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Use and perceived effectiveness of non-analgesic medical therapies for chronic pancreatitis in the United States

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Abstract

Background—Effectiveness of medical therapies in chronic pancreatitis (CP) has been described in small studies of selected patients.

Aim—To describe frequency and perceived effectiveness of non-analgesic medical therapies in CP patients evaluated at U.S. referral centers.

Methods—Using data on 516 CP patients prospectively enrolled in the NAPS2 Study, we evaluated how often medical therapies (pancreatic enzyme replacement therapy [PERT], vitamins/

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antioxidants [AO], octreotide, celiac plexus block [CPB]) were utilized and considered useful by physicians.

Results—Oral PERT was commonly used (70.3%), more frequently in the presence of exocrine insufficiency (EI) (87.8 vs. 61%, p<0.001), and pain (73.7 vs. 59.2%, p<0.002). On multivariable analyses, predictors of PERT usage were EI (OR 5.14, 95% CI 2.87-9.18), constant (OR 3.42, 95% CI 1.93-6.04) or intermittent pain (OR 1.98, 95% CI 1.14-3.45). Efficacy of PERT was predicted only by EI (OR 2.16, 95% CI 1.36-3.42). AO were tried less often (13.8%) and were more effective in idiopathic and obstructive vs. alcoholic CP (25% vs. 3.6%, p=0.03). Other therapies were infrequently used (CPB-5.4%, octreotide-6.6%) with efficacy generally <50%.

Conclusions—PERT is commonly utilized, but is considered useful in only subsets of CP patients. Other medical therapies are used infrequently and have limited efficacy.

Keywords

chronic pancreatitis; medical therapy; pancreatic enzymes; antioxidants; octreotide; celiac plexus block

Introduction

Chronic pancreatitis (CP) is a progressive inflammatory syndrome with multiple etiologies, multiple complications and highly variable outcome. Pancreatic injury and inflammation lead to dysfunction and/or loss of acinar cells, duct cells and islet cells. Loss of these cells results in clinical disorders of maldigestion, reduced bicarbonate secretion, and diabetes mellitus, respectively. The susceptibility of these specialized cells of the pancreas to injury, the inflammatory response and adaptation to recurrent injury are also variable between individuals, with each of these processes modified by genetic, epigenetic, environmental, and metabolic factors. The injured pancreas also contains inflammatory cells, pancreatic stellate cells (PSC) and sensory nerves which contribute to complications of fibrosis and pain. The deposition of calcified stones and ductal scarring or stricturing may impede the normal flow of pancreatic juice, and the loss of sufficient digestive enzymes leads to maldigestion of ingested nutrients with the clinical sequelae of bloating, cramping, abdominal pain, weight loss and malnutrition [1, 2]. The pancreatic pain syndrome is also very complex, with symptoms arising from multiple sources, including mechanical (obstructive) [3], vascular (ischemic) [4], inflammatory [5], neuropathic [6, 7] and possibly hyperstimulatory etiologies[8].

The medical treatment of symptomatic CP is difficult to standardize because of the complexity of the disease, the variability between patients and the changing characteristics of disease with progression of fibrosis or development of complications. Thus, a wide variety of empiric treatments are often tried for maldigestion and pain. The spectrum of analgesic requirements by CP patients ranges from acetaminophen and NSAIDs to powerful narcotic agents. Some patients with CP suffer from complications of duct obstruction that can be successfully treated with endoscopic therapy or surgery [3]. In addition, several non-analgesic, mechanism-targeting approaches have been introduced to help alleviate or reduce pain.

Pain from pancreatic hyperstimulation can theoretically be reduced at the duodenum by giving oral pancreatic enzyme replacement therapy (PERT) with meals to short-circuit the stimulation feed-back signals by increasing protease activity in the duodenum and decreasing CCK releasing factor [9]. A second approach is to block pancreatic stimulation with an inhibitory hormone analogue, octreotide, which activates the somatostatin receptor [10-12]. A third approach is to reduce acinar cell oxidative stress and injury by the use

of vitamins and/or antioxidants (AO) [13, 14]. A fourth approach is to directly block the stimulatory (vagal) and sensory nerves to the pancreas with a celiac plexus block (CPB). The use and perceived usefulness of these targeted approaches in clinical practice within the United States is unknown.

