Meta-analysis of prophylactic parenteral antibiotic use in acute necrotizing pancreatitis

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Key words: acute necrotizing pancreatitis; infected necrosis; antibiotic prophylaxis; metaanalysis.

Summary. Background. Acute pancreatitis is a potentially serious condition. It carries an overall mortality rate of 10–15%. Infectious complications account for approximately 80% of deaths from acute pancreatitis, and the question arises whether or not prophylactic antibiotics are useful in the prevention of these complications. Therefore, we performed an evidence-based analysis to assess the effect of available prophylactic antimicrobial treatment on the development of infected necrosis and sepsis, need for surgery, and mortality.

Methods. A comprehensive PubMed search was performed evaluating the value of prophylactic administration of parenteral antibiotics in patients with acute necrotizing pancreatitis. Only articles published in English language between January 1990 and May 2006 were included. The search strategy initially generated 692 articles related to antibiotics in the treatment of acute pancreatitis. This number was reduced to 97 publications related to clinical trials on the same topic. Finally, 10 randomized clinical trials concerning prophylactic parenteral antibiotics in patients with acute necrotizing pancreatitis were identified. We have performed a meta-analysis using the random-effects model to assess the impact of prophylactic antibiotics on development of infected pancreatic necrosis and sepsis, need for surgery, and overall mortality.

Results. Patients with necrotizing acute pancreatitis should receive effective antibiotic prophylaxis (i.e., carbapenems intravenously) to decrease the risk of infected necrosis and sepsis and need of surgery.

Conclusions. While providing new insights into key aspects of antibiotic prophylaxis, this evidence-based analysis highlights the need for further clinical trials regarding the indications for antibiotic prophylaxis.

Background

Acute pancreatitis is a potentially serious condition. Its incidence varies from 5 to 80 cases per 100 000 inhabitants per year, and it carries an overall mortality rate of 10-15% (1, 2). However, severity of the disease varies widely, ranging from mild and self-limiting to severe life-threatening disease, and most patients die from severe disease. Mortality rate approaches 40% in this group (3, 4). Infection occurs in 30–40% of patients who have over 30% necrosis of the pancreas. Furthermore, secondary pancreatic infection accounts for approximately 80% of deaths from acute pancreatitis, and the question arises whether or not prophylactic antibiotics are useful in the prevention of these complications (5–7).

The development of secondary infection, usually between the third and the fifth week of the disease, has now emerged as the principal determinant of survival. Although the mechanisms of bacterial contamination are still debated, experimental and clinical data suggest that translocation of microorganisms from the gastrointestinal tract to the pancreas is probable as colonization by gut pathogens often precedes the infection. Consequently, interest has focused on the identification of pancreatic necrosis and the potential benefits of prophylactic treatment with antibiotics to prevent secondary infection of pancreatic necrosis. The management of acute necrotizing pancreatitis (ANP) is still based on speculative and unproven paradigms in many centers. Therefore, we performed an evidencebased analysis to assess the effect of available prophylactic antimicrobial treatment on the development of infected necrosis and sepsis, need for surgery, and mortality.

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Materials and methods Literature search and study design

Using the PubMed system (service of the US National Library of Medicine that includes citations from MEDLINE and other life science journals for biomedical articles), we conducted a comprehensive literature search for randomized controlled trials assessing the value of antibiotic prophylaxis in ANP. Keywords for the search were acute pancreatitis, acute necrotizing pancreatitis, antibiotics and antibiotic prophylaxis, clinical trial (keyword and text word). Only articles published in English language between January 1990 and May 2006 were included. Dual publications were excluded. To be included in the meta-analysis, each article had to contain information about the diagnosis and verification of ANP, to specify antibiotic used for prophylaxis and comparator used in the control group. Rates of local pancreatic infections, sepsis, need for surgery, and mortality in each treatment arm of the individual trials were noted. Reported mean rates of pancreatic infection, sepsis, and mortality were used as a control for studies where two different prophylactic antibiotic regimens were compared (8). We performed meta-analyses to assess the overall effect of antibiotic prophylaxis and to compare different schemes of prophylactic antimicrobial treatment in patients with ANP.

Statistical analysis

A meta-analysis integrates the quantitative findings from separate but similar studies and provides a numerical estimate of the overall effect of interest.

