

Living FRIendly Summaries of the Body of Evidence using Epistemonikos (FRISBEE)

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Does *Helicobacter pylori* eradication play a role in immune thrombocytopenia (ITP)?

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Abstract

Helicobacter pylori infection has been implicated as trigger or disease modifier in immune thrombocytopenia (ITP). So, eradication treatment for this agent could have clinical benefits. Searching in Epistemonikos database, which is maintained by screening 30 databases, we identified four systematic reviews comprising 40 studies addressing the question of this article overall, including one randomized controlled trial. We combined the evidence using meta-analysis and generated a summary of findings following the GRADE approach. We concluded *Helicobacter* eradication might decrease risk of bleeding in patients with immune thrombocytopenia but the certainty of the evidence is low.

Problem

Helicobacter pylori is known for its influence on the development of gastrointestinal diseases. However, it could also play a role in diseases outside the digestive system such as immune thrombocytopenia (also called idiopathic or immune thrombocytopenic purpura - ITP). This condition is characterized by the presence of antibodies against platelets, and it has been postulated *Helicobacter* might act as a trigger, and also as a disease modulator by a mechanism not completely understood.

For this reason, it has been suggested eradication of *Helicobacter* could be beneficial. However, it is unclear whether this actually translates into clinical benefits.

Methods

We used Epistemonikos database, which is maintained by screening more than 30 databases, to identify systematic reviews and their included primary studies. With this information we generated a structured summary using a pre-established format, which includes key messages, a summary of the body of evidence (presented as an evidence matrix in Epistemonikos), meta-analysis of the total of studies, a summary of findings table following the GRADE approach and a table of other considerations for decision-making.

Key messages

- *Helicobacter* eradication might decrease bleeding risk in immune thrombocytopenia, but the certainty of the evidence is low.
- Adverse effects of *Helicobacter* eradication therapy are common but self-limiting and not severe.
- There is a substantial number of published and ongoing trials that have not yet been incorporated into systematic reviews in this topic, so a new review could provide further information on the matter.

About the body of evidence for this question

<p>What is the evidence. See evidence matrix in Epistemonikos later</p>	<p>We found four systematic reviews [1], [2], [3], [4], including 40 studies addressing the question of interest[5], [6], [7], [8], [9], [10], [11], [12],[13], [14], [15], [16],[17], [18], [19], [20], [21], [22], [23], [24], [25], [26], [27], [28], [29], [30], [31], [32], [33], [34], [35], [36],[37],[38], [39], [40], [41], [42], [43], [44]. However, only one corresponds to a randomized controlled trial [32]. This table and the summary in general are based on the latter, because the inclusion of the non-randomized studies did not provide additional relevant information or increase the certainty of the existing evidence.</p>
<p>What types of patients were included</p>	<p>The trial included adult patients between 18 and 75, with chronic immune thrombocytopenia and <i>Helicobacter pylori</i> infection confirmed with urea breath test.</p> <p>Patients were included only if secondary causes of thrombocytopenia had been clearly ruled out, including hepatitis B or C virus infection, HIV infection, lupus, antiphospholipid antibody syndrome, bone marrow failure syndromes, drug-induced thrombocytopenia, and malignancies such as chronic lymphocytic leukemia and malignant lymphoma.</p> <p>Patients with renal failure, severe liver failure, allergic to amoxicillin, clarithromycin or lansoprazole and patients with platelet counts below $20 \times 10^3/\mu\text{l}$ or above $100 \times 10^3/\mu\text{l}$ were also excluded.</p>
<p>What types of interventions were included</p>	<p>The trial evaluated eradication of <i>Helicobacter pylori</i> with amoxicillin 750 mg, clarithromycin 200 mg and lansoprazole 30 mg bid for one week. The trial compared against placebo.</p>
<p>What types of outcomes were measured</p>	<p>All of the systematic reviews evaluated only considered the outcome platelet response, measured in different ways. The randomized trial defined a platelet count of $150 \times 10^3/\mu\text{l}$ as complete response and a partial response over $50 \times 10^3/\mu\text{l}$.</p>