In the present study, we used the North American Pancreatitis Study 2 (NAPS2) cohort to obtain a cross sectional assessment of the frequency and physician-perceived effectiveness of PERT, AO, CPB and octreotide in CP patients evaluated at pancreas referral centers in the United States. In addition, we evaluated differences in use and perceived effectiveness based on the etiology of CP and on the presence or absence of exocrine insufficiency (EI) and pain. We assessed the use and efficacy of CPB with other medical therapies since CPB does not qualify as an endoscopic or surgical treatment.

Methods

North American Pancreatitis Study 2 (NAPS2)

The study population was identified from within the NAPS2, a 20 center, prospective, cross-sectional, observational cohort study from the United States consisting of 1000 subjects with pancreatitis (recurrent acute pancreatitis=460; CP=540), and 695 controls conducted between 2000 and 2006 [15]. The methodology of NAPS2 has been detailed previously [15]. The entry criteria for CP included definitive evidence on computed tomography (CT) scan and/or Endoscopic Retrograde Cholangiopancreatography (ERCP) with the Cambridge class II or more (83%) or documentation of CP using Magnetic resonance Cholangiopancreatography (MRCP), Endoscopic Ultrasound (EUS) or pancreatic histology in other enrollees [16]. Each study subject completed a detailed questionnaire on personal and family history, risk factors, symptoms and quality of life, and an additional questionnaire was completed by a physician-investigator with expertise in pancreatic diseases. The physician questionnaire contained questions relating to clinical phenotype, working diagnosis, risk factors, diagnostic and therapeutic interventions [15].

Physician Questionnaire

The information on use and effectiveness of medical therapies, presence of endocrine or EI, and etiology was obtained from responses provided by the enrolling physician in the Physician Questionnaire. In the section on therapies, physician was asked, “Which therapies were attempted, and which of these were helpful”, and given specific categories for medical (including PERT, AO, CPB and octreotide), endoscopic and surgical treatments. If the treatment had been tried the physician was asked to select between the following choices: *unchanged, worse, helpful or not sure*. Information on timing of treatment before study enrollment, dosage, duration and the formulation of PERT (enteric- or non-enteric coated) or AO therapy was not asked. A therapy was classified as effective if the physician chose “helpful” as a response. Patients could be counted for more than one treatment. From 540 patients in the NAPS2 cohort with CP, we excluded 24 (4%) patients in whom the enrolling physicians did not indicate a trial occurred with any of the therapeutic modalities (medical, endoscopic or surgical). The final sample size for analysis for this study was therefore 516/540 (96%) CP patients.

The enrolling physician indicated whether endocrine or EI was present and the method used to establish the diagnosis. We determined the etiology of CP based on physician's response to the question on working diagnosis. Physicians chose one or more working diagnosis from among the following choices: alcohol, idiopathic, hereditary, cystic fibrosis, pancreas divisum, hyperlipidemia, hypercalcemia, trauma, and other, with space provided for details. Since more than one working diagnosis could be selected, we used a hierarchical algorithm

to sequentially assign patients into etiologic groups. In summary, patients in whom "alcohol" was checked by itself or with other diagnoses were assigned to the "alcohol" group; among remaining patients, those with hereditary or cystic fibrosis diagnosis with or without another diagnoses were assigned to the "genetic" group; among remaining patients, those with autoimmune pancreatitis diagnosis with or without another diagnoses were assigned to the "autoimmune" group; among remaining patients, those with an obstructive etiology with or without another diagnoses were assigned to the "obstructive" group; among remaining patients, those identified with a specific etiology not included into any of the previous group were assigned to "other etiologies" group; all the remaining patients were then assigned to "idiopathic" group.

Patient Questionnaire

The information on demographics, and presence and pattern of pain was obtained from responses to the patient questionnaire. Patients were asked if they had abdominal pain, and to choose the pattern and severity of pain from a list consisting of five options [15, 17, 18]. Patients could characterize their pain experience as - A) episodes of mild to moderate pain, usually controlled by medication; B) Constant mild to moderate pain usually controlled by medication; C) Usually pain free with episodes of severe pain; D) Constant mild pain plus episodes of severe pain; E) Constant severe pain that does not change. We classified patients based on the pattern of pain (intermittent [Groups A or C] or chronic [Groups B, D, E]) and the severity of pain (mild to moderate [Groups A or B] or severe [Groups C, D, E]).

