Cigarette Smoking and Crohn's Disease: Are They Linked and What Is Being Done About It?

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ABSTRACT

Crohn's Disease is a serious inflammatory disease of the gastrointestinal tract. It is estimated that up to one million people in the United States alone suffer from an Inflammatory Bowel Disease. While the etiology of this disease is still unknown, there are many factors that are believed to contribute, both genetic and environmental. One environmental factor is cigarette smoking. It is estimated that one-third of our population of adults smoke. Studies at clinical centers show that at least 50% of patients with Crohn's disease are smokers. Research also shows that current and former smokers have a higher risk of developing Crohn's disease than nonsmokers do. Among people with the disease, smoking is associated with a higher rate of relapse, repeat surgery, and immunosuppressive treatment. Smoking also significantly increases the risk of disease recurrence after operation of Crohn's disease, especially in women. While there is no cure for Crohn's disease, many treatment options are available to help decrease the severity of Crohn's disease. These options include: medications, surgery, alternative medicine, nutrition, and strictureplasty.

INTRODUCTION

Cigarette smoking is a large part of our society today. Smoking causes a variety of life-threatening diseases, including lung cancer, emphysema, and heart disease. An estimated 400,000 deaths each year are caused directly by cigarette smoking. But what most don't realize is that smoking can have serious consequences on the digestive

system. One particular disease thought to be due to cigarette smoking is Crohn's disease. Crohn's disease is usually found in the ileum portion of the small intestine and 40 to 50 percent of the time goes through the ileocecal valve to the large intestine, but can occur in any section of the GI tract. (17) Crohn's disease usually causes diarrhea, cramp-like abdominal pain, often fever, and at times, rectal bleeding. Loss of appetite and subsequent weight loss may also occur. Symptoms may range from mild to severe, but, in general, people with Crohn's disease can lead active and productive lives. (16)

METHODS

Upon studying the gastrointestinal system in class, it became clear to me that most of the conditions being discussed had smoking as a related cause. This triggered me to investigate further. On November 24, 2001, I went to Logan College of Chiropractic Library. Bob Snyder, the librarian, and I conducted a few searches with different areas of upper GI carcinoma and their correlation with smoking (i.e. Esophageal carcinoma and smoking). Pub Med, Alta Vista, and EbscoOnline were used to conduct this search. Three total articles were found, all from 1999 and all from different sources.

After searching for titles contained in house, Mr. Snyder and I determined that Logan's library did not have much information on the subject of oncology. However, one area that was constantly coming up on our searches was the correlation of smoking and Crohn's disease.

A new search was conducted only using EbscoOnline, because we could print full text articles. The search was conducted using the keywords: Crohn's disease and smoking. Many titles were identified and all with full text availability were printed. 12 articles were printed, ranging from 1996 to 2001, citing 10 different sources.

On November 26, I also conducted my own search on the Internet and found the Crohn's and Colitis Foundation of America (CCFA). I emailed them and explained that I was doing a research project on Crohn's disease and it's relationship with cigarette smoking. I asked them to mail me any information that they thought pertinent to the subject. This search was conducted in the Logan College computer lab. Netscape Navigator was used to search the keywords Crohn's disease. The first and only thing identified and researched further was the CCFA website. I found no articles, but I was sent five articles. The articles ranged from 1999 to 2001, from five different sources. All five articles had the words smoking and Crohn's disease in the title.

The reason EbscoOnline was used is because it allows you to print full text articles. The twelve that were printed had the option of printing the full text article. All 12 articles printed were from referred journals. There were some search results older than 1996, but none were available in full text. There are 17 articles included in this literature review from 15 different sources. These 17 referred journal articles contain 11 investigations and 6 case studies.

DISCUSSION

Most people that smoke understand that they are doing harm to their bodies. They also do not realize that they are not just affecting their lungs, they are affecting other parts of their body as well. In a survey of 102 patients with Crohn's disease, forty-one of which were smokers and nineteen of which were ex-smokers, only thirteen patients were aware of the adverse affects of smoking on their Crohn's disease. Only five of the current or ex-smokers felt that smoking had influenced symptoms they associated with their Crohn's disease. (2)

In this same survey, 51 general practitioners were questioned to see if they knew the adverse relationship between cigarette smoking and Crohn's disease. Only two of the 51 general practitioners questioned knew of the adverse association between smoking and Crohn's disease. This survey indicates that many general practitioners and their patients with Crohn's disease are unaware that the incidence and course of Crohn's disease is influenced by smoking. Futhermore, some gastroenterologists do not provide their patients with this information. This is compounded by the fact that most smokers do not feel that smoking influences the symptoms they associate with Crohn's disease. (2)

