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[Intervention Review]

# Antibiotic therapy for prophylaxis against infection of pancreatic necrosis in acute pancreatitis

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## ABSTRACT

### Background

Pancreatic necrosis may complicate severe acute pancreatitis, and is detectable by computed tomography (CT). If it becomes infected mortality increases, but the use of prophylactic antibiotics raises concerns about antibiotic resistance and fungal infection.

### Objectives

To determine the efficacy and safety of prophylactic antibiotics in acute pancreatitis complicated by CT proven pancreatic necrosis.

### Search methods

Searches were updated in November 2008, in *The Cochrane Library* (Issue 2, 2008), MEDLINE, EMBASE, and CINAHL. Conference proceedings and references from found articles were also searched.

### Selection criteria

Randomised controlled trials (RCTs) comparing antibiotics versus placebo in acute pancreatitis with CT proven necrosis.

### Data collection and analysis

Primary outcomes were mortality and pancreatic infection rates. Secondary end-points included non pancreatic infection, all sites infection, operative rates, fungal infections, and antibiotic resistance. Subgroup analyses were performed for antibiotic regimen (beta-lactam, quinolone, and imipenem).

### Main results

Seven evaluable studies randomised 404 patients. There was no statistically significant effect on reduction of mortality with therapy: 8.4% versus controls 14.4%, and infected pancreatic necrosis rates: 19.7% versus controls 24.4%. Non-pancreatic infection rates and the incidence of overall infections were not significantly reduced with antibiotics: 23.7% versus 36%; 37.5% versus 51.9% respectively. Operative treatment and fungal infections were not significantly different. Insufficient data were provided concerning antibiotic resistance.

With beta-lactam antibiotic prophylaxis there was less mortality (9.4% treatment, 15% controls), and less infected pancreatic necrosis (16.8% treatment group, 24.2% controls) but this was not statistically significant. The incidence of non-pancreatic infections was non-significantly different (21% versus 32.5%), as was the incidence of overall infections (34.4% versus 52.8%), and operative treatment

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rates. No significant differences were seen with quinolone plus imidazole in any of the end points measured. Imipenem on its own showed no difference in the incidence of mortality, but there was a significant reduction in the rate of pancreatic infection ( $p=0.02$ ; RR 0.34, 95% CI 0.13 to 0.84).

### **Authors' conclusions**

No benefit of antibiotics in preventing infection of pancreatic necrosis or mortality was found, except for when imipenem (a beta-lactam) was considered on its own, where a significant decrease in pancreatic infection was found. None of the studies included in this review were adequately powered. Further better designed studies are needed if the use of antibiotic prophylaxis is to be recommended.

## **PLAIN LANGUAGE SUMMARY**

### **Use of antibiotics to prevent infection of dead pancreatic tissue in acute pancreatitis**

Acute pancreatitis is the inflammation of the pancreas, a serious emergency with no specific treatment. The pancreas, a digestive gland, can become inflamed for many reasons, but mainly as a complication from gallstones or excess alcohol intake. If severe, the pancreas may lose its blood supply, a complication called pancreatic necrosis that can be detected by computed tomography (CT) scanning. Death can occur either early in the disease process in association with uncontrolled inflammatory responses, causing multiple organ-system failure (MOSF), or late when the necrotic tissue becomes infected, which might necessitate major surgery to remove the infection, with the risk of death rising from 10% to over 40%. Antibiotics may prevent later infection and reduce the risk of death, but could also encourage bacterial antibiotic resistance and fungal infections. Controlled trials looking at the value of using prophylactic antibiotics have produced conflicting results.

This review aims to determine the effectiveness and safety of prophylactic antibiotics in CT-proven necrotising acute pancreatitis. A previous version published in 2006 suggested a survival advantage overall, and a decrease in pancreatic infections for some types of antibiotic therapy (beta-lactam antibiotics). Since that review, two further studies have been published: both were double-blinded, randomised, clinical trials (RCTs). These studies have now been included and our conclusions have changed as a result.

In the current review, data were found and analysed from 7 trials involving 404 patients randomly allocated to receive antibiotics or placebo. Although death occurred less after antibiotics (8.4%) than placebo (14.4%), as did infected pancreatic necrosis (19.7% versus 24.4%) and other infections (23.7% versus 36%), the differences were not statistically significant and so genuine benefit cannot be confirmed. There were no major problems with antibiotic resistance, and fungal infections were similar (3.9% versus 5%). The quality of studies was variable and only two were 'blinded', whereby investigators and patients were unaware of which treatment patients received. Many different regimens were used, and of the two main types of antibiotics used, a beta-lactam appeared to work better. Only one type of antibiotic (imipenem) was considered on its own, showing a significant decrease in infection of the pancreatic necrosis.

Although we cannot confirm benefit from the use of prophylactic antibiotics in this condition, consistent trends towards a beneficial effect nevertheless remain. Further, better designed studies, ideally with beta-lactam antibiotics, are required.