

Smoking and Acute Appendicitis

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Citation

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Abstract

Purpose: Appendectomy is the most commonly performed emergency surgical procedure. The aim of this retrospective case control study was to evaluate the association between smoking and acute appendicitis.

Material and methods: Retrospectively, 551 pathologically approved acute appendicitis cases were reviewed. They were compared with individuals from a healthy, age and sex matched group.

Results: When we evaluated both the patient and control group together, we found that smoking over 15 years and being a former smoker decreased the risk of acute appendicitis. We also found that smoking less than 5 years increased the risk of having acute appendicitis not statistically but clinically.

Conclusion: In the light of our findings, we suggest that smoking might not only decrease the risk of acute appendicitis but might also be protecting against it. But we still have limited information about how cigarette smoke affects the gut.

INTRODUCTION

Appendectomy is the most commonly performed emergency surgical procedure and accounts for 1-2% of all surgical operations. Acute appendicitis occurs in 1/7 to 1/17 people, mostly adolescents and young adults. It has a life-time risk of 7%. In the century since its recognition, no progress has been made in elucidating its etiology and pathogenesis. According to the leading theory, the initial event in the pathogenesis of acute appendicitis is obstruction of the lumen by factors like fecaliths, foreign bodies, intestinal parasites, tumors, or lymphoid follicular enlargement due to viral infections. However, obstructive elements have been identified in only 30%-40% of removed inflamed appendices. Currently, the mortality rate is 0.25% if all ages are considered.

Tobacco smoke has divergent roles as a deleterious factor in Crohn's disease (CD) and a protective agent in the development of ulcerative colitis (UC). The exact mechanisms of these apparently opposing effects have yet to be resolved. Smokers have approximately a twofold increased risk of developing CD 5 to 15 years after the initiation of smoking than nonsmokers. Both filtered tobacco smoke and nicotine have been demonstrated by Ko et al. to accelerate healing during active colitis, which also involves inhibition of neutrophil-derived free radicals and

downregulation of the pro-inflammatory chemokine and cytokine protein synthesis in the colonic tissue.

The aim of this retrospective study was to evaluate the association between smoking and acute appendicitis.

MATERIAL AND METHODS

We retrospectively reviewed the charts of patients in a medical center from January 2005 to July 2007 and found 551 (272 female, 279 male) histopathologically approved acute appendicitis cases (mean age 27 [\pm 9.6] years) that were compared with individuals from a healthy, age, sex, and socio-economically matched group (305 female, 313 male) (mean age 27 [\pm 10.1]). Candidates who had any medical disorder or any history of drug usage were excluded. We divided the patient and the control group into five sub-groups based on smoking histories (Table.1 and Table.2).

Figure 1

Table 1: Patient Group

| Smoking status | Female | Male |
|--------------------------|--------|------|
| Non-smoker | 162 | 137 |
| Smoking years <5 years | 51 | 64 |
| Smoking years 5-15 years | 37 | 46 |
| Smoking years >15 years | 10 | 17 |
| Stopped smoking* | 12 | 15 |

*Patients who had given up smoking at least a year before diagnosis.

Figure 2

Table 2: Control Group

| Smoking status | Female | Male |
|--------------------------|--------|------|
| Non-smoker | 166 | 120 |
| Smoking years <5 years | 56 | 52 |
| Smoking years 5-15 years | 38 | 74 |
| Smoking years >15 years | 11 | 43 |
| Stopped smoking* | 34 | 24 |

*Patients who had given up smoking at least a year before.

Data were analyzed to evaluate the effect of smoking on having acute appendicitis by Chi-square test. Descriptive statistics were shown as percentile. Odds ratio and 95%-CI were calculated for all groups. A multivariate analysis was also performed to adjust for the age effect on the incidence of appendicitis. Data were analyzed with the SPSS 11.5 package program.

RESULTS

There were no significant demographical differences between patient group and control group. Also, there were no statistically significant differences between demographical features of the subgroups. Two hundred ninety-nine individuals of the patient group (54.3%) and 286 of the control group (46.3%) had never been smokers. The prevalence of non-smoking in the patient group was found to be higher than in the control group (p=0.006).

When we evaluated both the patient and the control group together, we found that smoking over 15 years and being a former smoker decreased the possible risk of having acute appendicitis (p=0.003, p<0.001 respectively) (Table.3). Smoking less than 5 years had no influence (p=0.907) (OR: 1.02 [95%-CI 0.75-1.39]) on the risk of having acute appendicitis (Table.3). In the light of these findings we can suggest that smoking over 5 years can protect against having appendicitis.

Figure 3

Table 3

| Smoking status | Control | Patients | OR(95%-CI) | P |
|--------------------------|------------|------------|------------------|--------|
| Non-smoker | 286(46.3%) | 299(54.3%) | 1 | - |
| Smoking years <5 years | 108(17.5%) | 115(20.9%) | 1.02 (0.75-1.39) | 0.907 |
| Smoking years 5-15 years | 112(18.1%) | 83(15.1%) | 0.71 (0.51-0.98) | 0.039 |
| Smoking years >15 years | 54(8.7%) | 27(4.9%) | 0.48 (0.29-0.78) | 0.003 |
| Stopped smoking* | 58(9.4%) | 27(4.9%) | 0.44 (0.27-0.72) | <0.001 |

*Patients who had given up smoking at least a year before diagnosis.

The smoking prevalence in female patients and in the control group was statistically similar (p=0.214) but we can say that smoking decreased the incidence of having acute appendicitis in women (OR: 0.81 [95%-CI 0.58-1.13]). Women who had ever smoked had a lower risk of having acute appendicitis than women who had never smoked (Table.4). But this reduced risk was not a statistically

significant one, except for the women who had given up smoking at least 1 year before (p=0.004) (OR: 0.36 [95%-CI 0.18-0.72]).