Statistics

Descriptive analyses are presented as proportions for categorical data, and as mean ± standard deviation (SD) for continuous data. Univariate analysis for categorical data was performed using the chi-squared or Fischer's exact test as applicable to evaluate the proportion of patients in whom individual medical therapies were tried, and, if a therapy was tried, the proportion in whom physicians believed that it was effective. Univariate comparisons for continuous variables were made using the Student's-t test.

Multivariable logistic regression models were used to determine independent predictors for PERT use and efficacy. Due to small sample sizes for subjects in whom other medical therapies were tried (AO, CPB and octreotide), only univariate analyses were performed for the use and efficacy of these treatments. All variables showing a p-value of <0.10 in the univariate analysis were chosen for initial inclusion into the regression models, except for age and gender, which were forced into the models. A backwards selection technique was used to determine significant independent predictors. For class variables, all observations were entered if one value of the class was significant. Data were examined for collinearity but showed no significant interactions. Two-sided p-values <0.05 were considered significant. Data analysis was performed with R Project software (www.r-project.org) and SAS system version 9.2 (SAS Software Institute, Cary, NC).

Results

Demographics, etiology and use of medical therapies

The demographics of the overall NAPS2 cohort have been previously reported [15, 19]. In 516/540 (96%) patients with CP in the NAPS2 cohort, the enrolling physicians indicated the utilization and effectiveness of at least one of the therapeutic modalities (medical, endoscopic or surgical). The sample size for this study therefore consisted of 516 patients. The mean age of these 516 patients was 49.2 ± 15.6 years, 51.9% were male and 84.9% were Caucasian. Alcohol was considered as a single or contributing etiology in 43.8% patients, idiopathic CP in 28.9%, obstructive causes in 8.7%, while the remaining patients

were due to other etiologies. At least one of the four medical therapies was tried in 383/516 (74.2%) patients. In 283 (54.8%) only one medical therapy was utilized while two or more than two medical therapies were used in 89/516 (17.2%) and 11/516 (2.1%) patients, respectively.

Utilization of PERT

Overall, PERT was tried in 363/516 (70%) patients – by themselves in 263/363 (74.2%), and in combination with other medical therapies in 100/363 (25.8%) patients. A significant correlation was seen between PERT usage and the presence of symptoms (pain and/or EI) ($p<0.001$). Univariate analyses comparing PERT usage in different groups is provided in Table 1. There was no difference in PERT usage based on gender, race, etiology or presence of endocrine insufficiency. However, compared to almost 75% of patients younger than 65 years of age, PERT had been used in only ~50% of patients who were 65 years or older ($p=0.003$). PERT usage was also more frequent in patients with EI and/or pain.

On multivariate analysis (Table 2), the strongest predictors for PERT usage were presence of EI and presence of constant pain. Independent of the presence of pain, patients with EI were approximately 5 times more likely to have used PERT. Similarly, independent of the presence of EI, patients with intermittent pain were twice as likely to have used PERT, and those with constant pain were over 3 times more likely to have used PERT, than those with no pain. Patients less than 65 years of age were almost 3 times more likely to have used PERT compared to patients 65 years or older.

Effectiveness of PERT

In this study the physicians were not asked to specify whether PERT was effective for symptoms of maldigestion or pancreatic pain. PERT was considered by physicians to be effective in 158/362 (43.5%) patients. The reported effectiveness ranged from 27.9-79.2%. Univariate analyses comparing the efficacy of PERT in different groups are provided in Table 1. Physicians perceived PERT to be most effective in patients with EI without pain (19/24, 79.2%) followed by EI with pain (49/98, 50%), and least effective in either pain category without EI. In the univariate analysis, PERT was also perceived to be more effective in patients with endocrine insufficiency, younger patients, and patients without abdominal pain. The effectiveness of PERT appeared to be similar among patients in the three common etiologic groups.

On multivariate analysis, the only significant predictor for effectiveness of PERT was the presence of EI (Table 2). PERT was considered to be twice as effective in patients with EI versus those with no EI. The other significant predictors for effectiveness of PERT on univariate analyses were no longer significant in multivariate analyses.

