Original Article

Efficacy of *Helicobacter pylori* Eradication by Standard Triple Therapy in Patients with Chronic Idiopathic Thrombocytopenic Purpura in Pramongkutklao Hospital

Luksamana N
Piyanirun W

ABSTRACT

Background and Aim: Eradication of *Helicobacter pylori* was reported to increase the platelet counts in some *H. pylori*- positive patients with chronic idiopathic thrombocytopenic purpura (ITP). But the efficacy of the eradication was quite different according to previous reports. The aim of this study was to determine the effect of *H. pylori* eradication by standard triple therapy, on their platelet counts and the prevalence of *H. pylori* infection in ITP patients in Pramongkutklao Hospital.

Method: ITP patients were assessed for *H. pylori* infection by ^{14}C -urea breath test. *H. pylori* positive ITP patients were randomly assigned to either the eradication or the non-eradication group. In *H. pylori* eradication group, they received standard triple therapy for *H. pylori* eradication for 1 week. We evaluate the effect of *H. pylori* eradication on platelet recovery within 6 months after standard triple therapy.

Results: Of the 15 ITP patients, 5 (33.3%) were positive for *H. pylori*. Three patients were received triple therapy for *H. pylori* eradication. No significant increased in the mean platelet counts after 6 months of therapy.

Conclusion: The result from this study could not show the benefit of *H. pylori* eradication in term of improvement of platelet counts in ITP patients who infected with *H. pylori*. However further studies with large number of patients are needs to justify the result.

Key words : *Helicobacter pylori* infection, chronic idiopathic thrombocytopenic purpura, standard triple therapy.

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INTRODUCTION

Helicobacter pylori (H. pylori) is a gram-negative, spiral bacillus that colonizes the human gastric mucosa. It is causative of type-B gastritis and peptic ulcer disease, and plays an important role in the pathogenesis of gastric cancer and mucosal - associated lymphoid tissue (MALT) lymphoma[1,2]. Eradication of *H. pylori* is associated with an improvement of gastric mucosal inflammation, a reduced recurrence of peptic ulceration, and prevention of gastric cancer.

H. pylori infection has been implicated in the pathogenesis of non-digestive diseases such as vascular disease (coronary heart disease), autoimmune disease (Sjogren syndrome, hypothyroidism, and Schonlein-Henoch purpura), skin disease (chronic urticaria and rosacea)[3-5], and hematologic disease [iron

Department of Gastroenterology and Hepatology, Pramongkutklao Hospital, Bangkok 10400, Thailand.
Address for Correspondence: *Wanich Piyanirun, M.D., Department of Gastroenterology and Hepatology, Pramongkutklao Hospital, Bangkok 10400, Thailand.*

deficiency anemia[6], idiopathic thrombocytopenic purpura (ITP)[7]].

ITP is an acquired bleeding disorder prevalent in adults, in which autoantibodies bind to the platelet surface and cause platelet destruction in the reticuloendothelial system[8]. The exact mechanism involved in the pathogenesis of ITP is poorly understood.

In 1998, Gasbarrini *et al*.[7] In Italy, reported a notable increase of platelet counts following eradication therapy in patients with *H. pylori*-positive ITP. This study showed recovery of platelet counts in 6 of 8 ITP patients infected with *H. pylori*, after successful eradication of the bacteria. Current therapies for ITP include corticosteroids, immunosuppressive chemotherapy and splenectomy. All of which are associated with side effects and complications. If *H. pylori* eradication can truly lead to improvement of platelet counts in *H. pylori* positive ITP patients, it could well become a standard first-line non-invasive therapy for *H. pylori* positive ITP patients with low incidence of side effects.

In this study, we investigated the effect of *H. pylori* eradication by standard triple therapy on platelet counts, as well as looking into the prevalence of *H. pylori* infection in patients with ITP in Pramongkutklao Hospital.

PATIENTS AND METHODS

Patients

Adult patients with ITP who were followed up at the Hematologic Outpatient Clinic between May 2008 and February 2009 were enrolled into the study. ITP patients with platelet counts below 100×10^3 /μL, who were diagnosed more than 6 months previously, and who willing to participate in the study, were included. Patients with renal failure, or allergy to amoxicillin, clarithromycin, or omeprazole, or who had previously undergone *H. pylori* eradication therapy, were excluded. All patients gave an informed consent prior to the study.