Most studies agree with the information presented thus far that there is a strong correlation between smoking and Crohn's disease, but Odes et al in particular found otherwise. They said that in their patients with Crohn's disease, there were no significant differences in the number or percentage of hospitalizations and operations in nonsmokers and smokers. Further subdivision of the operations as abdominal or perineal in the Crohn's disease patients did not reveal significant differences between nonsmokers and smokers. (5)

All other studies however attest to the harmful effects that smoking has on the course of Crohn's disease. Cosnes et al showed in a prospective study of 622 French patients that there was a marked increase in Crohn's disease flare-ups in current smokers. They also showed that the morbidity of Crohn's disease rose when 16 or more cigarettes were smoked daily. (13)

Palli et al said that total cancer mortality tended to be increased in Crohn's disease, suggesting the existence of a pattern of increased exposure to environmental

carcinogens or some specific susceptibility. They also said that smoking habit seems to contribute significantly to the increased mortality observed in Crohn's disease. (6)

Hugot et al said the most important risk factor currently for an Inflammatory Bowel Disease is a familial history of the disease, but cigarette smoking is presently the only known environmental risk factor for Inflammatory Bowel Disease. (7)

Somerville et al said so little is known of the etiology and pathogenesis of Crohn's disease or the effect of smoking on the colon, that it is difficult to suggest a mechanism to account for the observed associations with smoking habit. Possible mechanisms include changes in bowel motility or in susceptibility to some as yet unidentified pathogen. In this respect, smoking has been reported to produce complex changes in immune function including reduced natural killer cell activity in peripheral blood leukocytes and decreased immunoglobulin concentrations. (12) Nicotine in cigarettes binds to acetylcholine receptors located both in the central nervous system and the peripheral nervous system. Presynaptic stimulation results in the release of neurotransmittors and local hormones, which in turn attributes to either suppression or not of the immune system. (10)

Stefan Targan, MD, said, "It's quite clear that environmental factors exacerbate Crohn's, and smoking is one of these." (14) In general, smokers with Crohn's disease have more severe disease. Smokers are less likely than nonsmokers to get better with medications, and more likely to get worse after surgery to remove the involved section of intestine. Modifying smoking behavior in Crohn's disease patients can improve the long-term course and reduce the number of flare-ups when patients stop smoking. (15)

Yamamoto and Keighley stated that smokers have more symptoms and have a greater risk of recurrence after surgery than non-smokers and that smokers appear to have an approximately twofold increased risk of postoperative recurrence of disease compared to non-smokers. Many patients with Crohn's disease are unaware that the incidence and course of the disease are influenced by cigarette smoking. Further education and encouragement of patients to stop smoking are required. (8)

Corrao et al showed a clear dose-effect relationship between the level of exposure to smoke and risk of Crohn's disease, especially in current smokers. (11)

Cosnes et al stated that the effect of smoking is clearly harmful in Crohn's disease, in both the short and the long-term, particularly in heavy smokers. On the other hand, this effect is not long-lasting and stops after smoking cessation. (19)

Yamamoto and Keighley demonstrated that smoking was associated with a high risk of recurrence after ileocolonic resection for ileocecal Crohn's disease. The exact mechanism of the effect that cigarette smoking has on Crohn's disease remains unclear, although reports that smoking may have a significant effect on the immune system or colon mucus have been documented. On the basis of these facts, it seems reasonable to advise patients with Crohn's disease to refrain from cigarette smoking. (9)

Not only is it understood that cigarette smoking is an environmental factor contributing to the cause of Crohn's disease, but it has also been shown that cigarette smoking is a possible cause for the faster reoccurrence of Crohn's disease. Smoking is an independent risk factor for clinical, surgical, and endoscopic recurrence in Crohn's disease. In a 10-year follow up of 174 patients the recurrence rate was 70% in smokers

and 41% in non-smokers. (2) In a study with only smoking as a habit at the time of operation significantly affected the cumulative proportion with a functioning ileorectal anastomosis; the 5-, 10- and 15-year cumulative proportions of patients with a functioning ileorectal anastomosis were 75, 54, and 48 percent respectively for smokers, compared with 89, 85, and 82 percent for non-smokers. (1)

Now that we understand what Crohn's disease is, how it is affected by cigarette smoking, and that most people with it do not know that their condition is complicated by it, we'll take a look at diagnostic tools and the most common methods for treating Crohn's disease at this time.

Crohn's disease can be extremely difficult to diagnose. Because these conditions share the symptoms of so many other intestinal illnesses, it sometimes takes years before a correct diagnosis is made. Physicians rely on a variety of procedures and laboratory tests to confirm a diagnosis. Some of these tests are also used to monitor patients' progress. (15) These tests can be categorized as follows:

1. blood and urine tests
2. stool examinations
3. radiological procedures
4. endoscopic procedures

Currently, there is no cure for Crohn's disease. Only symptom management is available. The current therapies being used at this time include: medications, surgery, resection and anastomosis, bypass, strictureplasty, alternative medicine, diet and nutrition.

