藥師於慢性胰臟炎疼痛控制的角色

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Outline

- Introduction
- Pain control
- Other consideration
- Conclusion

Chronic Pancreatitis

- Inflammatory condition
- Impaired endocrine and exocrine function
- Risk factor
  - Toxic-metabolic
  - Idiopathic
  - Genetic
  - Autoimmune
  - Recurrent and severe acute pancreatitis
  - Obstructive

Am Fam Physician 2007;76:1679-88

Chronic Pancreatitis

- Complications / confounders
  - Pancreatic cancer
  - Pseudocyst
  - Duodenal obstruction
  - Gastroparesis
  - Bile duct obstruction
  - Malabsorption

Chronic Pancreatitis

- Goal
  - Pain management
  - Management and prevention of complications
  - Correction of pancreatic insufficiency

Pain of Chronic Pancreatitis

- Most frequent and dominant symptom
- Highly variable clinical presentation
- No evidence-based protocol exist
- Mechanisms
  - Pancreatic duct hypertension
  - “Compartment syndrome”
  - Neural involvement
  - Genetic factors

Pain Management

- Life style modify
- Medical therapy
- Endoscopic therapy
- Surgical therapy
- Nerve blocks

Solid doctor-patient relationship

Medical Options

- Nonspecific supportive therapy
- Analgesics
- Adjunctive agents
- Antioxidants
- Enzymes
- Octreotide
- Others

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Analgesics

- Non-narcotic
- Narcotics
  - Low potency
  - High potency
- About ½ of patients with chronic pancreatitis use opioids

Analgesics

- Tramadol compared to morphine
  - Randomized trial, N=25
  - No difference in pain relief with less gastrointestinal side effects with tramadol
- Should begin with low potent agents

Adjunctive Agents

- Tricyclic antidepressants
- Selective serotonin reuptake inhibitors (SSRI)
- Combined serotonin and norepinephrine reuptake inhibitors (SNRI)
- $A_2\delta$ inhibitors

