Impaired intestinal permeability (IP) in patients with endometriosis: a pilot study

Shanti I. Mohling, MD, FACOG\textsuperscript{1}, Robert S. Furr, MD, FACOG\textsuperscript{1, 2}

\textsuperscript{1} University of Tennessee College of Medicine, Chattanooga, Tennessee, Department of Obstetrics and Gynecology, Division of Minimally Invasive Gynecologic Surgery
\textsuperscript{2} Women’s Surgery Center, Chattanooga, Tennessee

\textbf{Objective:} To determine whether patients with a surgical diagnosis of \textbf{endometriosis} have \textbf{impaired intestinal permeability} as compared with healthy controls.

\textbf{Methods:} \textbf{40 female patients} were enrolled between June 2016 and February 2018. 24 patients with pelvic pain preparing to undergo surgery for suspected endometriosis and 16 healthy age-matched control patients from 2 clinics were invited to participate. \textbf{18 pain patients} completed the study and \textbf{6 control patients} completed the study. All patients were screened for alcoholism, celiac disease or other autoimmune diseases, which can also be associated with IP. Both control patients and pain participants underwent evaluation for IP using a lactulose/ mannitol (L/M) oral challenge. Each subject ingested an oral preparation of Lactulose 5 gm, Mannitol 1gm and water. Urine was collected for six hours and measured for levels of lactulose, mannitol and a ratio of L/M. A urinary L/M ratio >2 Standard Deviations above the reference range is consistent with impaired IP. Patients with an elevation of both lactulose and mannitol above 2 Standard Deviations were also considered to have impaired IP. Pelvic pain patients underwent previously scheduled surgery, as planned. When endometriosis was identified, it was excised and sent to pathology for confirmation.

\textbf{Results:}
The categories analyzed:
1) Pelvic pain with surgical and biopsy-proven evidence of endometriosis.
2) Pelvic pain with a history of surgically identified endometriosis.
3) Pain without surgical evidence of endometriosis.
4) Control patients with no history of chronic pelvic pain or other autoimmune disease.

\begin{itemize}
\item None of the control patients had impaired IP
\item Of patients with Impaired IP, 100% had current or historical surgically proven endometriosis
\item 60\% of patients with endometriosis had impaired IP
\end{itemize}

<table>
<thead>
<tr>
<th></th>
<th>Impaired IP</th>
<th>Normal IP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endometriosis</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>No Endo</td>
<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>

The Fisher exact test statistic value is 0.2059. The result is not significant at \(p < .05\)
Impaired intestinal permeability (IP) in patients with endometriosis

**Background:** Impaired IP is known to be associated with a number of inflammatory conditions and immune-mediated disease states. Impaired IP could explain activation of the dendritic system which causes a shift in Th1/Th2 immunity and over-expression of certain cytokines.

**Limitations of our study:**
- The 6-hour urine collection may have discouraged patients, especially control patients
- All patients may not have adequately collected their specimens
- History of diagnosed endometriosis could not be confirmed with pathology in all cases.

**Conclusions:**
There is a trending correlation between IP and endometriosis. The potential significance of impaired IP and its relationship to peritoneal inflammation warrants continued research. This is interim data and the trial is ongoing.

**Understanding Intestinal Permeability:**
- Over the past two decades, research has correlated immune-related disease with impaired intestinal permeability. This can be seen with a number of autoimmune disease states including, but not limited to, Celiac disease, Type 1 Diabetes, Crohn’s, SLE, Rheumatoid arthritis, Multiple Sclerosus, inflammatory bowel disease and ankylosing spondylitis.
- Increased intestinal permeability allows for exposure of the immune system to environmental antigens that normally would not breach the intestinal barrier leading to a perpetuation of the autoimmune process.
- New understanding of the role of increased intestinal permeability suggests a new paradigm: Genetic predisposition + Environmental triggers + Impaired Intestinal Permeability = Disease

**Intestinal Barrier:**
Immunofluorescence microscopy of mouse small intestine in cross section demonstrates the proximity of the intestinal lumen to the immune system.

Increased intestinal permeability allows for increased exposure of the immune system to environmental antigens that normally would not breach the intestinal barrier. This leads to a perpetuation of a dysfunctional immune process.
Impaired intestinal permeability (IP) in patients with endometriosis

References:
6. MC Buscarinu et al. Intestinal Permeability in Relapsing-Remitting Multiple Sclerosis. *Neurotherapeutics*. [https://doi.org/10.1007/s13311-017-0582-3](https://doi.org/10.1007/s13311-017-0582-3).

This research was made possible by a grant from the Endometriosis Foundation of America