Research Unit

Improving outcomes for patients with autoimmune platelet disorders

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In brief…

Platelet disorders are difficult to diagnose and treat. Researchers are improving the accuracy of diagnosis and helping determine the best treatments.

What is this research about?

Immune thrombocytopenia (ITP) is a blood disorder characterized by bleeding due to a shortage of platelets. The symptoms of ITP are highly variable, ranging from tiny bruises to life-threatening brain hemorrhages. Identifying ITP is difficult because there are no specific diagnostic criteria or biomarkers, apart from a low platelet count with no apparent other causes.

Multiple mechanisms may be involved in ITP. Many ITP patients have antibodies and immune cells that target their platelets for destruction. Some patients may also have problems producing new platelets. ITP is treated in many ways, but the most common first-line treatments to control ITP-related bleeding are corticosteroids and intravenous immune globulin (IVIg). IVIg, a plasma-derived product, has a limited supply and is very costly. In addition, IVIg and corticosteroids, as well as other treatments for ITP, may cause side effects that are difficult for the patient to tolerate.

Researchers at McMaster University are using a multi-faceted approach to refine the diagnosis and treatment process for ITP, ensuring that each patient receives the best possible care.

What did the researchers do?

The four studies presented here were done to determine the best strategies for diagnosing and treating ITP. In the first study, researchers compared independent diagnoses from three experienced hematologists presented with the medical records for patients with low platelet counts. The researchers assessed the level of agreement between the hematologists and compared patient characteristics in cases where there was disagreement versus agreement. In the second study, the researchers did a meta-analysis combining the results from nine randomized control trials of different corticosteroid treatments for ITP patients. The meta-analysis examined platelet counts and side effects for ITP patients treated with two different corticosteroids (high-dose dexamethasone versus prednisone). In the third study, researchers examined how another ITP treatment (rituximab) affected patient antibodies, with the goal of finding a biomarker to identify patients who would respond to the therapy. In the fourth study, researchers identified ITP patients who had been prescribed a new treatment for ITP (romiplostim) and compared the number of IVIg treatments given before versus after starting romiplostim therapy. The researchers also determined the cost impact for the health-care system.

What did the researchers find?

- Agreement was moderate between the experienced hematologists. They identified patient characteristics that most consistently led to an ITP diagnosis, including a platelet count below 20×10^9 per litre and an increase in the platelet count to at least 30×10^9 per litre after treatment.
- The meta-analysis showed that ITP patient responses (increased platelet counts) were similar for the two treatments examined, but patients treated with the high-dose dexamethasone responded faster and reported fewer side effects than patients treated with prednisone.
- Rituximab treatment reduced platelet antibody levels. However, the loss of the antibody after treatment was not associated with a response to rituximab. Investigators noted that the patients who had antibodies that persisted after treatment responded poorly.
- Romiplostim increased platelet counts and decreased IVIg use for most patients and was cost-neutral for the health-care system.

How can you use this research?

Diagnosis of ITP is currently a difficult and subjective process, and even experienced hematologists often do not agree on a diagnosis. Hematologists typically diagnose ITP when platelet counts fall below 100 x 10^9 per litre with no underlying other causes (e.g. fever, enlarged spleen, etc.). However, they could increase the consistency of their ITP diagnoses by using the more specific clinical criteria identified by the McMaster research team (a platelet count below 20 x 10^9 per litre and an increase in the platelet count to at least 30 x 10^9 per litre after treatment).

The meta-analysis provides valuable information to assist health-care providers in choosing between two common corticosteroid treatments for ITP. Although prednisone and high-dose dexamethasone resulted in similar platelet count improvements overall, the meta-analysis indicates that high-dose dexamethasone might be a better choice for some patients, particularly those with severe ITP who require a rapid increase in platelet count.

Although the rituximab study did not show a consistent correlation between loss of anti-platelet antibodies and treatment response, most patients with persistent antibodies did not achieve a clinical response to treatment, suggesting that this could represent a group of patients with severe disease.

Romiplostim treatment effectively increased platelet counts and reduced IVIg use, suggesting that it could help ease the strain on the system by decreasing the amount of IVIg needed for ITP patients. The overall cost to the health-care system did not change with romiplostim treatment.

The research on corticosteroids is providing evidence for new, updated guidelines for ITP management. More accurate diagnosis of ITP and more targeted treatments will improve the experience and outcomes for ITP patients and could also reduce the need for IVIg.

About the research team: Dr. Donald Arnold, who is a professor of medicine at McMaster University and the director of the McMaster Centre for Transfusion Research, was the lead or senior author on all four studies. A Canadian Blood Services medical officer, Dr. Michelle Zeller, also contributed to one study. Other authors include researchers at the McMaster Centre for Transfusion Research and collaborators from the University of Montreal, the Windsor Regional Hospital and the London Health Sciences Centre.

This ResearchUnit is derived from the following publications:

1. Salib M et al. Difficulties in Establishing the Diagnosis of Immune Thrombocytopenia: An Agreement Study. American Journal of Hematology 2016; 91: E327-9.

2. Mithoowani S et al. High-Dose Dexamethasone Compared with Prednisone for Previously Untreated Primary Immune Thrombocytopenia: A Systematic Review and Meta-Analysis. Lancet Haematol 2016; 3: e489-e96.

3. Arnold DM et al. The Effect of Rituximab on Anti-Platelet Autoantibody Levels in Patients with Immune Thrombocytopenia. Br J Haematol 2017; 178: 302-7.

4. Zeller MP et al. Effect of a Thrombopoietin Receptor Agonist on Use of Intravenous Immune Globulin in Patients with Immune Thrombocytopenia. Transfusion 2016; 56: 73-9.

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