

Review: Antibiotic prophylaxis of pancreatic necrosis in acute pancreatitis reduces mortality and sepsis

Villatoro E, Larvin M, Bassi C. Antibiotic therapy for prophylaxis against infection of pancreatic necrosis in acute pancreatitis. *Cochrane Database Syst Rev.* 2004;(2):CD002941.

QUESTION

In patients with severe acute pancreatitis who have developed pancreatic necrosis, what is the effectiveness of prophylactic antibiotic therapy?

DATA SOURCES

Published and unpublished studies in any language were identified by searching MEDLINE (1966 to June 2003), EMBASE/Excerpta Medica (1980 to June 2003), CINAHL (1982 to June 2003), the Cochrane Library (Issue 2, 2003), lists of conference abstracts, and bibliographies of relevant studies; and by contacting experts.

STUDY SELECTION AND ASSESSMENT

Studies were selected if they were randomized controlled trials (RCTs) that compared prophylactic antibiotic therapy for preventing infection of pancreatic necrosis within 7 days of the onset of the attack with placebo or best supportive care; included patients with severe acute pancreatitis associated with pancreatic necrosis; and measured all-cause mor-

tality and rates of microbiologically proven infected pancreatic necrosis. Study quality was assessed for allocation concealment, method of randomization, blinding, follow-up, and intention-to-treat analysis.

OUTCOMES

All-cause mortality, pancreatic sepsis, extrapancreatic infection, operative treatment, fungal infection, and length of hospital stay.

MAIN RESULTS

4 RCTs (218 patients, mean age range 41 to 52 y) were included. Antibiotic prophylaxis against infection of pancreatic necrosis in acute pancreatitis reduced all-cause mortality

and pancreatic sepsis (Table), but did not differ from supportive medical therapy for rates of extrapancreatic infection, operative treatment, or fungal infection; or length of hospital stay.

CONCLUSION

In patients with severe acute pancreatitis who have developed pancreatic necrosis, prophylactic antibiotic therapy reduces all-cause mortality and pancreatic sepsis.

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Antibiotic prophylaxis vs supportive medical therapy for infection of pancreatic necrosis in acute pancreatitis at 10 days to clinical recovery*

Outcomes	Weighted event rates		RRR (95% CI)	NNT (CI)
	Antibiotics	Supportive medical therapy		
All-cause mortality	6%	17%	65% (16 to 85)	10 (6 to 34)
Pancreatic sepsis	21%	32%	36% (1 to 58)	9 (5 to 100)

*Abbreviations defined in Glossary; weighted event rates, RRR, NNT, and CI calculated from data in article using a fixed-effects model.

COMMENTARY

Superinfection of pancreatic necrosis is the most common cause of death in patients with necrotizing pancreatitis, having a mortality of up to 40% (1). Infection typically sets in 2 to 3 weeks after the onset of severe pancreatitis, providing a window for giving prophylactic antibiotics to prevent this complication. Several studies addressing this topic have provided mixed results, however, and the risks associated with empirical broad-spectrum antibiotics, including fungal infection and the selection of resistant organisms, are well known, particularly in patients with serious illness in the intensive care setting.

The meta-analysis by Villatoro and colleagues included 4 RCTs involving 218 patients, all of whom had pancreatitis with pancreatic necrosis documented on computed tomography scan. Villatoro and colleagues' analysis offers fairly strong evidence for a reduction in the risk for superinfection of necrotic tissue and overall mortality in patients treated with prophylactic antibiotics. No difference was noted in the incidence of fungal infections, but information on the selection for resistant organisms was not available. None of the studies included in the meta-analysis were double-blinded, however, and the studies varied in case mix, choice and duration of antibiotics, and methodological quality. Also of note, since the publication of this systematic review, the first double-blind RCT studying this issue has been published, and it did not show a difference in rates of infected pancreatic necrosis between treatment and control groups (2).

Guidelines established by the American College of Gastroenterology and other organizations suggest that it may be reasonable to initiate prophylactic antibiotics in patients with pancreatic necrosis, a practice already taking place in many centers (3, 4). The review by Villatoro and colleagues gives us further evidence to support this practice, but definitive studies answering this question have yet to be done.

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