Unfortunately, none of the current medications used to treat Crohn's disease provide a cure. However, most people respond favorably to careful, well-directed, long-term medical management. Current therapies can help control disease by:

- Suppressing the abnormal and destructive immune response
- Promoting healing of intestinal tissue
- Relieving symptoms of diarrhea, abdominal pain, and fever

There are four groups of medications for these illnesses:

Anti-Inflammatory Drugs – Sulfasalazine, Corticosteroids, 5-ASA drugs
Immunomodulators - 6-mercaptopurine, Azathioprine, Cyclosporine, ethotrexate
Antibiotics – Metronidazole, Ciprofloxacin
Antidiarrheal Agents – Loperamide, Diphenoxylate/atropine, Cholestyramine (7)

Approximately two thirds to three quarters of individuals with Crohn's disease undergo at least one surgical procedure during the course of their illness. Unfortunately, though surgery can alleviate the symptoms of Crohn's disease, it is not a cure. In fact, 40-50% of people with Crohn's disease require a second operation. Because of this, physicians try to avoid surgery if possible.

Reasons for Elective Surgery include:

- Symptoms (e.g., fatigue, weight loss, stomach pain) that cannot be controlled by medications
- Cancer or Severe Dysplasia (pre-cancerous condition): The risk of cancer in Crohn's disease is not as high as it is in ulcerative colitis. Indeed, the incidence appears to be too low to warrant routine exams of the colon. Though extremely rare, malignancies of the small bowel, usually seen in very inflamed and ulcerated portions of the intestine, have been found in patients with long-term disease.
- Growth failure in children

Reasons for Emergency Surgery include:

- Severe bleeding: May occur from any segment of affected bowel. Usually responds well to transfusion and steroids. Only about five percent of patients require surgery.
- Recurrent small bowel obstruction: Usually occurs only in patients with long-term disease. Caused by indigestible foods, inflammation, and intestinal scarring. Responds well without surgery, if treated early.
- Abscess: Caused when intestinal contents leak through bowel wall. Surgery is usually needed to drain abscess.

- Fistula: An abnormal passage between the intestine and another organ, caused by inflammation. May lead to an abscess. Need for surgery depends on individual case. (Many types of fistulas respond to medications.)
- Free perforation: Rare in Crohn's disease. Caused when a deep ulcer in the bowel wall produces a hole into a peritoneal cavity. Bowel contents leak through this hole, causing peritonitis. Type of surgery depends on location of tear and extent of disease.
- Toxic megacolon: Severe inflammation of colon, which creates danger of perforation. Unusual in Crohn's disease. Always requires surgery. (17)

Resection and anastomosis is the standard operation for Crohn's disease. It is necessary when:

- Medications are no longer effective
- Side effects from medications become severe or intolerable
- Life-threatening complications (e.g., abscess, obstruction, perforation, bleeding) develop

Procedures include:

- Resection: Diseased segment of intestine is removed.
- Anastomosis: The two cut ends are rejoined.

The surgeon's goal is to remove as little of the intestine as possible. Unless the rectum is severely affected, it is almost always possible to restore intestinal continence, avoiding an ostomy. Crohn's disease is patchy and segmental by nature. Therefore, a surgeon may need to remove more than one portion of diseased intestine. But he will not touch a mildly affected area that doesn't appear to cause trouble. (18)

The bypass operation once was favored by surgeons over resection and anastomosis. But this surgery is performed much less often today, because:

- Complications, such as recurrence of disease, cancer, and perforation, can occur in bypassed loops of intestine
- Techniques for resection and anastomosis have improved greatly, resulting in fewer surgical complications

Procedures include:

- Diseased portion of intestine is left in place.
- Creation of a new connection between the healthy bowel and the colon, which bypasses diseased intestine.

Total bypass is favored by most surgeons, since it completely excludes the diseased intestine. Waste material doesn't flow through the bypassed segment. This helps promote healing. Once part of the intestine has been bypassed, it can't be reconnected, even after it heals. It is either left in place or removed at a later date. (10)

Candidates for bypass are patients who:

- Are too sick to undergo resection and anastomosis
- Have inflammation so extensive that removing the diseased intestine may damage surrounding structures This procedure is the standard operation for Crohn's disease. It is necessary when:
- Medications are no longer effective
- Side effects from medications become severe or intolerable
- Life-threatening complications (e.g., abscess, obstruction, perforation, bleeding) develop

Since physicians today know that surgery cannot cure Crohn's disease, they strive to remove as little of the intestine as possible. Strictureplasty is a newer operation that enables surgeons to widen narrow segments of intestine (strictures) that cause obstructions. This procedure does not require removal of any part of the intestine. Since strictures often are multiple and can involve long or widely separated parts of the bowel, strictureplasty is an attractive alternative to resection. (16)