All meta-analyses were performed on studies that compared two groups with respect to a dichotomous endpoint (like mortality or development of sepsis). Thus, each study provides estimates of two proportions in each group (odds ratio, relative risk, etc.). The goal was to obtain global estimates of these proportions and to test whether they differ significantly. Global estimate of a proportion can be obtained by simply pooling together the data of each study. However, a test for significance cannot be applied to such pooled data, as these studies are heterogeneous with respect to study population and treatment protocols. Therefore, individual trials were pooled, and the overall rates of pancreatic infection, sepsis, surgery, and mortality, together with their 95% confidence intervals (CI), were calculated for each treatment arm. Under the fixedeffects model, it is assumed that all studies come from a common population, and that the effect size (relative risk, odds ratio, etc.) is not significantly different among the different trials. This assumption was tested by the

"heterogeneity test" using the Cochran Q statistics. We considered that in our case, the random-effects model (DerSimonian and Laird method) may be more appropriate to use since it takes into account both the random variation within the studies and the variation among different studies, especially because in some cases the heterogeneity test yielded a low P value, and the mean I^2 (inconsistency) value was 29.65±16.75 in our study. The later findings indicated that the fixedeffects model might be invalid. Indeed, the randomeffects model tends to give a more conservative estimate (*i.e.* with wider confidence interval), but the results from the two models usually agree well. We used the standard χ^2 methodology to test whether odds ratio significantly differed from value 1. If the value 1 was not within the 95% CI, then the odds ratio was considered statistically significant at the 5% level (P<0.05). Publication bias was assessed visually using a funnel plot and statistically by means of a regression asymmetry test (Egger's test) and a rank correlation test (Begg's test) (9, 10). No evidence of publication bias was found.

Results

Infection of pancreatic necrosis with consecutive sepsis belongs to the most serious complications of severe AP with a high mortality rate (11). Although the prevention of this complication by antibiotic prophylaxis is believed to decrease mortality, the actual benefit of antibiotic prophylaxis is controversial (12). Pancreatic necrosis is best assessed by contrast-enhanced computed tomography (CT) scan; therefore, only series with CT-proven pancreatic necrosis were included in our meta-analysis (13, 14). The search strategy initially generated 692 articles related to antibiotics in the treatment of acute pancreatitis. This number was reduced to 97 publications related to clinical trials on the same topic. Finally, 12 randomized clinical trials concerning prophylactic antibiotics in patients with ANP were identified.

Golub *et al.* included all studies on antibiotic prophylaxis published from 1966 to 1997 into a metaanalysis (15). Early studies using penicillins were separately evaluated and did not show any beneficial effect in this meta-analysis. Moreover, penicillins are known to have very poor penetration into pancreatic tissue; therefore, we excluded these studies from further analysis (16). Sharma *et al.* meta-analyzed three trials and found significantly reduced risks of sepsis and mortality (17). A meta-analysis by Bassi *et al.* also showed a significant decrease in the incidence of infected necrosis and pancreatic abscesses during