Pregabalin

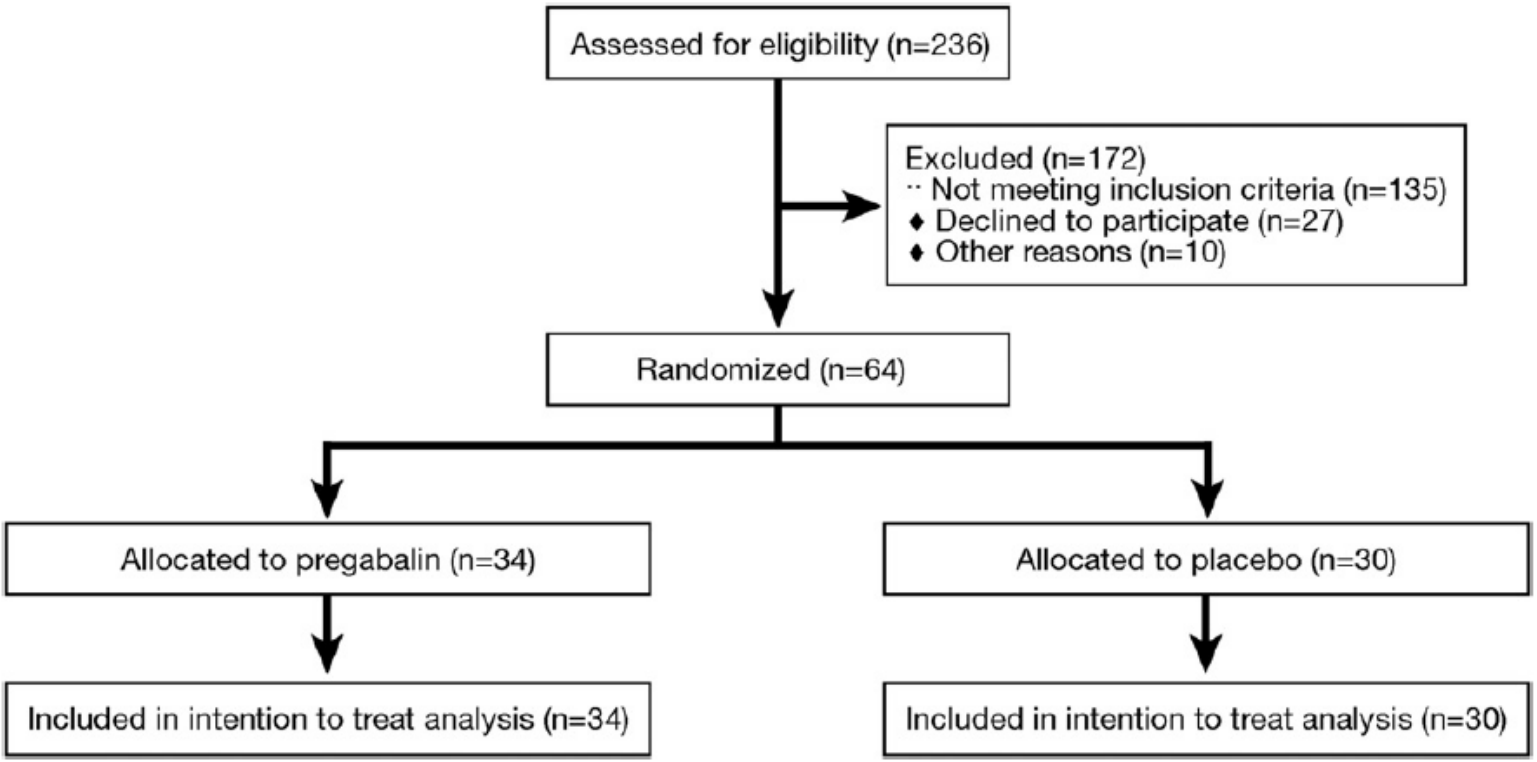

Figure 1. Study enrollment and randomization.

Gastroenterology 2011;141:536-43

Pregabalin

Table 2. Changes in Primary and Secondary End Points After Three Weeks of Study Treatment

Variable	Pregabalin (n=34)	Placebo (n=30)	Pregabalin vs placebo	*P* value
Average diary pain score	−36% (−43%–−29%)	−24% (−31%–−16%)	−12% (−22%–−2%)	.02
Maximal diary pain score	−32% (−38%–−26%)	−22% (−28%–−16%)	−10% (−19%–−2%)	.02
PGIC				
Very much improved	1 (3)	2 (7)		.048
Much improved	13 (41)	4 (14)		
Minimally improved	8 (25)	7 (24)		
No change	7 (22)	11 (38)		
Minimal worse	0 (0)	4 (14)		
Much worse	2 (6)	1 (3)		
Very much worse	1 (3)	0 (0)		
BPI				
Pain score	−1.2 (−2.2–−0.2)	−0.4 (−1.1–−0.4)	−0.8 (−2.0–−0.4)	.19
Interference score	−1.3 (−2.2–−0.3)	−1.0 (−1.7–−0.2)	−0.3 (−1.5–−0.9)	.61

NOTE. Pain diary data were available for 33 patients (97%) in the pregabalin group and 29 patients (97%) in the placebo group; 2 patients in the pregabalin group left the study after 11 days and 18 days; their data were included until then. Patients' global impression of change (PGIC) and brief pain inventory short form (BPI) were available for 29 patients (97%) in the placebo group. In the pregabalin group, PGIC data were available for 32 patients (97%) and BPI data for 31 patients (94%). Changes in pain diary data and BPI scores are reported as mean changes (95% confidence interval). PGIC is reported as numbers (%).

