Smoking Cessation in a Chronic Pancreatitis Population

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Abstract

Objectives—Smoking is a known risk factor for developing chronic pancreatitis and accelerates disease progression. Smoking cessation remains an important treatment recommendation, but little is known about its effects. This study evaluated smoking cessation in this population and its impact on quality of life.

Methods—27 smokers with chronic pancreatitis participated in a smoking cessation program incorporating the QuitWorks program and individual counseling. Their smoking cessation rates were compared with a control population (n=200) consisting of in-patients without chronic pancreatitis who smoked. Smokers were also compared with non-smokers (n=25) with chronic pancreatitis in terms of quality of life indicators.

Results—0/27 patients had quit smoking at 6 months, 1/27 at 12 months, and 0/27 patients at 18 months. There was a 19% quit rate in the control population at the 6-month period. Smokers had a worse quality of life, higher rates of depression and anxiety, and worse coping skills than non-smokers.

Conclusions—Smoking cessation in the chronic pancreatitis population is extremely challenging, as shown by our 0% quit rate after 18 months. Given that smokers with chronic pancreatitis also experience a worse quality of life, it becomes even more important to stress the importance of smoking cessation in these patients.

Keywords

Smoking Cessation; Chronic Pancreatitis

Introduction

Chronic pancreatitis has become a global problem, with worldwide prevalence estimated to be near 50/100,000 individuals.[1–4] Most often a result of alcohol consumption, chronic pancreatitis may also be attributed to genetic deficiencies (Cystic Fibrosis, SPINK1, and cationic trypsinogen mutations), as well as metabolic abnormalities (hyperlipidemia and

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hypercalcemia).[2] It is well known to affect many aspects of a patient's health, including physical health, such as pain and nutritional status, financial health, and emotional health.[5–6] This impact translates into a large financial burden on healthcare with an estimated $638 million spent yearly in the US on pain control alone.[7]

Traditionally, improving quality of life depends on ceasing alcohol intake, eating small, low-fat meals, and using pancreatic enzyme supplementation.[8–11] In addition, patients in pain often require symptom relief through the use of chronic opioid analgesia, celiac plexus blocks, or surgery.[12–16] Recently, another approach that has been suggested for the management of these patients is smoking cessation as a number of findings seem to suggest that smoking is an independent risk factor in the development of chronic pancreatitis. Tolstrup et al found a dose-dependent association between smoking and chronic pancreatitis.[17,18] Smoking has also been found to hasten the age of first diagnosis as smokers with chronic pancreatitis have been found to have an earlier age of diagnosis compared to non-smokers, along with a significantly higher risk of developing pancreatic calcifications.[19] On a molecular level, Wittel et al demonstrated that high-dose smoke exposure in rats led to pancreatic damage with features similar to chronic pancreatitis and Chowdhury et al showed that nicotine had significant accumulation in the pancreas of rats, suggesting that nicotine may be the active ingredient in smoking that leads to pancreatic inflammation.[20–23]

The goal of this study was to evaluate the effectiveness of smoking cessation in chronic pancreatitis patients and its impact on their quality of life.

Materials and Methods

This is a longitudinal prospective study, approved by our institutional review board, designed to evaluate the impact of smoking cessation on the quality of life in patients with chronic pancreatitis.

Patients with chronic pancreatitis at our institution, a tertiary academic medical center, who met the inclusion/exclusion criteria (Table 1), were identified and invited to participate. This enrollment period occurred during January, 2013 to June, 2013. Recruitment for chronic pancreatitis patients occurred during their normally scheduled outpatient visits. Those who agreed signed the informed consent and returned for the following visits: a) initiation visit, b) intervention visit, and c) follow-up visits. All visits were conducted by one physician who regularly sees all the chronic pancreatitis patients in the outpatient clinic.