Assessment of *H. pylori* infection and therapy for *H. pylori* eradication

H. pylori infection was assessed by means of ^{14}C urea breath test (UBT; PY test®). In this test, the cut-off value for positive *H. pylori* infection was defined as being above 199 dpm (disintegration per minute). *H. pylori*- positive ITP patients were randomly allocated to the *H. pylori* eradication group (Group A) or the *H. pylori* non-eradication group (Group B). In group A, patients received standard triple therapy for *H. pylori* eradication (amoxycillin 1 gm twice a day, clarithromycin 500 mg twice a day, omeprazole 20 mg twice a day) for 1 week. Eradication was assessed by ^{14}C urea breath test at least four weeks after the eradication therapy.

Assessment of response and follow up

In the *H. pylori* eradication group (Group A), platelet counts were examined at 1 and 6 months after *H. pylori* eradication. In the other *H. pylori* non-eradication group (Group B), platelet counts were also examined at 1 and 6 months after the initial *H. pylori* infection assessment. We evaluated the effect of H. pylori eradication on platelet recovery within 6 months after standard triple therapy. A complete response (CR) was defined as platelet counts greater than 120×10^3/μL. A partial response (PR) was defined as an increment of platelet counts more than 30×10^3/μL from the baseline platelet counts. No response (NR) was defined as any significant increase in the platelet count.

Statistical analysis

Clinical characteristics and demographic data of *H. pylori* positive and *H. pylori* negative patients, as well as of the *H. pylori* eradication and *H. pylori* non-eradication groups, were analyzed using the mean ± standard deviation (SD). The changes of platelet count in the *H. pylori* eradication group (Group A) and the *H. pylori* non-eradication group (Group B) were analyzed by using the Mann-Whitney, Wilcoxon test.

RESULTS

Patient characteristics and Outcome

Fifteen ITP-patients were enrolled in this study. Six were male (40%) and nine were female (60%), ages ranging from 20 to 81 years (mean age, 49.5 ± 16.9

Table 1. Clinical characteristics of all patients.

Demographic data	Patient (N = 15)
Gender	
male	6 (40%)
female	9 (60%)
Age (years)	49.5 ± 16.9
Platelet Count ($\times 10^3$ /μL)	64.2 ± 28.6
Disease Duration (months)	95.6 ± 101.6