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| Clinical study | Treatment groups | u | Inclusion criteria | NdI | Surgery | Sepsis | Mortality |
|---------------------------------------|----------------------------------------------------------------------|----------|--------------------------------------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|
| Pederzoli et al., 1993 (28) | Imipenem (14 days) Control | 41 33 | CT-proven pancreatic necrosis | 5/41 (12.2%) 10/33 (30.3%) | 12/41 (29.3%) 11/33 (33.3%) | 11/41 (26.8%) 26/33 (78.8%) | 3/41 (7.3%) 4/33 (12.0%) |
| Sainio <i>et al.</i> , 1995 (29) | Cefuroxime (14 days) Control | 30 30 | CT-proven pancreatic necrosis CRP>120 mg/L | 9/30 (30.0%) 12/30 (40.0%) | 7/30 (23.3%) 14/30 (46.6%) | 4/30(13.3%) 8/30(26.6%) | 1/30 (3.3%) 7/30 (23.3%) |
| Delcenserie et al., 1996 (23) | Ceftazidime (10 days)* Control | 11 12 | CT-proven pancreatic necrosis | 0/11 (0.0%) 3/12 (25.0%) | Ι | 0/11 (0.0%) 7/12 (58.3%) | 1/11 (9.1%) 3/12 (25.0%) |
| Schwarz et al., 1997 (30) | Oflox + Metro (prophylactic)** Oflox + Metro (on demand >10 days) | 13 13 | CT-proven pancreatic necrosis | 8/13 (62.0%) 7/13 (54.0%) | I | 4/13 (31.0%) 6/13 (46.0%) | 0/13 (0.0%) 2/13 (15.0%) |
| Bassi et al., 1998 (22) | Pefloxacin (14 days) Imipenem (14 days) | 30 30 | CT-proven pancreatic necrosis (>50% of pancreatic volume) | 10/30(34.0%) 3/30(10.0%) | Ι | 13/30 (44.0%) 6/30 (20.0%) | 7/30 (24.0%) 3/30 (10.0%) |
| Takeda <i>et al.</i> , 2000 (20) | Imipenem + protease inhibitor *** | 156 | CT-proven pancreatic necrosis | 20/156(12.8%) | Ι | Ι | 29/156(18.6%) |
| Nordback et al., 2001 (27) | Imipenem (prophylactic) Imipenem (on demand) | 25 33 | CT-proven pancreatic necrosis CRP>150 mg/L | 2/25 (8.0%) 14/33 (42.0%) | 2/25 (8.0%) 14/33 (42.0%) | Ι | 2/25 (8.0%) 5/33 (15.0%) |
| Manes <i>et al.</i> , 2003 (25) | Meropenem (>14 days) Imipenem (>14 days) | 88 88 | CT-proven pancreatic necrosis | 10/88 (11.4%) 12/88 (13.6%) | 15/88 (17.0%) 16/88 (18.2%) | 19/88 (21.6%) 21/88 (23.9%) | 12/88 (13.6%) 10/88 (11.4%) |
| Isenmann <i>et al.</i> , 2004 (24) | Cipro + Metro (14 days) **** Placebo | 37 33 | CT-proven pancreatic necrosis or CRP>150 mg/L | 7/37 (18.9%) 5/33 (15.2%) | 8/37 (21.6%) 5/33 (15.2%) | Ι | 3/37 (8.1%) 3/33 (9.1%) |
| Maravi-Poma <i>et al.</i> , 2004 (26) | lmipenem/cilastatin (14 days) lmipenem/cilastatin (>14 days) | 46 46 | CT-proven pancreatic necrosis SAP | 13/46(28.0%) 14/46(30.4%) | I | 5/46(11.0%) 7/46(15.0%) | 9/46 (19.6%) 8/46 (17.4%) |
| * Ceftazidime + amikacin + m | ietronidazole; **ofloxacin + metronidazol | e; ** | *protease inhibitor = nafamostat me | ssilate, gabexate | mesilate, or uri | nastatin; | |

CT - computed tomography; CRP - C-reactive protein; SAP - severe acute pancreatitis; IPN - infectious pancreatic necrosis.

**** ciprofloxacin + metronidazole; "-" - not reported in original publication; n - number of patients in each group.

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severe acute pancreatitis (18). The trial by Luiten *et al.* was excluded from analysis since enteral (oral and rectal) antibiotics were used to achieve intestinal decontamination in their study (19). This trial showed less infected pancreatic necrosis without a difference in mortality rate. Other important study carried out by Takeda *et al.* in Japan was included into our meta-analysis since it provided data on the use of continuous regional arterial infusion of carbapenems and/or protease inhibitors (*i.e.* gabexate mesilate) (20). However, the overall effect was presumably produced by parenteral administration of antibiotics, since recent meta-analysis defined protease inhibitors to have no effect on outcome in patients with severe acute pancreatitis (21).

Based on our inclusion criteria and on the results of earlier publications, we have selected a total of 10 randomized or randomized controlled studies for the new meta-analysis (Table 1) (20, 22–30). There were 1279 patients included in the meta-analysis, of whom 641 received prophylactic antibiotics and 638 were allocated to control group.

Primary outcomes

Infected necrosis

Secondary infection of necrotic tissue was reported in all the trials. Three hundred twenty-four patients suffered from infected necrosis: 113 in the prophylactic antibiotic group and 211 in the control group. Overall, antibiotic prophylaxis was associated with a significant reduction in the risk of occurrence of infected necrosis (RR=0.57, 95% CI 0.418-0.784; P=0.0005). Forest plot of odds ratio (95% CI) for occurrence of infected pancreas necrosis is represented in Fig. 1. There was no significant heterogeneity among studies (Q=20.68; df=12; P=0.06) (Fig. 1). When stratified by the type of prophylactic antibiotic (carbapenems vs. others), there was no significant reduction in infected pancreatic necrosis rate in the group of patients treated with fluoroquinolones or cephalosporins (RR=0.96, 95% CI 0.662-1.388; P=0.824) (Fig. 1, Table 2). On the contrary, carbapenems (i.e., imipenem, meropenem) significantly reduced the incidence of infected pancreatic necrosis (RR=0.45, 95% CI 0.325-0.630; P<0.0001) (Fig. 1, Table 2). There was no significant heterogeneity in carbapenem studies (Q=12.06; df=7; P=0.098) or in studies with other prophylactic antibiotic (Q=2.67; df=4; P=0.613).

