Nicotine and ulcerative colitis – Saint or sinner?

By Dr Lisa Nissen

Ulcerative colitis is a form of inflammatory bowel disease that causes chronic inflammation of the digestive tract. It is generally characterised by abdominal pain and bloody diarrhea. It can be extremely debilitating and can sometimes lead to life-threatening complications. The complications include: severe bleeding, perforated colon, severe dehydration, liver disease, osteoporosis, inflammation of skin, joints and eyes, an increased risk of colon cancer and toxic megacolon. It is estimated that around 10,000 Australians suffer from ulcerative colitis, with men and women affected equally.

Ulcerative colitis, unlike Crohn’s disease, usually affects one continuous section of the innermost lining of the large intestine (colon) and rectum. The course of ulcerative colitis varies, with periods of acute illness often alternating with periods of remission. However, over time the severity of the disease usually remains constant. Ulcerative colitis symptoms can vary, depending on the severity of inflammation and where it occurs. For this reason, it is classified according to its location (Table 1).

<table>
<thead>
<tr>
<th>Type</th>
<th>Location</th>
<th>Signs and symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ulcerative proctitis  (Mildest form)</td>
<td>Confined to the rectum</td>
<td>Rectal bleeding may be only sign</td>
</tr>
<tr>
<td>Proctosigmoiditis</td>
<td>Rectum and the lower end of the colon</td>
<td>Bloody diarrhoea, abdominal cramps and pain are common</td>
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<tr>
<td>Left-sided colitis</td>
<td>Extends from the rectum up the left side through the sigmoid and descending colon</td>
<td>Bloody diarrhoea, abdominal cramping and pain on the left side, and unintended weight loss</td>
</tr>
<tr>
<td>Pancolitis</td>
<td>Affecting the entire colon</td>
<td>Bloody diarrhoea (may be severe), abdominal cramps and pain, fatigue, and significant weight loss</td>
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<tr>
<td>Fulminant colitis. (flare, life threatening)</td>
<td>Affects the entire colon</td>
<td>Severe pain, profuse diarrhoea and, sometimes, dehydration and shock</td>
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</tbody>
</table>

|immune system suppressors| (e.g. azathioprine, mercaptopurine, cyclosporine, infliximab). Although effective, these treatments carry the risk of significant side-effects. More recently however, it is the unusual epidemiological relationship between smoking and inflammatory bowel disease that has given rise to the investigation of potential therapeutic benefits of nicotine for ulcerative colitis. Interestingly, while smoking appears to exacerbate the effects of Crohn’s disease, there is compelling epidemiological evidence that smoking may have a protective effect against ulcerative colitis. The risk of developing the disease is significantly lower in smokers than non-smokers, with ulcerative colitis patients who resume or start smoking often experiencing clinical improvement. A significant proportion of newly diagnosed patients are former smokers who have quit within the previous four years.

Now, in no way does this mean that the significant health risks of smoking itself are outweighed for this patient group and it would never be recommended as a means of treating ulcerative colitis. However, the nicotine contained in cigarettes seems to provide a potential benefit. Although the exact mechanism by which nicotine exerts its benefits in ulcerative colitis is still unknown, it has been speculated that nicotine may assist through; increasing the thickness of colon mucous (enhancing the protection of the intestinal mucous), influencing the cellular and humoral immune system (interferes with the inflammatory response) and affecting gut motility.

There have been a number of studies, including randomized placebo controlled trials; cohort and case studies, which have shown that nicotine can assist in bringing on remission after a flare-up of ulcerative colitis alone and in combination with mesalazine and/or prednisone. These studies have primarily focused on the use of transdermal nicotine (for ease of delivery) in doses varying between 15-30 mg/day for between 4-6 weeks. However, this benefit is not shown in maintenance of remission. Unfortunately, as would be expected the nicotine therapy also caused side effects including nausea, light headedness and headaches. These side effects tended to be more troublesome in people who were non-smokers.
What we can learn from this is that nicotine can provide a potential benefit for ulcerative colitis patients who do not respond to, or have contraindication to conventional therapies (e.g. corticosteroids). However, further investigation is needed into the potential risks and benefits of this type of therapy and more needs to be known about the mechanisms by which nicotine acts in reducing flare-ups in ulcerative colitis patients.

Useful references
- Thomas GO, Rhodes J, Green JT. Inflammatory bowel disease and smoking—a review. Am J Gastroenterol. 1998;93:144-9

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- reduces the need for syringing
- facilitates syringing

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<table>
<thead>
<tr>
<th>Indication</th>
<th>Dose</th>
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<tbody>
<tr>
<td>Nicotine replacement therapy (transdermal)</td>
<td>Initiation (patients smoking &gt; 10 cigarettes / day): 21 mg/day patch should be used for the first 6 weeks, followed by 14 mg/day for 2 weeks, then 7 mg/day for the last 2-4 weeks.</td>
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<tr>
<td>Ulcerative colitis</td>
<td>Nicotine 15-30mg/day (transdermal) for 4-6 weeks in combination with mesalazine during flare-ups</td>
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</tbody>
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