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Pregabalin

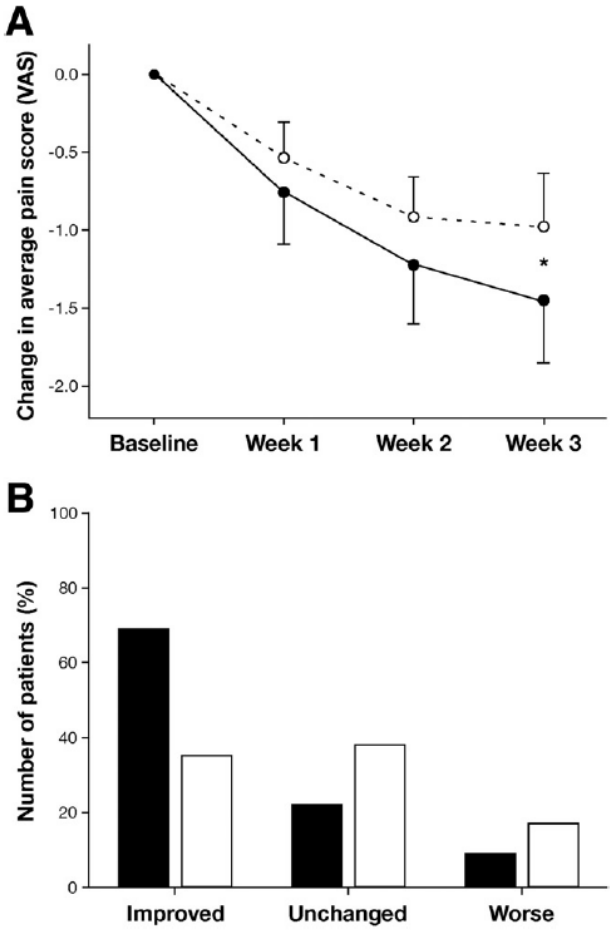

Figure 2. Primary and secondary outcomes. (*A*) Changes in average pain score (VAS). The *black circles* and *solid line* represent pregabalin-treated patients, and the *white circles* and *dashed line* represent patients receiving placebo. *Bars* are standard errors. $^{*}P = .02$ comparing pregabalin and placebo. (*B*) PGIC at the end of the study. *Black bars* represent pregabalin-treated patients, and *white bars* represent patients receiving placebo. There was a better treatment response in the pregabalin group ($P = .048$).

Gastroenterology 2011;141:536-43

Pregabalin

Table 4. Adverse Events During the Study Period

		n *(%)*			
	Event	Pregabalin (n=34)	Placebo (n=30)	Risk ratio (95% CI)	*P* value
	Any adverse event	31 (91)	16 (53)	1.7 (1.2–2.4)	.001
Central nervous system	Feeling drunk	12 (35)	2 (7)	5.3 (1.3–21.8)	.007
	Mild/moderate/severe	4/7/1	0/2/0		
	Light-headedness	8 (24)	1 (3)	7.1 (0.9–53.2)	.03
	Mild/moderate/severe	6/2/0	1/0/0		
	Dizziness	13 (38)	5 (17)	2.3 (0.9–5.7)	.09
	Drowsiness	12 (35)	6 (20)	1.8 (0.8–4.1)	.27
	Trouble concentrating	3 (9)	1 (3)	2.6 (0.3–24.1)	.62
	Headache	4 (12)	4 (13)	0.9 (0.2–3.2)	1.00
	Amnesia	2 (6)	0 (0)	—	.49
	Migraine attack	1 (3)	0 (0)	—	1.00
	Myoclonus	2 (6)	0 (0)	—	.49
	Tremor	1 (3)	0 (0)	—	1.00

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Adjunctive Agents

- In patients requiring chronic opioid, a trial of a pregabalin can be considered
- The effect of tricyclic antidepressants and SSRI is not known

Antioxidants

- Oxidative stress can be documented in chronic pancreatitis
- 4 randomized trials
  - Different antioxidants
  - Different duration of treatment
  - Different result
- Dose and components

