

# Pancreatic cancer and the use of enzymes: A review of the literature

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# Aims

- Determine evidence behind the use of pancreatic enzyme replacement therapy (PERT) in pancreatic cancer patients.
- Investigate evidence behind dosage recommendations of PERT in pancreatic cancer.

# Literature search

- **Guidelines**- NICE guidelines, National Library of Guidelines, Clinical Knowledge Summaries, International Guidelines.
- **Evidence based reviews**- Cochrane Library, DARE, DUETs.
- **Databases**- Medline, CINHALL, EMBASE, PubMed.

# Guidelines

## **Guidelines for the management of patients with pancreatic cancer periampullary and ampullary carcinomas (GUT 2005)**

- 'Pancreatic enzyme supplements should be used to maintain weight and increase quality of life'.
- Evidence is graded at A: at least 1 randomised control trial (RCT).

# Bruno et al 1998

- Double blind randomised placebo control trial.
- 21 subjects with unresectable cancer of the pancreatic head with biliary stent insitu.
- Subjects were given placebo or PERT therapy.
- All patients received dietary counselling.

# Bruno et al 1998

## PERT therapy details

- Panzytrat 25000 'enteric coated pancreatin microsphere preparation'.
- 25000 PhEur units of lipase.
- 2 capsules given with main meals.
- 1 capsule given with snacks.
- Followed up for 8 weeks.

# Bruno et al 1998

## **PERT subjects**

↑ 1.2 % body weight

↑ 12 % fat absorption

Total energy intake of  
8.42 MJ/day

## **Placebo subjects**

↓ 3.7 % body weight

↓ 8 % fat absorption

Total energy intake of  
6.66 MJ/day

# Bruno et al 1998

- Only RCT available.
- Very small sample size.
- No power calculation undertaken.



# Perez et al 1983

- 12 subjects with pancreatic cancer
- 4 meals per day, 8 pancreatin tablets with each meal.
- 6 subjects with moderate to severe fat malabsorption 'improved with pancreatin'.
- Subjects with mild fat malabsorption 'had no improvement'.
- Many problems with study including very small sample size.

# Review articles

- No systematic reviews found in Cochrane library specific to pancreatic cancer and PERT.
- Reviews found frequently described authors own practice and lacked supporting references.
- Several review authors quote references which are not specific to pancreatic cancer. (e.g. Ferrone et al 2007)

# Review articles

<b>Author</b>	<b>Dose of PERT advocated (units of lipase per meal)</b>
Smith 2008	20000 - 50000
Damerla et al 2008	50000*
Nakakura & Warren 2007	25000 - 40000 <sup>‡</sup>
Keller & Layer 2005	25000 - 40000 <sup>‡</sup>
Bruno et al 1995	20000 - 70000*

\*Authors do not quote supporting references

<sup>‡</sup>Supporting references are not specific to pancreatic cancer

# PERT and pancreatic cancer surgery

- Several authors support the use of PERT post pancreatic cancer surgery due to the level of exocrine insufficiency found in their studies (Tran et al 2008; Matsumoto & Traverso 2006; Ohtsuka et al 2001; Sato et al 1998).
- No studies found advocating specific doses of PERT.

# Summary of evidence

- National guidelines and RCT support the use of PERT in pancreatic cancer.
- Lack of studies, specific to pancreatic cancer, investigating specific dosage.
- Some review articles available describing current practice of authors working in this field.

# Discussion points

- Should all pancreatic cancer patients receive PERT?
- Level of exocrine insufficiency in pancreatic cancer patients?
- Quality of life?
- Further research?