Procedures include:

A small balloon, attached to a catheter, is moved along the intestine. Wherever its path is blocked, which indicates a stricture, the intestine is cut and opened lengthwise and then closed in the opposite direction. This procedure may be performed alone or along with other operations (i.e., resection plus strictureplasty). Surgeons may attempt to correct all narrow areas of intestine in a single operation, including segments not currently causing problems. (16)

Note: An alternative to strictureplasty is endoscopic dilation of strictures. A means of avoiding or postponing surgery, this technique is not yet in general practice, nor has its long-term effectiveness been proven. In endoscopic dilation, the physician uses an endoscope, a specially lighted tube, to expand the intestine. This procedure can only be performed on areas of the intestine within reach of the endoscope.

People who have Crohn's disease must cope with pain, complications (e.g., arthritis), and drugs, which can have serious side effects. It's no wonder that many individuals are eager to try every therapeutic avenue. Can hypnosis and biofeedback help control pain? Can acupuncture ease depression? These are among the questions that the Office of Alternative Medicine (OAM), a division of the National Institutes of Health, is trying to answer. Alternative therapy is also known as "holistic medicine," because it purports to treat the "whole person," body and mind. As such, it covers a broad spectrum of therapies, from meditation to homeopathy. The federal government created OAM in 1993. That year, a survey published in the *New England Journal of Medicine* reported that about a third of all Americans had used some type of alternative therapy in 1990--many without their doctors' knowledge. Clearly, some people are not comfortable discussing such options with their physicians, fearing ridicule or rejection. This is understandable. In the past, most physicians attributed the possible benefits of holistic medicine to the "placebo effect," claiming that a treatment worked (temporarily) because the patient believed that it would work. But the success of some treatments, such as hypnotherapy, in controlling pain and promoting healing, has caused physicians and researchers to take a new look at this phenomenon. (17)

Indeed, new research is exploring the "mind-body connection." One emerging field, known as psychoneuroimmunology, seeks to explain how the brain, the nervous system, and the immune system are connected. For example, the gut has its own nervous system, which receives messages from the brain and transmits information to it. Is it possible to harness the power of the mind to control the complex processes of the immune system? Could any alternative therapies play a role in preventing the inflammation and pain of Crohn's disease? This new field could provide important clues.

Deficiencies of essential nutrients may occur in Crohn's disease, depending on the location and extent of the disease. The primary nutrients are: protein; calories; vitamins A, D, C, B-12 and folic acid; calcium; iron; and zinc. The best protection is to eat a variety of foods from the four basic food groups (see below), choosing sources that are rich in the nutrients you need and that conform to any dietary modifications that you may require. Some people also may need vitamin or mineral supplements. While diet cannot cure these illnesses, good nutrition can help in the following ways:

- It can reduce disease symptoms and replace lost nutrients.
- Medications may be more effective when your nutritional state is not depleted.
- Retarded growth in children may be alleviated when proteins and calories are increased. (6)

Unless your dietary history suggests a specific food intolerance, there is no need to avoid a particular food. For the diet and/or supplements that are right for you, talk to your physician or nutritionist. Recommended Daily Allowances (RDAs), established for the general population, can be useful as a starting point in planning your diet. To meet these RDA's, eat daily helpings of the following:

- Meat and meat substitutes - 2 servings
- Dairy - 2-4 servings

- Cereal and grains - 4 servings
- Fruits and vegetables - 5 servings

Food Sources of Important Vitamins:

Vitamin A
- Liver, eggs, dairy products, fish liver oils, dark green leafy vegetables (e.g., green peas, spinach)

Vitamin D
- Sunlight, liver, fish liver oil, fortified food products (e.g., milk, butter, cereals)

Vitamin C
- Fruits (e.g., citrus fruits, bananas, apples)

Folic Acid
- Liver, beets, corn, legumes, green leafy vegetables

Vitamin B-12
- Meat, fish, poultry

Calcium
- Cheese, ice cream, milk, yogurt, sardines

Iron
- Red meat, fish, poultry, eggs

Zinc
- Animal protein (e.g., beef, chicken), plant foods, (e.g., legumes, bran, green peas) (14)

CONCLUSION

In this literature review, we have discussed the possible etiologies, signs and symptoms, and treatments of Crohn's disease. While most of us know that cigarette smoking causes many things, we can now understand that it affects our lives in many ways we didn't even think possible. Granted, the etiology of Crohn's disease is still unknown, but there seems to be a strong link between causation and reoccurrence of Crohn's disease. Understanding this correlation, we can further help and provide those patients suffering from this disease with the knowledge that will help them make the proper choices to decrease the severity of Crohn's disease in their body.

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