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Pancreatic Enzymes

- A negative feedback inhibition to the pancreas
- Cholecystokinin (CCK)

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Pancreatic Enzymes

- 7 RCTs
  - All use crossover design
  - 2 demonstrate benefit using uncoated enzymes
  - Significant heterogeneity in outcome measures
- 2 observational studies & 1 meta-analysis
  - No benefit
- Management of exocrine insufficiency > pain control
  - Concurrent use of proton pump inhibitors

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Octreotide

- Inhibition of pancreatic secretion
- 4 RCTs
  - No effect: 2
  - Benefit : 1
  - Benefit only in subgroup analysis: 1
- The longevity of possible benefit was not established

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Other Consideration

- Dependent on heavy narcotic use
- Act and regulations

慢性胰臟炎病人使用成癮性麻醉藥品之臨床指引

- 病患衛教：低油飲食
- 先使用非成癮性止痛劑，建議飯前服用，輔以酵素療法
- 長期依賴止痛劑之病人，如病情需要可適時增加以下療法：
  - Octreotide 注射
  - Celiac plexus block
  - 內視鏡治療
  - 外科治療

醫師為非癌症慢性頑固性疼痛病人長期處方成癮性麻醉藥品注意事項

- 非癌症相關之慢性頑固性疼痛病人
  - 非癌症引起且無法以其他藥物或治療緩解
  - 因燒燙傷、重大創傷等需住院反覆手術
- 長期使用
  - 連續使用超過14天
  - 三個月內累積使用28天
- 應使用其他藥物及方式控制疼痛無效始得考慮麻醉藥品

醫師為非癌症慢性頑固性疼痛病人長期處方成癮性麻醉藥品注意事項

- 需成立管制藥品管理委員會
  - 醫學中心或區域醫院
    - 麻醉/疼痛、精神、神經、內科、外科專科醫師
    - 藥師
  - 疼痛衛教
  - 病例評估、審查、追蹤
- 會診：填寫新個案通報表
  - 10工作日內完成：疼痛科、精神科、其他相關科
  - 一致同意始得續用；意見不一致提會討論

醫師為非癌症慢性頑固性疼痛病人長期處方成癮性麻醉藥品注意事項

- 使用中
  - 填寫同意書：告知副作用及注意事項
  - 至少每四個月提委員會討論
  - 至少每半年重填同意書及會診精神科評估
  - 診斷改變：重新填寫及會診
- 以口服劑型為主
  - 處方限制：口服14日、貼片15日、針劑7日
  - 廢貼片、空安瓿應於再處方時繳回

麻醉藥品臨床使用規範

- 用藥原則
  - 嚴格依臨床適應症用藥
  - 不得應病人要求濫用藥品
  - 盡量採口服給藥
  - 採取階段式給藥
  - 依照規定處方，不得以電話處方
- 給藥間期
  - Codeine：3-4次/天
  - Morphine口服速效劑型：q4h
  - Morphine sulfate長效錠：q8-12h

藥局交付麻醉藥品時應辦理事項

- 應核對領藥人身分
- 請領藥人於麻醉藥品專用處方箋上憑[1]身分證明[2]簽名領受
  - 病患本人無法親自領藥時，可由家屬代理
- 發給麻醉藥品居家治療用藥紀錄表
  - 複診時交醫師審視
- 未按規定確實填寫，再處方麻醉藥品時，酌予減少交付天數
  - 情節重大者，並應拒絕再處方交付麻醉藥品
- 未用完之藥品如不再使用時，應併同麻醉藥品居家治療用藥紀錄表繳回

Conclusion

- Painless chronic pancreatitis is rare
- Cause of pain is usually multifactorial
- A varying degree to the pain
- Lifestyle modify
- Medications may be useful but not in any situation
- Endoscopic therapy、nerve blockade or surgical treatment are alternative