Utilization and efficacy of other medical therapies

In contrast to PERT, other therapies were used infrequently in patients with CP: the second most commonly used modality was AO, in 71/516 (13.8%), followed by CPB in 34/516 (6.6%) and octreotide in 28/516 (5.4%) patients. Similar to PERT, the usage of other therapies correlated with the presence of symptoms ($p< 0.01$). Univariate analyses comparing the usage and efficacy of AO, CPB and octreotide in different groups is provided in Table 4. Although no significant differences were seen in the proportion of patients in whom individual therapies were used, largely due to small sample sizes, interesting trends were noted. Not surprisingly, CPB was used more often in patients who reported constant or severe pain, and in patients with alcohol or idiopathic etiologies, and was used less often in those over age 65 years. Octreotide was tried more often in patients who reported pain, had no EI and had obstructive or idiopathic etiologies.

As indicated in Table 4, the efficacy of AO was generally considered to be poor, with the best efficacy of ~25% in patients who were young, and in those who had obstructive and idiopathic rather than alcoholic etiologies (p=0.03). When used, the efficacy of CPB and octreotide was highly variable, ranging from 20-100%.

Subgroup analyses

The results of subgroup analyses by sex were generally similar to the overall analyses (data not shown).

Discussion

The present study reports on the use and perceived effectiveness of medical therapies that are used for treating pain in CP by targeting possible pain-generating mechanisms. A number of observations from this study confirm and strengthen previous observations, and add perspective to a complex condition. The primary finding was that PERT were widely used, while the use of AO, CPB and octreotide in clinical practice in the United States is relatively infrequent. In this group, more than half of the patients treated did not have EI. As expected, PERT were very helpful in treating patients with EI, although physicians still considered it helpful in one-third of subjects with pain, but without EI. AO appeared to be most useful in patients with non alcohol-related CP, although it was ranked as the least helpful of the three medications under all conditions. Octreotide appeared to be most helpful treatment in patients with alcohol-related CP.

The present study has major strengths and limitations. The strengths include its multi-center approach, the use of pancreatic experts for phenotyping, and the use of best available tools for this study. The primary limitation is that this was a single visit analysis of a large, cross-sectional cohort of CP patients evaluated at expert centers in the United States, and therefore reflects the therapies tried until the time of enrollment and may not fully reflect the practice of the expert consultant. Secondly, the indication(s) for prescribing medical therapies were unknown. Third, the specific dosage or formulation of PERT (enteric- or non-enteric coated) or AP was not evaluated. Fourth, as in all observational studies, it was not possible to standardize treatment dose or duration, the measures of effect, and/or end point(s) and there were no placebo controls limiting our ability to address potential physician bias. There may also be a referral bias of patients from the community to referral centers who failed standard therapies. The study was also limited by small number of patients in whom AO, octreotide and CPB were attempted. Furthermore, comparison of subjects by presence and type of pain was based on the time of enrollment, and not necessarily at the time of attempted treatment. These factors limit the analysis of the data set to observations of the use of medical therapies in the community, and their perceived usefulness under typical practice conditions. However, it provides very important information about current use of these therapies in the United States, and may be very useful in determining feasibility and power in future prospective studies.

Pancreatic Enzyme Supplements

PERT is used both for treating maldigestion and for treating pain. There is no controversy as to whether PERT is both useful and medically necessary in the treatment of patients with EI (e.g. cystic fibrosis, advanced CP, pancreatic resection). Defining the physiologic threshold for pancreatic insufficiency is complicated by poorly defined or inconsistent endpoints (e.g. biochemical measures of protein nutrition [20], fecal elastase concentrations [21, 22], steatorrhea [23]), by the varying nutritional needs and meal sizes of individual patients. Furthermore, the threshold for prescribing PERT by the managing physician is also variable, often depending on the signs and symptoms of maldigestion (e.g. unexplained weight loss,

bloating, abdominal cramping, diarrhea, steatorrhea) and patient complaints rather than relying on measures of pancreatic exocrine function and nutritional needs. The findings of the present study strongly support the role of PERT in the treatment of patients with EI with and without pain.