# Exocrine insufficiency in Pancreatic Cancer

<b>Author</b>	<b>% subjects exocrine insufficient</b>
Matsumoto & Traverso 2006	68 %
Kato et al 1993	92 % (pre-op)
	80 % (post-op)
Ihse et al 1977	87 %

# Any questions





# References

- BRUNO, M.J., HAVERKORT, E.B., TIJSSEN, G.P., TYTGAT, G.N. and VAN LEEUWEN, D.J., 1998. Placebo controlled trial of enteric coated pancreatin microsphere treatment in patients with unresectable cancer of the pancreatic head region. *Gut*, 42(1), 92-96.
- BRUNO, M.J., HAVERKORT, E.B., TYTGAT, G.N. and VAN LEEUWEN, D.J., 1995. Maldigestion associated with exocrine pancreatic insufficiency: Implications of gastrointestinal physiology and properties of enzyme preparations for a cause-related and patient-tailored treatment. *American Journal of Gastroenterology*, 90(9), 1383-1393.
- DAMERLA, V., GOTLIEB, V., LARSON, H. and SAIF, M.W., 2008. Pancreatic enzyme supplementation in pancreatic cancer. *Journal of Supportive Oncology*, 6(8), 393-396.
- FERRONE, M., RAIMONDO, M. and SCOLAPIO, J.S., 2007. Pancreatic enzyme pharmacotherapy. *Pharmacotherapy*, 27(6), 910-920.
- IHSE I, ARNESJO B, KUGELBERG C, LILJA P. Intestinal activities of trypsin, lipase and phospholipase after a test meal. An elevation of 474 examinations. *Scandinavian Journal of Gastroenterology* 1977;12:663-668.
- KATO H, NAKAO A, KISHIMOTO W, NONAMI T, HARADA A, HAYAKAWA T, ET AL. 13C-labeled trioctanion breath test for exocrine pancreatic function test in patients after pancreatoduodenectomy. *American Journal of Gastroenterology* 1993;88(1):64-69.
- KELLER, J. and LAYER, P., 2005. Human pancreatic exocrine response to nutrients in health and disease. *Gut*, 54, vi1-vi28.
- MATSUMOTO, J. and TRAVERSO, L.W., 2006. Exocrine function following the whipple operation as assessed by stool elastase. *Journal of Gastrointestinal Surgery*, 10(6), 1225-1229.
- NAKAKURA, E.K. and WARREN, R.S., 2007. Palliative care for patients with advanced pancreatic and biliary cancers. *Surgical Oncology*, 16(4), 293-7.

# References cont.

- OHTSUKA, T., YAMAGUCHI, K., CHIJIWA, K. and TANAKA, M., 2001. Postoperative pancreatic exocrine function influences body weight maintenance after pylorus-preserving pancreatoduodenectomy. *American Journal of Surgery*, 182(5), 524-529.
- PEREZ, M.M., NEWCOMER, A.D., MOERTEL, C.G., GO, V.L. and DIMAGNO, E.P., 1983. Assessment of weight loss, food intake, fat metabolism, malabsorption and treatment of pancreatic insufficiency in pancreatic cancer. *Cancer*, 52(2), 346-352.
- SATO, N., YAMAGUCHI, K., YOKOHATA, K., SHIMIZU, S., MORISAKI, T., CHIJIWA, K. and TANAKA, M., 1998. Short-term and long-term pancreatic exocrine and endocrine functions after pancreatectomy. *Digestive Diseases & Sciences*, 43(12), 2616-2621.
- SATO, N., YAMAGUCHI, K., YOKOHATA, K., SHIMIZU, S., NOSHIRO, H., MIZUMOTO, K., CHIJIWA, K. and TANAKA, M., 1998. Changes in pancreatic function after pancreatoduodenectomy. *American Journal of Surgery*, 176(1), 59-61.
- SMITH, B., 2008. The use of pancreatic enzyme replacement therapy in cancer. *Oncology Nutrition Connection*, 16(3), 11-15.
- TRAN, T.C., VAN'T HOF, G., KAZEMIER, G., HOP, W.C., PEK, C., VAN TOORENENBERGEN, A.W., VAN DEKKEN, H. and VAN EIJCK, C.H., 2008. Pancreatic fibrosis correlates with exocrine pancreatic insufficiency after pancreatoduodenectomy. *Digestive Surgery*, 25(4), 311-318.
- GUIDELINES FOR THE MANAGEMENT OF PATIENTS WITH PANCREATIC CANCER PERIAMPULLARY AND AMPULLARY CARCINOMAS. *Gut* 2005. Pancreatic Section of the British Society of Gastroenterology, Pancreatic Society of Great Britain and Ireland, Royal College of Pathologists, Special Interest Group for Gastro-Intestinal Radiology.