistance. In the study by Dajani et al,² the mean age was 37.5 years (17-64 years). However the mean age of our patients was 13.9 ± 2.7 years.¹ Prof. Al-Mendalawi pointed out that the resistance rate of *H. pylori* to the commonly used anti-*H. pylori* antibiotics used is increasingly reported. It is true that the efficacy of STT for *H. pylori* infection has been decreasing progressively. Recent studies⁶ report ERs below 75% in adults, and it has been approximately 61% in our country. Pediatric studies from Turkey⁷ showed that ER with STT has decreased from 75.5% in 2001 to 55% in 2012. In our study,¹ *H. pylori* ER was 68.9% for the STT group. In adults, a recent meta-analysis have demonstrated that sequential therapy administered as *H. pylori* eradication therapy was consistently significantly better than the triple therapy with a significant effect on ERs.⁷ We join

others in concluding that although sequential therapy is promising, further high-quality RCTs in other settings are needed, particularly in children for whom evidence is still limited.

Antibiotic resistance is an important factor in treatment success. Data on clarithromycin resistance in Turkey are usually derived from adult studies.⁷ In these studies, clarithromycin-resistant *H. pylori* strains were detected in 40-48% of the cases.^{8,9} In a study that was conducted in children, the overall incidence of clarithromycin resistance was 25.7%, which is a high percentage,⁷ but it did not explain the very high rate of treatment failure per se in our study.¹ The virulence of *H. pylori* changes geographically, and the presence of different virulence factors. The importance of antibiotic-susceptibility testing and tailored therapy becomes more pronounced in the pediatric population, which is exposed to antibiotics very frequently, and sometimes unnecessarily. Although current data suggest an eradication strategy on the basis of antibiotic-susceptibility testing before the initiation of the treatment, this may not be technically and practically possible all the time. It has been recognized that probiotics can exhibit an inhibitory ability against *H. pylori*. We can agree that starting the probiotic before initiating anti-*H. pylori* therapy may improve *H. pylori* ER.

Probiotics supplementation has been considered a new choice in anti-*H. pylori* therapy. In recent years, more and more studies have been carried out to investigate this topic in children, but the efficacy of probiotics supplementation in children undergoing *H. pylori* eradication therapy has not been entirely established.¹⁰ The current limited evidence suggests that probiotics supplementation in triple therapy for *H. pylori* infection may have beneficial effects on the eradication and therapy-related side effects, however, it seems that the beneficial effects are strain specific. Most of the studies have shown that probiotics have beneficial effects, especially on uneventful effects of antibiotics used in the eradication therapy. It is known that the microbiota is not distributed homogeneously along the intestinal tract. There are minimum amount of microbiota in the stomach, despite the maximum density in the colon. Therefore, probiotics may have minimal effect on the stomach environment and ER. Antibiotics used in eradication may lead to side effects via dysbiosis. Probiotics can decrease the side effects by support, and helps to restore the healthy microbiota. In our opinion, there are not enough studies to reach a definite conclusion on this issue. Further well-designed and large-scale trials on this topic are needed to confirm these findings. Such future studies should focus on clarifying which probiotic preparation is preferred for pediatric patients, in what dosage, and for how long.

It is true that yogurt is one of the best-known food that contain probiotics. Yogurt may act on gut health by modulating the gastrointestinal flora and immune response. The nutritional composition of yogurt is also affected by the species and strains of bacteria used in the fermentation process. Also, we agree with Prof. Al-Mendalawi that yogurt consumption provides good nutrition, and probiotics-containing yogurt may also have many positive contributions. However, we cannot comment on this, as yogurt was not used in our study.

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