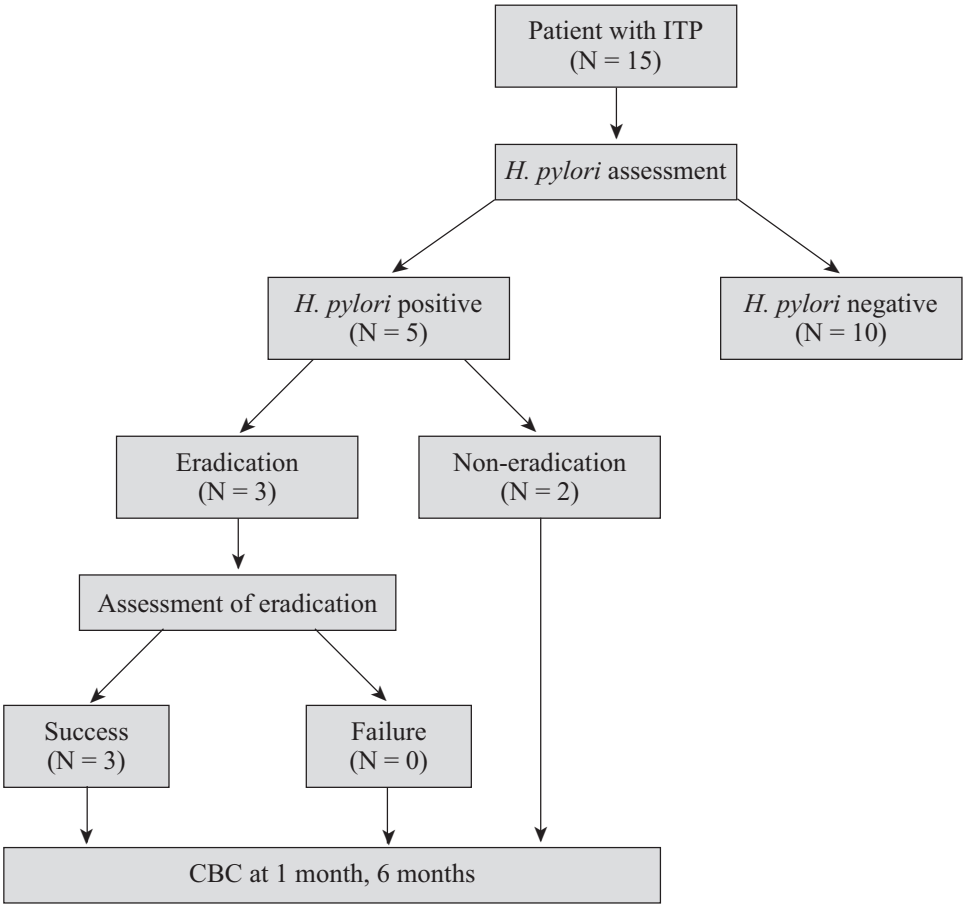

Figure 1. Flow diagram of ITP patients in the study.

Table 2. Clinical characteristics of *H. pylori*-positive and *H. pylori*-negative ITP patients.

	***H. pylori* positive (n = 5)**	***H. pylori* negative (n = 10)**	***p*-value**
Gender (M:F)	3:2	3:7	0.329
Age (years)	50.8 ± 10.9	48.9 ± 19.8	0.846
(range)	(43-70)	(20-81)	
Platelet Count ($\times 10^3$ /μL)	70.4 ± 29.3	61.2 ± 29.3	0.577
(range)	(29-100)	(10-100)	
Disease Duration (months)	94.8 ± 92	96 ± 110.8	0.984
(range)	(6-228)	(6-360)	
Previous treatment for ITP			
None	0	1	
Prednisolone only	5	7	
Prednisolone + other	0	1	
Other	0	1	
History of peptic ulcer	3	5	

years) (Table 1). As shown in Figure 1, of the 15 ITP-patients assessed for *H. pylori* infection, 5 patients (33.3%) were positive for *H. pylori* and 3 cases were designated as the eradication group (Group A) while the other 2 cases were allocated to the non-eradication group (Group B). Successful eradication was achieved in all 3 cases (100%). Comparison between the clinical characteristics of *H. pylori* positive and *H. pylori* negative patients revealed no differences in age, sex, disease duration, previous treatment for ITP, history of peptic ulcer disease, and mean platelet count (Table 2). Subgroup analysis in the *H. pylori* positive group also revealed no difference in sex, previous treatment for ITP, and history of peptic ulcer disease, between the eradication group (Group A) and the non- eradication group (Group B), although the mean age, and the duration of disease were higher in the non-eradication group (Group B) (Table 3). Prior to the study, the mean platelet count in the non-eradication group (Group B, $98.5 \pm 21.2 \times 10^3$ /μL) was higher than in the eradication group (Group B, $51.6 \pm 20.2 \times 10^3$ /μL) (Table 3). In Group A, no patients reported serious side effects during the eradication therapy. As shown in Figure 2 and Table 4, the mean platelet count 6 months after *H. pylori* eradication ($52.3 \pm 16.4 \times 10^3$ /μL) did not significantly increase. According to this result, there is no important of platelet count after *H. pylori* eradication in ITP patients.

Table 3. Clinical characteristic of *H. pylori*-positive patients.

	(Group A) Eradication group (n = 3)	**(Group B) Non-eradication group (n = 2)**
Gender (M:F)	2:1	1:1
Age (years)	45.3 ± 2.5	59.0 ± 15.5
Platelet count ($\times 10^3$ /μL)	51.6 ± 20.2	98.5 ± 21.2
Disease Duration (months)	38.0 ± 50.3	180 ± 67.8
Previous treatment for ITP		
None	0	0
Prednisolone only	3	2
Prednisolone + other	0	0
Other	0	0
History of peptic ulcer	2	1