a. Initiation visit: During this visit, baseline information was obtained from the patient. This included demographic data in conjunction with 10 previously validated questionnaires designed to capture a holistic view of the quality of life of these patients. This included: 1) the Pancreatitis Quality of Life Instrument (PANQOLI), a questionnaire specifically designed to measure quality of life in patients with chronic pancreatitis,[23] 2) the Short Form-12 (SF-12), a generic measure of quality of life,[24] 3) the Michigan Alcohol Screening Test (MAST) to assess for alcoholism[25] 4) the Drug Alcohol Screening Test (DAST) to detect drug misuse and

abuse,[26] 5) the Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R) was used to assess opioid addiction potential,[27] 6) the Brief Cope 24 was used to assess coping skills,[28] 7) the Hospital Anxiety and Depression Scale (HADS) was used to identify depression and anxiety,[29] 8) the Malnutrition Universal Screening Test (MUST) was used to screen for malnutrition,[30] 9) a Visual Analog Scale (VAS) was used for pain assessment,[31] and 10) the Karl Fagerström Nicotine Tolerance questionnaire was used to evaluate the level of nicotine dependence in patients identified as smokers.[32] Active smokers, as defined by smoking 1 cigarette/day were offered smoking cessation programs as described below. Non-smokers were defined as those who never smoked. These patients also had baseline information collected including demographic information as well as all the questionnaires described above with the exception of the Fagerström Nicotine Tolerance questionnaire, which is not applicable to non-smokers.

b. Intervention visit: Those active smokers who were interested in smoking cessation were all given a referral to QuitWorks. This is a free, evidence-based smoking cessation service run by the state of Massachusetts which works in collaboration with the majority of health plans available in the state.[33] Once a referral was made, the service contacted the patient by phone, and provided them with a 2-week supply of nicotine patches, followed by a phone counseling session for those interested to help provide the patient a plan for smoking cessation and to help set a quit date. The service also contacted the referring provider with the patient's progress, and set up an additional 4 phone sessions with the patient to help them coordinate relapse prevention and everyday strategies to stay smoke-free. A follow-up intake was then done at 6 months to evaluate the patient's progress.

In addition to the to a QuitWorks referral, all patients in our study were also offered face-to-face individual sessions with a smoking cessation specialist at our institution in an effort to expand the resources patients had in reaching their goal of quitting smoking. If a subject elected to receive this second service, an initial assessment with the smoking cessation specialist gathered information regarding the patient's tobacco use, including previous quit attempts, and a carbon monoxide (CO) breath meter was used to create a baseline carbon monoxide (CO) level, while a blood test was done to measure the serum carboxyhemoglobin percentage (COHb). A quit date was set for the next appointment (1 month later), and patients were offered nicotine replacement products as well as FDA-approved medications, including bupropion or varenicline based on patient preference and safety profile. Patients were then seen on a monthly basis and seen for up to 18 months. Repeat CO and COHb testing was also offered at these follow-up visits to monitor carbon monoxide levels.

c. Follow-up visits: Patients were brought back for follow-up visits at 6, 12 and 18 months. It was expected that quality of life differences would become measurable at 6-month intervals. During those visits, patients were asked to answer the same 10 questionnaires as the original inclusion visit for comparison. Smoking cessation rates were also determined during these visits.

Control population

To evaluate the impact of Quitworks on smoking cessation in our patient population, 200 consecutive in-patients who smoked, but did not have chronic pancreatitis, were referred to the QuitWorks smoking cessation program while hospitalized at our institution. This number reflected the amount of patients able to be recruited for the control population during the enrollment period. This population was followed by QuitWorks following discharge from the hospital for up to 6 months to evaluate their smoking cessation rates. Demographic data was collected from this population, but no quality of life measures were assessed as this population was followed solely for the purpose of evaluating smoking cessation rates.

Statistical Analysis

The primary outcome of this study was the smoking cessation rate of patients with chronic pancreatitis. Secondary outcomes included quality of life assessments of both smokers and non-smokers with chronic pancreatitis, and smoking cessation rates of the control population.

Demographic data was expressed as mean ± SD or number (%). Baseline measures were compared with T-test for variables meeting assumptions of normality and Chi-square test for categorical variables. Quality of life measures were compared using multivariate regression (IBM SPSS Version 21.0, Chicago, Ill). $p < 0.05$ was considered as the level of significance.

Results

Patient Characteristics

52 patients with chronic pancreatitis agreed to participate in this study. Diagnostic criteria of the chronic pancreatitis patients are detailed in Table 2. Of these 52 patients, 27(51.9%) were active smokers. The average age was 48.7 and females constituted 59.6% of the population. In terms of racial distribution, 86.5% of the population was Caucasian. Noticeably, there was a high unemployment rate (48.1%), disability rate (23.1%) and unmarried rate (including single, widowed, and divorced - 61.5%). All chronic pancreatitis patients were on narcotics. The only variables that were significantly different between the two groups were the presence of diabetes, and the daily pain medication requirements (Table 3).

