H. pylori infection in childhood chronic immune thrombocytopenic purpura

Several studies have reported remission of immune thrombocytopenic purpura (ITP) after eradication of a coexistent *Helicobacter pylori* infection in adults. Data in children are limited. Here we report the results of a prospective study of *Helicobacter pylori* determination and eradication in children with chronic ITP in the Netherlands.

Haematologica 2007; 92:576

Chronic immune thrombocytopenic purpura (cITP) is a rare disease, developing in 10-20 % of children diagnosed with ITP. In adult cITP patients, several groups have reported platelet recovery in half of the patients following eradication of a coexistent *Helicobacter pylori* (*H. pylori*) infection.[1,2] However, these results are contradicted in other studies in which no significant platelet response was seen.[3,4] Reports in children are limited.[5] This prospective study was conducted to establish the prevalence and clinical relevance of eradication of H. pylori infection in children diagnosed with cITP in the Netherlands. All Dutch children, aged up to 16 years, with an isolated platelet count <100×10^9/L persisting for more than one year, otherwise unexplained, were eligible for the study. Pediatricians were repeatedly informed about the study and asked to enter patients. Patients and their families were informed through the ITP patient support group. Children were enrolled from July 1 2003 to January 1 2005. Data regarding patient characteristics were obtained from the child's paediatrician. For detection of *H. pylori* a commercially available stool antigen test (HpSA, Meridian Bioscience Europe, sensitivity of 89-98%; specificity >90%)[6] was performed at time of inclusion. Patients infected with *H. pylori* were treated with a combination of amoxicillin 15 mg/kg, clarithromycin 7.5 mg/kg bd. and omeprazol 2 mg/kg od. for two weeks. Platelet counts were determined at the time of inclusion and three and six months thereafter. Complete remission (CR) was defined as the achievement of a platelet count >150×10^9/L. Partial remission (PR) was defined as a platelet count above 50×10^9/L and at least a doubling of the initial count. The study was approved by the institutional ethical committee of the University Medical Centre Groningen. Written informed consent was provided by the patient or parents.

Forty-seven patients, 18 male (38.3%), 29 female (61.7%) were enrolled (*Table 1, online appendix*). No child underwent splenectomy before or during the study. Three patients (6.4%) were infected with *H. pylori* and received treatment according to protocol. No other platelet enhancing treatment during the study period was prescribed. Two children achieved PR at 3 months, one achieved CR. At the end of the study period 2 children remained in PR. By mistake, one child's platelet count was checked at 9 months instead of at 6. HpSA tests performed at the time of last reported platelet count were negative in all three patients. Follow-up data was available on thirty of the forty-four (68%) *H. pylori*-negative patients. During six months of follow-up, none of these patients achieved PR or CR.

Our study shows that eradication of *H. pylori* might be beneficial in treating chronic ITP. However, while the group studied represents approximately 65% of children with cITP in the Netherlands (estimated prevalence: 1/45,000; pediatric population: 3.2 million), this study is obviously too small to draw definitive clinical conclusions. cITP is a disease characterised by spontaneous remissions especially in the first year after diagnosis.[7] To minimise confusion between spontaneous remission and treatment effect, we defined cITP as a thrombocytopenia persisting for more than one year. Similarly, to prevent small fluctuations in platelet count in children at the higher end of the spectrum qualifying as CR, a platelet count of < 100×10^9/L was used as criterion instead of 150×10^9/L. No follow-up data are available for a third of the control group. Thus data are possibly biased. The fact that these children did not need medical attention during the study period underscores the benign nature of their disease. Similar to adults, the prevalence of *H. pylori* infection (6.4%) in children with cITP is not significantly different from that reported in the general pediatric population (10%),[8] suggesting that a causative relationship is unlikely. All three *H. pylori* positive children initially responded to eradication treatment. Spontaneous remission cannot be excluded but such a variation was not present in the control group. At the end of the study period a downward trend in platelet count is discernible although two children remain in PR. Therefore, with a relatively short follow-up period we cannot exclude the possibility that the platelet response is only transient. A non-specific effect of the medication is unlikely. In a previous study *H. pylori* negative patients did not respond to eradication therapy.[4] To summarize, prevalence of *H. pylori* in pediatric cITP patients is similar to that in the general pediatric population. Three *H. pylori* positive children responded to eradication therapy with an increased platelet count.

Veronica M.E. Neefjes Harriët Heijboer,° Rienk Y.J. Tamminga#*

**Department of Paediatrics, Royal Aberdeen Children's Hospital, United Kingdom; °Emma Children's Hospital, Academic Medical Centre Amsterdam, the Netherlands; #Beatrix Children's Hospital, University Medical Centre Groningen, the Netherlands*

Funding: This study was made possible by a grant from the New Investigations Fund (Starterssubsidie) of the Beatrix Children's Hospital of the UMCG, Groningen, the Netherlands.

Acknowledgments: The authors wish to express their gratitude to all the children and parents who participated in this study. The authors also gratefully acknowledge all pediatricians for their help in entering children in the study.

Key words: immune thrombocytopenic purpura, platelets, Helicobacter pylori.

Correspondence: Veronica Neefjes, Consultant Paediatric Oncologist, Royal Aberdeen Children's Hospital, Westburn Road, Aberdeen, AB25 2ZG. Phone: international +01224.5503564. Fax: international:+ 01224-550704. E-mail: Veronica.Neefjes@nhs.net

References

1. Gasbarrini A, Franceschi F, Tartaglione R, Landolfi R, Pola P, Gasbarrini G. Regression of autoimmune thrombocytopenia after eradication of Helicobacter pylori. Lancet 1998;352:878.
2. Suzuki T, Matsushima M, Masui A, Watanabe K, Takagi A, Ogawa Y, et al. Effect of Helicobacter pylori eradication in patients with chronic idiopathic thrombocytopenic purpura-a randomized controlled trial. Am J Gastroenterol 2005;100: 1265-70.
3. Jarque I, Andreu R, Llopis I, De la RJ, Gomis F, Senent L, et al. Absence of platelet response after eradication of Helicobacter pylori infection in patients with chronic idiopathic thrombocytopenic purpura. Br J Haematol 2001; 115:1002-3.
4. Michel M, Cooper N, Jean C, Frissora C, Bussel JB. Does Helicobacter pylori initiate or perpetuate immune thrombocytopenic purpura? Blood 2004;103:890-6.
5. Jaing TH, Yang CP, Hung IJ, Chiu CH, Chang KW. Efficacy of Helicobacter pylori eradication on platelet recovery in children with chronic idiopathic thrombocytopenic purpura. Acta Paediatr 2003;92:1153-7.
6. Suerbaum S, Michetti P. Helicobacter pylori infection. N Engl J Med 2002;347:1175-86.
7. Reid MM. Chronic idiopathic thrombocytopenic purpura: incidence, treatment, and outcome. Arch Dis Child 1995; 72:125-8.
8. Roosendaal R, Kuipers EJ, Buitenwerf J, van UC, Meuwissen SG, van Kamp GJ, et al. Helicobacter pylori and the birth cohort effect: evidence of a continuous decrease of infection rates in childhood. Am J Gastroenterol 1997;92:1480-2.