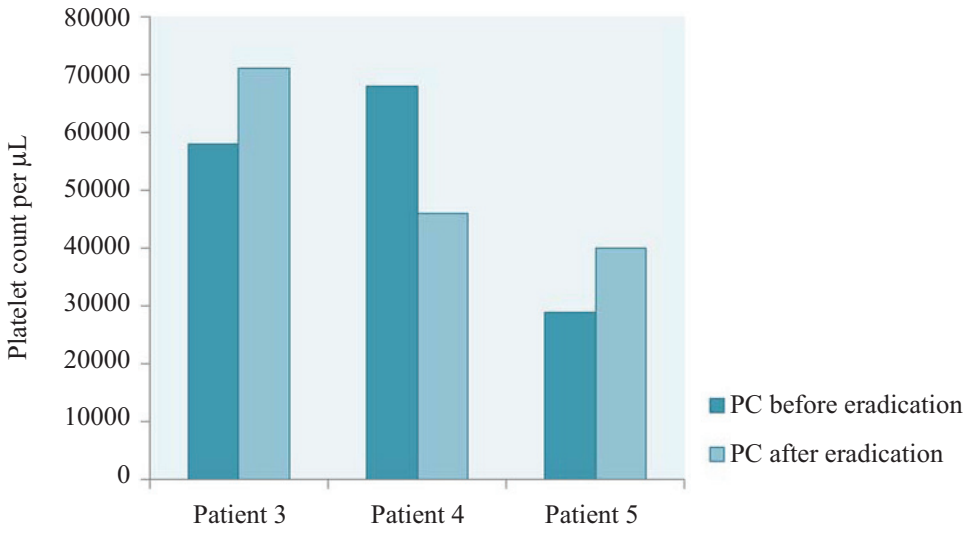

Figure 2. Changes in platelet count before and after *H. pylori* eradication.

Table 4. Changes in platelet count before and after *H. pylori* eradication (per μL).

	Platelet count before eradication	Platelet count after eradication
Patient 3	58000	71000
Patient 4	68000	46000
Patient 5	29000	40000

	before eradication	after eradication	*p*-value
Platelet Count ($\times 10^3$ /μL)	51.6 ± 20.2	52.3 ± 16.4	0.958

DISCUSSION

ITP is an autoimmune disorder characterized by production of antiplatelet autoantibodies and destruction of platelets in the reticuloendothelial system mediated by these auto antibodies. Takahashi *et al*.[9] have demonstrated cross-reactivity between platelet-associated immunoglobulin G (PAIgG) and *H. pylori* cytotoxin-associated gene A (CagA) protein. PAIgG from *H. pylori*-positive patients with ITP reacted with *H. pylori* CagA protein and the reaction decreased after successful *H. pylori* eradication, suggesting that molecular mimicry by CagA of an unknown platelet antigen was crucial in the pathogenesis of a subset of ITP cases. Cross reactivity between an anti-CagA antibody and platelet protein caused the destruction of platelet by an immunologic mechanism.

Gasbarrini *et al*.[7] (1998) from Italy first reported that six of eight *H. pylori* -eradicated ITP exhibited an increase in platelet count. In contrast, Jarque *et al*.[10] (2001) from Spain reported only 3 out of 23 *H. pylori*-eradicated ITP showed an increase in platelet count. Thus, the effect of eradication of *H. pylori* for ITP patients remains controversial. Long-term use of corticosteroids, immunosuppressive drug and splenectomy are still the mainstays of therapy in ITP patients. All such treatment modalities are invasive and have several side-effects. If *H. pylori* eradication therapy can truely improve platelet counts in *H. pylori* positive ITP patients, it could become a standard first-line non-invasive therapy for *H. pylori* positive ITP patients, with low side effects.

We therefore carried out this randomized controlled study to evaluate the effect of *H. pylori* eradication on platelet counts by standard triple therapy in patients with ITP. Secondarily, the study aimed to determine the prevalence of *H. pylori* infection in ITP patients with platelet counts below 10×10^3 /μL. Our data showed that the mean platelet counts at 6 months after eradication by standard triple therapy did not significantly increase, compared to the mean baseline platelet count. This contrasted with some previous studies. The reason may be due to small number of patients, as most ITP patients do not fit in with our inclusion criteria.

In Thailand, the prevalence of *H. pylori* infection in adults is as high as 74%. A previous study in Bangkok and in the rural provinces[11-14] showed an infection rate of about 50-80% in adults and 25.4% in pediatric groups. In this study, the prevalence of *H. pylori* infection in ITP patients with platelets below 10×10^3 /μL was 5 of 15 patients (33.3%), which appeared to be lower than average in the general population.

In summary, our study showed that *H. pylori* eradication therapy did not improve platelet counts in *H. pylori* positive patients. Further studies with larger numbers of ITP subjects are needed for a name meaningful interpretation.

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