Smoking Cessation Rates

All 27 patients who actively smoked agreed to enroll in the smoking cessation program. 27/27 patients were referred to QuitWorks and all of them enrolled within the QuitWorks program (completed the initial assessment interview and agreed to follow-up sessions).

Additionally, 14/27 (51.9%) agreed to meet with our smoking cessation specialist and have monthly follow-up appointments. Please see Table 4 for further details.

At the 6-month period, 0/27 patients (0%) had quit smoking, defined as being smoke-free for >7 days. At the 12-month period, 1/27 patients (3.7%) had quit, with the single patient having quit for a period of 3 months. At the 18-month period, however, 0/27 patients had quit at that time period. In comparison, the control population was reported by QuitWorks at 6-months to have a 19% quit rate (38/200). The control population's demographics are presented in Table 5.

Quality of Life Comparison

Quality of life measures were evaluated using the questionnaires as described above. A baseline comparison was made between smokers and non-smokers in these quality of life measures. Smokers had a significantly worse PANQOLI score (47.5 vs. 56.0, $p<0.05$), worse physical component score (PCS, $p<0.006$) on the Short-Form 12, worse coping score ($p<0.04$) on the Brief Cope, and worse anxiety ($p<0.005$) and depression ($p<0.05$) scores on the HADS. There were no significant changes in any of these scores during the follow-up periods within the smoking group. Please see Table 6.

Discussion

Smoking Cessation rate

The most notable finding of this study was the lack of success in smoking cessation in chronic pancreatitis patients. To our knowledge, this is the first study to evaluate smoking cessation rates in this population.

Although QuitWorks yielded little success in our program, this technique has been utilized in over 22,000 patients since its inception in 2002 with a 17% success rate (quit smoking for >30 days).[33–36] Furthermore, our control population had a similar success rate indicating that it was not a problem with the intervention or its practice locally since at the 6-month period, QuitWorks had reported a 19% quit rate in our control population. Rigotti et al recently performed a randomized trial on hospitalized patients who wished to quit, providing the intervention group with automated telephone calls which promoted cessation, a 90-day supply of any smoking cessation medication, and counseling as needed.[37] The control group was recommended to call 1–800-QUIT-NOW, a national service provided for smoking cessation, and found that at the 6-month follow-up period, the intervention group had a confirmed 7-day tobacco abstinence rate of 26% vs. 15% in the control group. Our study's control population's 19% quit rate was comparable to these results, which again emphasizes the enormous difficulty our chronic pancreatitis patients had in quitting, despite the use of proven cessation strategies.

To try to improve our results, patients were offered individual appointments with a smoking cessation specialist. As the cessation specialist incorporated counseling services based on social learning theory with motivational interviewing techniques and cognitive behavioral strategies in-person, we believed this would supplement the aid QuitWorks gave patients over the phone as a recent meta-analysis demonstrated the overall effectiveness of these

techniques in smoking cessation.[38] One patient who met with the cessation specialist did indeed quit for a period of 3 months by the 12-month follow-up period, but by the 18-month period had relapsed. Nevertheless, this additional method did not help our group of patients.

This failure in smoking cessation has left the chronic pancreatitis patients in a poor state as determined by our questionnaire analysis. As compared to non-smokers, patients with chronic pancreatitis who were smokers had a higher divorce rate, lower percentage of diabetes, and a higher amount of opiate use. Some studies have shown a link between the acceleration of disease activity and smoking. In a study by Maisonneuve et al, cigarette smoking was associated with earlier development of calcifications and diabetes in chronic alcoholic pancreatitis.[19] This appears to be supported by the increased use of pain medications in smokers in our study. These findings may also explain the poorer quality of life in smokers in our study as demonstrated by the PANQOLI, Brief Cope 24, and HADS. These findings are similar to the NAPS2 (North American Pancreatitis Study 2) study, which used the Short Form-12 as a marker for quality of life and found that smoking was a risk factor for a worse mental component score (MCS).[39] While the lower incidence of diabetic patients in our group appear to be conflicting with the results from Maisonneuve et al, a closer evaluation would be needed to sort out potential confounding variables that may not have been included in our data analysis such as BMI, history of alcohol use and family history of type I diabetes. Each of these could have increased the risk for diabetes in our patient population independent of the severity of the patients' chronic pancreatitis.