Isaksson et al [24] reported a double-blinded, placebo controlled, randomized trial of non-enteric coated PERT in patients with CP for the treatment of pain. Fifteen of 19 (79%) patients treated with a pancreatic enzyme supplement during the one week treatment period had an average pain reduction of 30% [24]. Four additional studies were subsequently published, including one positive study using non-enteric coated enzymes [25] and three negative studies using enteric coated enzymes [26-28], but the individual, and combined results [9] failed to demonstrate significant benefit over placebo. However, an argument has been made that this approach is effective in minimal change, or "small duct" CP, and requires the use of high potency, uncoated pancreatic enzymes [12], preferably with acid suppression [29]. After reviewing this literature Brown et al [9] concluded that what is needed is an adequately powered study, with emphasis on minimizing patient and drug heterogeneity and use of enzyme preparations that provide adequate concentrations of proteases in the duodenum. The present study does suggest that many physicians treating CP patients with pain but without EI have used PERT. There appears to be perceived usefulness in treating patients without EI, and this effect appeared to be similar in patients with (36%) and without pain (34.6%). Due to the cross-sectional design, it is unclear if PERT were used in the latter group to treat symptoms of maldigestion or pain without clinically obvious EI or whether this apparent improvement in symptoms reflects of placebo effect. However, in patients with pain, PERT was judged to be more useful in patients with EI (50%) than those with pain alone (36.3%). Thus, PERT appear to have an important role in the treatment of CP patients, but the effect on pain is smaller than on EI alone (79.2%). The possibility that PERT are effective in a special subset of patients with "small duct" disease [12], or hereditary pancreatitis [30] has not been excluded. Whether PERT is helpful in patients with pain alone need to be addressed in prospective trials with appropriate study design and follow up.

Vitamins / Antioxidants

A non-significant result for perceived effectiveness between etiologies overall could be due to small sample sizes (resulting in a Type-II error) which limits our ability to draw definite conclusions. However, when comparing effectiveness of AO in subgroup analyses, physicians did report a significantly higher effectiveness for AO in patients with idiopathic and obstructive etiologies (p=0.03) when compared to alcohol-related CP (Table 4).

While early trials on the use of a single AO were disappointing [13], two recent studies suggest that combination AO may be useful for the treatment of pain in a subset of patients with CP [14, 31]. In the study by Kirk at al. [31], 36 patients with CP were recruited, but only 23 patients completed the study. Data from pain diaries were disregarded and the results represented the data from the SF-36 questionnaires completed by patients who completed the study. This study showed that a combination AO improved abdominal pain and several aspects of quality of life in patients with CP. It is hard to compare the results of this study to ours because the etiology of CP was not specified [31]. On the other hand, a more recent study from India evaluated AO in 127 patients, most of whom had idiopathic CP [14]. It showed combination AO (much higher doses comparing to the previous study) was effective in reducing the number of painful days per month, requirement of analgesics, need for hospitalization, and the percentage of patients who became pain free. However, significant post-randomization dropouts and other methodological issues limit the strength of the conclusion of this trial [32]. Our study suggest that providers considered AO to be more helpful in obstructive and idiopathic CP than alcoholic CP, but the 25% effectiveness rate is similar to placebo in many randomized trials of abdominal pain.

Celiac Plexus Block

The utility of CPB for pancreatic pain was first recognized in patients with pancreatic cancer [33]. Wiersema first demonstrated that celiac plexus block could be done using EUS [34], and Gress et al [35] went on to demonstrate that it could provide significant improvement in pain scores with reduction in pain medication usage in half of treated patients. In the current study, CPB was used in 5.6% of men and 7.7% of women. Although the numbers are small, it appears that this therapy was used more often in patients with constant pain but was more effective in those with mild-moderate pain.

Octreotide

Octreotide has been evaluated for pain in CP mainly when other medical therapies have failed. Octreotide is a potent inhibitor of pancreatic exocrine secretion [36] and may work through several mechanisms [37], including a direct effect [38] and inhibiting neural stimulation [39]. It may have anti-inflammatory properties [40] and reduce sphincter of Oddi pressure [41].