Summary of findings

The Information on the effects of *Helicobacter pylori* eradication in patients with immune thrombocytopenia is based in only one randomized trial including 25 participants [32]. The trial measured increase in platelet count after the eradication of *Helicobacter pylori*, which was used as indirect evidence of the effect on the risk of bleeding. The summary of findings is as follows:

- *Helicobacter* eradication might decrease bleeding risk in immune thrombocytopenia, but the certainty of the evidence is low.
- Adverse effects of *Helicobacter* eradication therapy are common but self-limiting and not severe. The certainty of the evidence is high.

<i>Helicobacter pylori</i> eradication for immune thrombocytopenia				
Patients	Immune thrombocytopenia + <i>Helicobacter</i> (+)			
Intervention	Eradication of <i>Helicobacter pylori</i>			
Comparison	Placebo			
Outcomes	Absolute effect*		Relative effect (IC 95%)	Certainty of the evidence (GRADE)
	WITHOUT eradication	WITH eradication		
	Difference: patients per 1000			
Bleeding	This outcome was not reported, but can be indirectly estimated through the probability of partial or complete platelet response, which was higher with eradication (RR 12.07; 95%, 0.75 to 193).		--	⊕⊕○○ ^{1,2,3,4} Low
Adverse effects	The trial does not report adverse effects. However, based on other studies we know eradication therapy produces adverse effects in 14% to 27% of patients, mainly abdominal pain, diarrhea, headache and vomiting [45].		--	⊕⊕⊕⊕ High

RR= Risk ratio.
Margin of error = 95% confidence interval (CI).
GRADE: evidence grades of the GRADE Working Group (see later in this article).

* The risk **WITHOUT eradication** is based on the risk in the control group of the trial. The risk **WITH eradication** (and its margin of error) is calculated from relative effect (and its margin of error).

¹ The trial has serious limitations, so we downgraded the certainty of the evidence in one level because of risk of bias.
² We downgraded the certainty of the evidence in one level for imprecision since the confidence interval is extremely wide.
³ We downgraded the certainty of the evidence in one level for indirectness. Platelet response constitutes a reliable surrogate outcome, so we only downgraded it in one level.
⁴ We upgraded the certainty of the evidence in one level for large effect size.

About the certainty of the evidence (GRADE)*

⊕⊕⊕⊕

High: This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different† is low.

⊕⊕⊕○

Moderate: This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different† is moderate

⊕⊕○○

Low: This research provides some indication of the likely effect. However, the likelihood that it will be substantially different† is high.

⊕○○○

Very low: This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different† is very high.

*This concept is also called 'quality of the evidence' or 'confidence in effect estimates'.

† Substantially different = a large enough difference that it might affect a decision.

Other considerations for decision-making

To whom this evidence does and does not apply

- The evidence presented in this summary is widely applicable to *Helicobacter pylori* positive adults with immune thrombocytopenia.
 - While some observational studies have suggested a role in patients without demonstrated *Helicobacter* infection, it does not seem reasonable to extrapolate to this group in the absence of more certain evidence.
 - This evidence does not apply to secondary immune thrombocytopenia, since there is no role of *Helicobacter* in these cases.
-

About the outcomes included in this summary

- Bleeding and adverse effects were considered as critical outcomes for decision-making according to the opinion of the authors of this summary.
 - Platelet count corresponds to a surrogate outcome that allegedly has good correlation with bleeding, so we considered it as indirect evidence for bleeding risk.
-

Balance between benefits and risks, and certainty of the evidence

- From other studies we know adverse events related to *Helicobacter* eradication treatment are frequent, but self-limiting and mild [36]. In addition, there may be benefits in relation to the decrease of bleeding risk, although the certainty of the evidence is low.
 - Eventually, other benefits associated with the eradication of *Helicobacter* not related to immune thrombocytopenia could be considered, which could tip the balance in favor of treatment.
-