Limitations

Although a significant difference was noted in the smoking cessation rate between patients with chronic pancreatitis (0/27) and those without (38/200), it is not clear whether there was an underestimation of the smoking cessation rate in one group and its overestimation in the other. After all, the 19% quit rate was not confirmed biochemically and therefore may have provided an overestimation. Similarly, the 6 month period may have been too short for patients with chronic pancreatitis to develop enough lifestyle changes to quit smoking given their multiple other difficult psychosocial issues. Therefore, a larger, longer study at multiple centers may provide more data. However, for now, it seems that conventional approaches to smoking cessation in this group of patients are at best suboptimal.

Conclusion

This study demonstrated a decreased smoking cessation rate in a chronic pancreatitis population compared to patients without chronic pancreatitis. Given the risk of disease progression, and the likely negative effects on quality of life that smoking has on these patients, smoking cessation should be one of the major goals in the management of smokers with chronic pancreatitis. In addition to improving quality of life, such an approach may also translate into economic savings as seen in other chronic conditions.[40] However, given that conventional smoking cessation approaches may be less than effective in this group of patients, one has to look at other potential approaches. One such approach may be the use of the practice of mindfulness which was found to be beneficial in other patients with difficulty quitting.[41] While it remains unclear whether chronic pancreatitis patients are more prone to

addictions, this study illustrates the enormous difficulty they have in quitting smoking and highlights the need for the development of further strategies and medications for smoking cessation.

Acknowledgments

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Table 1

Inclusion-Exclusion Criteria for Chronic Pancreatitis Patients

Inclusion Criteria		Exclusion Criteria	
Patient must have abdominal pain, not related to other identifiable etiologies in conjunction with one of the following two features:		Patient to be excluded from the study if they have one of the following features:	
a.	Presence of pancreatic calcification as demonstrated by an imaging study such as CT scan or KUB imaging	a.	Age less than 18 years
b.	Presence of five out of nine criteria of pancreatic injury by endoscopic ultrasound in conjunction with a positive secretin stimulation test to confirm pancreatic insufficiency.	b.	Comorbidities such as end-stage cancer (estimated survival < 6 months), HIV (T4 cell count < 50), end-stage congestive heart failure, end-stage chronic obstructive pulmonary disease, uncompensated cirrhosis, renal failure (on dialysis or with CrCl <25), or pre-existing diabetes mellitus
		c.	Non-English speakin

CT indicates computed tomography; KUB, kidney, ureter, and bladder; CrCl, creatinine clearance

Table 2

Diagnostic Criteria of Chronic Pancreatitis Patients

Diagnostic Criteria	
Calcifications on CT or KUB (n=52)	40.4% (21/52)
Endoscopic Ultrasound findings (n=40):	
Hyperechoic foci	77.5% (31/40)
Hyperchoic strands	80% (32/40)
Lobular contour	97.5% (39/40)
Cysts	35% (14/40)
Main duct dilatation	45% (18/40)
Duct irregularity	82.5% (33/40)
Hyperechoic margins	95% (38/40)
Visible side branches	22.5% (9/40)
Stones	30% (12/40)
Positive secretin stimulation test (n=40)	100% (40/40)

Table 3

Patient Characteristics

	Chronic Pancreatitis Population (n=52)	Non- smokers (n=25)	Smokers (n=27)	*p*
Age (years)	48.7 ± 9	49.3±11	48.1 ± 8	0.322
Sex	Male (40%) Female (60%)	Male (52%) Female (48%)	Male (26%) Female (74%)	0.053
Race				
Caucasian	86.54%	80%	92.6%	0.184
Hispanic	5.77%	12%	0%	0.064
Black	5.77%	8%	3.7%	0.507
Asian	1.92%	0%	3.7%	0.331
Relationship Status				
Single	25%	24%	25.9%	0.873
Married	38.5%	36%	40.7%	0.726
Divorced	17.3%	8%	25.9%	0.088
Unmarried Couple	9.6%	12%	7.4%	0.575
Single Parent	5.8%	12%	0%	0.064
Education Level				
High School	50%	50%	50%	1.000
College	34.1%	27.3%	40.1%	0.340
Masters	9.09%	13.6%	4.5%	0.262
Employment Status				
Unemployed	48.1%	48%	48.2%	0.991
Disability	23.1%	24%	22.2%	0.879
Employed (Full or part time)	19.2%	16%	22.2%	0.569
Job Seeking	1.92%	4%	0%	0.294
Retired	1.92%	4%	0%	0.294
Diabetes (%)	22.6%	36%	11.1%	0.033
Morphine (oral) mg/day	145 ± 140	114.4 ± 130	179 ± 144	0.048

Bold values are statistically significant.