A few small studies published in abstract form [42-44] or as full manuscripts [11, 45, 46] have reported on the efficacy of octerotide in painful CP. In 1993, in a placebo controlled, double blind, dose finding study, octreotide 200 μg given three times a day was reported to be more effective than placebo in reducing pain [43]. The benefit was more prominent in the subgroup of patients with constant daily pain [43]. An open label extension published in 1994 [44] suggested that by 6 weeks 50% of patients still had continued pain relief for 6 weeks [44]. In contrast, a small German study showed no differences in pain control or analgesic use during a short-term (3 days) double-blind cross-over study [11]. In 2009, a study from the US compared long acting octreotide to short acting octreotide in the treatment of painful CP in a small open label, unblinded pilot study [46]. Lieb et al[46] reported that in 7 patients with severe CP and constant daily pain once monthly depo-octreotide, (Octreotide LAR®, Novartis, East Hanover, NJ, USA,) 60 mg intramuscular injection, may be a useful substitute for short acting octreotide that must be injected three times a day. We found that octreotide was seldom used in the clinical practice of gastroenterologists at the NAPS2 sites but was judged by the provider to be of some benefit in a few patients.

Summary and Conclusion

The current report provides a cross-sectional perspective on the current use of non-analgesic medical therapies in CP in the United States. The major finding is that PERT is the most commonly used treatment in this class, and provides a significant perceived benefit for EI; but also for pain in a subset of patients, especially those with EI. The second finding is that AO do appear to be useful in patients with non-alcohol related, but not in alcoholic CP. Thirdly, CPB and octreotide treatment may be useful in a small subset of patients, but the limited use of these therapies limits any further interpretations.

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Appendix

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Table 1

Univariate associations for the use and efficacy of PERT in chronic pancreatitis patients in the North American Pancreatitis Study 2

Attribute	% in sample (N=516)	%enzymes Tried	p-value[$]	% enzymes Effective	p-value[#]
Gender					
Male	51.9	68.3		41.5	
Female	48.1	72.6	0.29	45.6	.44
Age:					
<35	18.2	76.6		38.9	
35-44	21.3	79.1		37.9	
45-64	44.2	70.2		46.9	
65+	16.3	52.4	**.003**	50.0	.36
Race					
White	84.9	69.4		44.1	
Other	15.1	75.6	.27	40.7	.63
Etiology					
Alcohol	43.8	69.9		46.8	
Obstructive	8.7	77.8		48.6	
Idiopathic	28.9	68.5		47.1	
Other	18.6	70.8	.68	27.9	**.04**
Pain					
Yes	76.7	73.7		40.4	
No	23.3	59.2	**.002**	56.3	**.015**
Pain					
No pain	23.3	59.2		56.3	
Constant	43.2	80.7		40.0	
Intermittent	33.5	64.7	**<.0001**	41.1	**.05**
Pain					
No pain	23.3	59.2		56.3	

Attribute	% in sample (N=516)	%enzymes Tried	p-value[$]	% enzymes Effective	p-value[#]
Mild	17.1	69.3		36.1	
Severe	59.7	75.0	**.005**	41.6	**.04**
Exocrine Insufficiency (n=480)					
Yes	29.0	87.8		55.7	
No	71.0	61.0	**<.0001**	36.1	**.0005**
Patient group (n=480)					
Pain (+), EI (-)	57.0	66.4		36.3	
Pain (+), EI (+)	22.7	89.9		50.0	
Pain (-), EI (+)	6.3	80.0		79.2	
Pain (-), EI (-)	14.0	38.8	**<0.001**	34.6	**<0.001**
Endocrine Insufficiency (n = 480)					
Yes	26.2	68.5		55.1	
No	73.8	69.7	.80	38.8	**.008**

EI – exocrine insufficiency; PERT – pancreatic enzyme replacement therapy

"% in sample" - proportion of overall study sample (i.e. patients in whom any medical, endoscopic or surgical treatment modality was utilized, n = 516); "% enzymes tried" – proportion of individual subgroup in whom PERT was tried; "%enzymes effective" – among patients receiving PERT, proportion in whom they were considered to be effective.

[$] p-value – differences in proportion for utilization of enzymes

[#] p-value – differences in proportion for effectiveness of enzymes

Table 2

Independent predictors of PERT use in chronic pancreatitis patients in the North American Pancreatitis Study 2 based on multivariate analyses.