What would patients and their doctors think about this intervention

- Considering the nature of the adverse effects, some patients and their doctors may be inclined to use this intervention, despite doubts about benefits.
 - Other patients may not want to be exposed to adverse effects from an intervention whose effectiveness has low level of certainty.
-

Resource considerations

- It is a relatively low-cost intervention, so probably this factor is not determinant in the decision.
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Differences between this summary and other sources

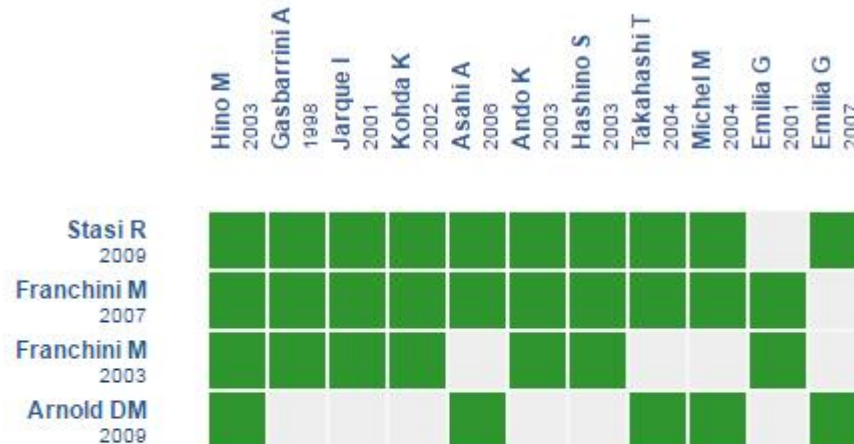
- The conclusions of this article partially agree with the identified systematic reviews, noting eradication could have benefits. However, our summary puts more emphasis on the limitations of the existing evidence
 - The conclusions of this summary do not agree with one of the main guidelines on this subject [46], which recommends against routine eradication in asymptomatic patients with chronic immune thrombocytopenia. Importantly, the guideline does not include most of the evidence discussed in this summary.
-

Could this evidence change in the future?

- The probability that the conclusions of this summary change with future evidence is high, due to the existing uncertainty.
 - We identified at least three ongoing studies evaluating this question [47],[48],[49], and some already published but not yet incorporated into systematic reviews [50],[51],[52],[53]. So, it is very likely that a new systematic review would offer relevant information.
-

How we conducted this summary

Using automated and collaborative means, we compiled all the relevant evidence for the question of interest and we present it as a matrix of evidence.



Starting from any systematic review, Epistemonikos builds a matrix based on existing connections in the database.

The author of the matrix can select relevant information for a specific health question (typically in PICO format) in order to display the information set for the question.

The rows represent systematic reviews that share at least one primary study, and columns display the studies.

The boxes in green correspond to studies included in the respective reviews.

Follow the link to access the **interactive version**: [Helicobacter pylori eradication for immune thrombocytopenia \(ITP\)](#)

Notes

The upper portion of the matrix of evidence will display a warning of "new evidence" if new systematic reviews are published after the publication of this summary. Even though the project considers the periodical update of these summaries, users are invited to comment in *Medwave* or to contact the authors through email if they find new evidence and the summary should be updated earlier. After creating an account in Epistemonikos, users will be able to save the matrixes and to receive automated notifications any time new evidence potentially relevant for the question appears.

The details about the methods used to produce these summaries are described here <http://dx.doi.org/10.5867/medwave.2014.06.5997>.

Epistemonikos foundation is a non-for-profit organization aiming to bring information closer to health decision-makers with technology. Its main development is Epistemonikos database (www.epistemonikos.org).

These summaries follow a rigorous process of internal peer review.

Conflicts of interest

The authors do not have relevant interests to declare.

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