Table 4

Characteristics of Smokers With Chronic Pancreatitis

Category	Smoking Cessation Specialist and QuitWorks (n=14)	QuitWorks only (n=13)
Age, y	49.1 ± 7.9	47.8 ± 5.4
Sex (p<0.03)	1 Male (7.7%) 13 Female (92.3%)	6 Male (46.2%) 7 Female (53.8%)
Pack-years (years)	29.4 ± 16.4	21.9 ± 11.8
Baseline ppd	1.1 ± 0.52	1.0 ± 0.39
18-month ppd	0.95 ± 0.55	0.73 ± 0.52
Baseline CO level (parts per million)	25.5 ± 12.1	NA
18-month CO level (parts per million)	28.3 ± 18.3	NA
Baseline COHb (%)	4.7 ± 1.9	NA
18-month COHb (%)	5.5 ± 3.1	NA
Smoking cessation product	Nicotine Patch (35.7%) Electronic Cigarette (28.6%) Varenicline (7.1%)	Nicotine Patch (46.2%) Electronic Cigarette (15.4%) Varenicline (15.4%)
Concomitant drug use	Marijuana (21.4%)	Marijuana (23.1%)
Fagerström nicotine tolerance questionnaire	Low Risk (28.6%) Medium Risk (35.7%) High Risk (35.7%)	Low Risk (38.5%) Medium Risk (30.8%) High Risk (30.8%)
Quit rate at 6 months	0%	0%
Quit rate at 12 months	7.10%	0%
Quit rate at 18 months	0%	0%

ppd indicates packs per day; CO, carbon monoxide; COHb, carboxyhemoglobin

Table 5

Description of Control Population

Age	62.2 years
Sex	57% Males 43% Females
Race	Caucasian (74%) Hispanic (13%)
In-patient diagnosis	Pneumonia (29.5%) Urinary Tract Infection (23.5%)
Smoking cessation rate	19%

Table 6

Quality of Life Comparison

Questionnaires	Quality of Life measure	Smokers (n=27)	Non-Smokers (n=25)	p-value
PANQOLI	Quality of Life	47.5 ± 9.9 (IQR 40.5–57.5)	56.0 ± 14.2 (IQR 47–65)	**p<0.04**
Short-Form 12	PCS	30.9 ± 8.9 (IQR 27.5–39.7)	37.2 ± 9.7 (IQR 31.5–41.4)	**p<0.006**
	MCS	36.2 ± 10.2 (IQR 29.3–40.3)	37.6 ± 10.7 (IQR 27.7–46.8)	p<0.31
MAST	Alcoholism	29.6%	16%	p<0.24
DAST	Drug Disorder	3.7%	8.0%	p<0.56
	Drug Abuse	0%	0%	p<0.99
SOAPP-R	Opioid addiction	33.3%	24.0%	p<0.45
Brief Cope 24	Coping ability	103.2 ± 19.3 (IQR 88–109)	92.1 ± 24.7 (IQR 83.5–105)	**p<0.05**
HADS	Anxiety	9.8 ± 4.6 (IQR 7–14)	6.6 ± 3.9 (IQR 4–9)	**p<0.005**
	Depression	8.2 ± 4.0 (IQR 6–11)	6.2 ± 4.4 (IQR 2–8)	**p<0.05**
MUST	Malnutrition	55.6%	48%	p<0.56
VAS for pain	Pain level	54.5 ± 26.7 (IQR 37.5–78)	46.5 ± 24.8 (IQR 40–70)	p<0.13

PANQOLI: Pancreatitis Quality of Life Instrument; PCS: Physical Component Score; MCS: Mental Component Score; MAST: Michigan Alcohol Screening Test; DAST: Drug and Alcohol Screening Test; SOAPP-R: Screener and Opioid Assessment for Patients with Pain-Revised; HADS: Hospital Anxiety and Depression Scale; MUST: Malnutrition Universal Screening Test; VAS: Visual Analog Scale

Bold values are statistically significant.