Figure 4

Table 4: Female Group

| Smoking status | Control | Patients | OR(95%-CI) | P |
|--------------------------|------------|------------|------------------|-------|
| Non-smoker | 166(54.4%) | 162(59.6%) | 1 | - |
| Smoking years <5 years | 56(18.4%) | 51(18.8%) | 0.93 (0.60-1.44) | 0.756 |
| Smoking years 5-15 years | 38(12.5%) | 37(13.6%) | 0.99 (0.60-1.65) | 0.993 |
| Smoking years >15 years | 11(3.6%) | 10(3.7%) | 0.93 (0.38-2.25) | 0.875 |
| Stopped smoking* | 34(11.1%) | 12(4.4%) | 0.36 (0.18-0.72) | 0.004 |

*Patients who had given up smoking at least a year before diagnosis.

Smoking had a statistically significant protecting effect against acute appendicitis in men (p=0.008) (OR: 0.64 [95%-CI 0.46-0.89]). Smoking less than 5 years had a small effect on having acute appendicitis in men, not statistically (p=0.738) but clinically (OR: 1.08 [95%-CI 0.69-1.67]). But smoking 5 to 15 years or over 15 years statistically and clinically decreased the risk of having appendicitis. Smoking given up at least 1 year before reduced the risk of having acute appendicitis in men but this result was not statistically significant (p=0.087) (Table.5).

Figure 5

Table 5: Male Group

| Smoking status | Control | Patients | OR(95%-CI) | P |
|--------------------------|------------|------------|------------------|--------|
| Non-smoker | 120(38.3%) | 137(49.1%) | 1 | - |
| Smoking years <5 years | 52(16.6%) | 64(22.9%) | 1.08 (0.69-1.67) | 0.738 |
| Smoking years 5-15 years | 74(23.6%) | 46(16.5%) | 0.54 (0.35-0.85) | 0.007 |
| Smoking years >15 years | 43(13.7%) | 17(6.1%) | 0.35 (0.19-0.64) | <0.001 |
| Stopped smoking* | 24(7.7%) | 15(5.4%) | 0.55 (0.27-1.09) | 0.087 |

*Patients who had given up smoking at least a year before diagnosis.

The smoking status was statistically significantly different in the two groups by univariate analysis, and then we proceeded to multivariate analysis. But we did not find any other statistically significant differences.

DISCUSSION

In animal studies, interesting regional differences emerged: in the normal rat jejunum, chronic nicotine administration decreased PGE2 generation and increased NOS activity, but had no effect on the microcirculation; whereas microcirculation in the colon was enhanced, but NOS activity or PGE2 generation were not affected in the normal rat colon by nicotine administration₆.

In order to further assess the different effects of nicotine on the colon and small intestine, Eliakim et al. have studied the effects of nicotine administration on the cytokine profile in small bowel, colonic mucosa and blood of normal rats and have found that acute nicotine administration (1 or 2 days) significantly decreased jejunal IL-2 and IL-10 levels and increased IL-6 levels, while chronic administration (7 days)

caused an increase in IL-6 and a decrease in IL-10 levels. On the other hand, colonic mucosa IL-2 levels have decreased significantly, with no change in IL-6 or IL-10 mucosal levels. Thus, the colonic cytokine profile behaved totally differently to nicotine exposure compared to small bowel mucosa. Nicotine administration decreased the anti-inflammatory mediator IL-10 levels in the small bowel and increased the level of the pro-inflammatory mediator IL-6, possibly contributing to mucosal damage in that region. Nicotine decreased the levels of the pro-inflammatory mediator IL-2 in colonic mucosa. Similar effects of smoking have been found for the pro-inflammatory mediators IL-8 and IL-1beta in human colonic mucosa. Smokers with inflammatory bowel disease had a significant reduction in cytokine levels, specifically IL-1beta and IL-8 in patients with UC and IL-8 in patients with CD₈.

Furthermore, nicotine administration significantly increased both somatostatin and intestinal trefoil factor mRNA expression in the colon but not in the jejunum of IL-10 knock-out mice.

Montgomery suggested that smoking is a cofactor which increases the risk of having acute appendicitis, in the light of the unadjusted odds ratio which he found to be 2.34 (95%-CI 1.52-3.59) for appendectomy associated with cigarette smoking₁₀. We found that smoking less than 5 years does not affect the risk of having acute appendicitis. Oppositely, we found that smoking over 15 years and being a former smoker decreased the incidence of having acute appendicitis ($p=0.003$, $p<0.001$ respectively). Also, we can say that smoking decreased the risk of having acute appendicitis in women (OR: 0.81 [95%-CI 0.58-1.13]). Moreover, smoking had a statistically significant protecting effect against acute appendicitis in men (OR: 0.64 [95%-CI 0.46-0.89]).

Women who had ever smoked had a lower risk of having acute appendicitis than women who had never smoked (Table.4). But this reduced risk was not a statistically significant one, except for the women who had given up smoking at least 1 year before ($p=0.004$) (OR: 0.36 [95%-CI 0.18-0.72]). Can we suggest that cigarette smoke may change the inflammatory response of the bowel for a while? The same hypothesis is not statistically significant in men. Does cigarette smoke have a gender-specific effect on the

bowel? Unfortunately, we have little knowledge about the effects of cigarette smoke on the bowel. Nor do we know if smoking has a gender-specific effect especially on the bowel.

CONCLUSION

In the light of our findings we suggest that smoking might not only decrease the risk of acute appendicitis but that it might also be protecting against it. But we still have limited information about how cigarette smoke affects the gut.

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