Variable	Odds ratio	95% Confidence Interval
Male Gender vs. female	0.86	0.56 – 1.32
Age		
<35 vs. 35-44	1.03	0.50 – 2.09
45-64 vs. 35-44	0.62	0.34 -1.10
65+ vs. 35-44	0.35	0.18-0.71
Pain:		
Constant vs. no pain	3.42	1.93- 6.04
Intermittent vs. no pain	1.98	1.14 – 3.45
Exocrine Insufficiency	5.14	2.87 – 9.18

PERT – pancreatic enzyme replacement therapy

Gender and age were forced into the model. Other variables entered into the model were severity of pain, endocrine insufficiency, etiology and race. Interaction between pain and exocrine insufficiency was not significant.

Table 3

Independent predictors of PERT efficacy in chronic pancreatitis patients in the North American Pancreatitis Study 2 based on multivariate analyses.

Variable	Odds ratio	95% Confidence Interval
Male Gender vs. female	0.83	0.53 – 1.29
Age		
<35 vs. 35-44	1.16	0.59 – 2.31
45-64 vs. 35-44	1.51	0.85 -2.69
65+ vs. 35-44	1.67	0.76-3.66
Exocrine Insufficiency	2.16	1.36 – 3.42

PERT – pancreatic enzyme replacement therapy

Gender and age were forced into the model. Other variables entered into the model were frequency of pain, severity of pain, endocrine insufficiency and race

Table 4

Univariate associations for the use and efficacy of vitamins and antioxidants, celiac plexus block, and octreotide in chronic pancreatitis patients in the North American Pancreatitis Study 2

Attribute	% in sample (N=516)	VITAMINS/ANTIOXIDANTS		CELIAC PLEXUS BLOCK		OCTREOTIDE	
		% Tried	% Effective	% Tried	% Effective	% Tried	% Effective
Gender							
Male	51.9	16.0	16.3	5.6	40.0	5.2	64.3
Female	48.1	11.3	10.7	7.7	36.8	5.7	42.9
Age:							*
<35	18.2	17.0	25.0	6.4	66.7	5.3	20.0
35-44	21.3	11.8	7.7	9.1	40.0	6.4	57.1
45-64	44.2	13.6	16.1	7.0	25.0	5.7	76.9
65+	16.3	13.1	0.0	2.4	50.0	3.6	0.0
Race							
White	84.9	13.9	14.8	6.4	39.3	5.3	56.5
Other	15.1	12.8	10.0	7.7	33.3	6.4	40.0
Etiology							
Alcohol	43.8	12.4	3.6	6.6	40.0	3.5	75.0
Obstructive	8.7	15.6	28.6	2.2	100.0	8.9	50.0
Idiopathic	28.9	16.8	24.0	9.4	35.7	7.4	54.5
Other	18.6	11.5	9.1	4.2	25.0	5.2	40.0
Pain							
Yes	76.7	13.4	11.3	7.6	40.0	6.3	56.0
No	23.3	15.0	22.2	3.3	25.0	2.5	33.3
Pain							
No pain	23.3	15.0	22.2	3.3	25.0	2.5	50.0
Constant	43.2	13.9	12.9	12.6	35.7	6.7	60.0
Intermittent	33.5	12.7	9.1	1.2	100.0	5.8	33.3

Attribute	% in sample (N=516)	VITAMINS/ANTIOXIDANTS		CELIAC PLEXUS BLOCK		OCTREOTIDE	
		% Tried	% Effective	% Tried	% Effective	% Tried	% Effective
Pain				*			
No pain	23.3	15.0	22.2	3.3	25.0	2.5	33.3
Mild-moderate	17.1	11.4	10.0	4.6	75.0	6.8	33.3
Severe	59.7	14.0	11.6	8.4	34.6	6.2	63.2
Exocrine Insufficiency (n=480)						*	
Yes	29.0	15.8	18.2	8.6	25.0	1.4	54.2
No	71.0	12.0	7.3	5.6	47.4	7.0	100.0
Endocrine Insufficiency (n=480)							
Yes	26.2	13.1	11.8	7.7	30.0	3.9	60.0
No	73.8	13.1	10.4	6.0	45.5	6.0	54.6

* $p < 0.05$

"% in sample" - proportion of overall study sample (i.e. patients in whom any medical, endoscopic or surgical treatment modality was utilized, n = 516); "% tried" – proportion of individual subgroup in whom treatment was tried; "% effective" – among patients who received treatment, proportion in whom it was considered to be effective.