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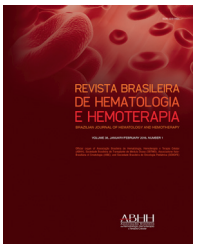

Original article

Platelet count response to *Helicobacter pylori* eradication for idiopathic thrombocytopenic purpura in northeastern Brazil

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ABSTRACT

Background: Several studies have demonstrated that platelet counts in *Helicobacter pylori*-positive patients with chronic idiopathic thrombocytopenic purpura improved significantly after successful eradication of the infection. However, depending of the geographical region of the study the results have been highly divergent.

Objective: The purpose of this study was to evaluate the effect of *H. pylori* eradication therapy on platelet count in a cohort of chronic idiopathic thrombocytopenic purpura patients from northeastern Brazil.

Method: *H. pylori* status was determined in 28 chronic idiopathic thrombocytopenic purpura patients using the rapid urease test and histology. *H. pylori*-positive patients received standard triple therapy for one week. The effect of the eradication therapy was evaluated using the 13C-urea breath test two to three months after treatment.

Results: The prevalence of *H. pylori* infection was similar to that found in the general population. Twenty-two patients (78.5%) were *H. pylori*-positive. Fifteen were treated, 13 (86%) of whom successfully. At six months, 4/13 (30%) displayed increased platelet counts, which remained throughout follow-up (12 months). Platelet response was not associated to mean baseline platelet count, duration of chronic idiopathic thrombocytopenic purpura, gender, age, previous use of medication, or splenectomy.

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Conclusions: *H. pylori* eradication therapy showed relatively low platelet recovery rates, comparable with previous studies from southeastern Brazil. The effect of *H. pylori* eradication on platelet counts remained after one year of follow-up suggesting that treating *H. pylori* infection might be worthwhile in a subset of chronic idiopathic thrombocytopenic purpura patients.

Introduction

Helicobacter pylori, a gram-negative microorganism first isolated by Warren & Marshall in 1984, colonizes the human stomach and may cause type B gastritis and peptic ulcers. Colonization of the stomach by *H. pylori* is associated with increased risk of gastric cancer,[1] and a number of other non-gut-related disorders, such as coronary disease[2] and autoimmune diseases including autoimmune thyroiditis[3] and chronic idiopathic thrombocytopenic purpura (cITP).[4]

cITP is a poorly understood acquired hemorrhagic disease which involves the destruction of platelets in the reticuloendothelial system induced by anti-platelet antibodies.[5] To date an effective and safe treatment for cITP has not been established. cITP treatment has been restricted to therapies with the potential of causing significant toxicity and risks including immunosuppressive agents, such as corticosteroids, intravenous immunoglobulin therapy (IVIg), anti-D immunoglobulin (anti-D), rituximab and salvage splenectomy. Furthermore, 20–30% of cITP patients are resistant to these therapies.[6]

After the discovery by Gasbarrini that platelet counts in *H. pylori*-positive cITP patients improved significantly after successful eradication of the infection,[4] several authors from different geographical regions have evaluated the effect of *H. pylori* eradication therapy on platelet counts in this patient population. However, results have been highly variable (0–100%).[7]

The highest response rates (>50%) are of cohorts in Italy,[8] Japan,[9] Korea[10] and Colombia.[11] On the other hand, in a study from Spain, only 13% experienced a significant increase in platelet counts as a result of *H. pylori* eradication,[12] whereas a study from the United States found no difference between groups.[13]

Differences in the genetic background of the host and in the virulence of *H. pylori* strains may explain the discrepancies observed in studies on *H. pylori* eradication therapy in cITP patients. This bacterium has several virulence genes, showing a high variability of distribution with the most important being the *vacuolating cytotoxin A* gene (*VacA*) and *cytotoxin-associated* gene A (*cagA*). The *cagA* gene is part of a 40 kb cluster of genes (cag pathogenicity island) that codes a type IV secretion system that injects the CagA protein into gastric epithelial cells and is also associated with increased secretion of interleukin-8, a strong proinflammatory chemokine.[14] It has been postulated that CagA evokes host systemic immune responses, producing autoantibodies that cross-react with host platelet surface antigens promoting platelet aggregation via immune complex formation with augmented platelet clearance rates resulting in thrombocytopenia.[15]

The few Brazilian studies that have evaluated the role of *H. pylori* infection in adult cITP patients were based on cohorts from southeastern Brazil.[16] Although the prevalence of *H. pylori* infection is high (80%) in northeastern Brazil[17] and infection is often intrafamilial with onset in early childhood.[18] No study to our knowledge has evaluated the association between *H. pylori* and cITP in cohorts from this region.

Objective

The purpose of the present study was therefore to evaluate the effect of *H. pylori* eradication therapy on platelet counts in a cohort of cITP patients from northeastern Brazil.

Methods

This prospective, observational, study evaluated 28 patients with cITP selected from those who attended the *Centro de Hematologia e Hemoterapia do Ceará*, a referral center for cITP in Fortaleza, Ceara, Brazil. Patients, recruited through convenience sampling from August 2013 to August 2014, were followed up for one year.

cITP was diagnosed according to the guidelines of the American Society of Hematology.[19] Inclusion criteria were i) platelet count $<100 \times 10^9$/L for over six months, ii) normal or increased bone marrow megakaryocytes, and iii) no other thrombocytopenia-related conditions or factors. The exclusion criteria were i) platelet counts $\geq 100 \times 10^9$/L and $\leq 25 \times 10^9$/L, ii) treatment with corticosteroids, immunosuppressants or other specific drugs for cITP as well as splenectomy during the study period, iii) treatment with antimicrobial drugs, steroidal or non-steroidal anti-inflammatory agents or proton pump inhibitors in the 30 days preceding the study, iv) active gastrointestinal bleeding, v) pregnancy, vi) history of treatment for *H. pylori* infection, and vii) history of gastric surgery. cITP patients with platelet counts $\leq 25 \times 10^9$/L were excluded to reduce the confounding effect of concomitant cITP therapies during the study period.

Gastroendoscopy was performed at the university hospital Walter Cantideo, Fortaleza, Ceara, Brazil. All cITP patients were submitted to upper gastrointestinal endoscopy including biopsy of the gastric mucosa from the five sites recommended

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