Mortality

Mortality rates were reported in all the trials. Two hundred nine patients died: 88 in the prophylactic antibiotic group and 121 in the control group. The administration of prophylactic antibiotics in general was associated with a significant reduction in mortality rate (RR=0.76, 95% CI 0.586–0.976; P=0.032). Forest plot of odds ratio (95% CI) for mortality rate is shown in Fig. 2. There was no significant heterogeneity among



Fig. 1. Forest plot of odds ratio (95% CI) for infected pancreatic necrosis

studies (Q=7.56; df=12; P=0.818) (Fig. 2). However, when stratified by type of antibiotic (carbapenems *vs.* other antibiotics), the administration of neither carbapenems (RR=0.77, 95% CI 0.583–1.009; P=0.058) nor

other prophylactic antibiotics (RR=0.62, 95% CI 0.271–1.399; P=0.247) resulted in a significant reduction in mortality rate (Fig. 2, Table 2). There was no significant heterogeneity either in carbapenem



Fig. 2. Forest plot of odds ratio (95% CI) for mortality

| Table 2. | Comparison | of carba | penems | and | other | antibiotics | in | treatment |
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| Antibiotic | Relative risk | 95% CI | χ^{2} (df=1) | Р | Significance |
|----------------------------------------------------------------------------------------------------------------|-------------------------|-------------------------------------------|------------------------|----------------------------|--------------|
| Development of infected pancreas necrosis Carbapenems Other i/v antibiotics Total (random effects) | 0.452 0.958 0.572 | 0.325–0.630 0.662–1.388 0.418–0.784 | 21.98 0.05 12.05 | P<0.01 P=0.82 P<0.01 | n.s. |
| Need for surgery Carbapenems Other i/v antibiotics Total (random effects) | 0.509 0.797 0.566 | 0.331-0.781 0.286-2.223 0.384-0.833 | 9.55 0.18 8.30 | P<0.01 P=0.67 P<0.01 | n.s. |
| Prevalence of sepsis Carbapenems Other i/v antibiotics Total (random effects) | 0.376 0.634 0.423 | 0.299–0.474 0.358–1.120 0.327–0.548 | 68.98 2.46 42.55 | P<0.01 P=0.12 P<0.01 | n.s. |
| Mortality Carbapenems Other i/v antibiotics Total (random effects) | 0.767 0.616 0.756 | 0.583–1.009 0.271–1.399 0.586–0.976 | 3.59 1.33 4.60 | P=0.06 P=0.25 P=0.03 | n.s. n.s. |

n.s. - insignificant effect.

studies (Q=2.86; df=7; P=0.898) or in other prophylactic antibiotic studies (Q=4.87; df=4; P=0.300).

Secondary outcomes

Need for surgery

Data regarding the need for surgical intervention for the management of ANP were available from five studies. One hundred sixty-seven patients underwent surgery: 59 in the group with antibiotic prophylaxis and 108 in the control group. Treatment with antibiotics was associated with a significant reduction in the need for surgery (RR=0.57, 95% CI 0.384–0.833; P=0.004). Forest plot of odds ratio (95% CI) for the need for surgery is represented in Fig. 3. There was no significant heterogeneity among studies (Q=8.77; df=5; P=0.118) (Fig. 3). When stratified by type of the antibiotics (carbapenems vs. other prophylactic antibiotics), there was no reduction in the need for surgery in "other" antibiotic group (RR=0.80, 95% CI 0.286-2.223; P=0.666) (Fig. 3, Table 2), whereas the administration of carbapenems demonstrated a significant reduction in the need for surgery (RR=0.51, 95%) CI 0.331–0.781; P<0.01) (Fig. 3, Table 2). There was no significant heterogeneity either in carbapenem studies (Q=4.74; df=3; P=0.192) or in other prophylactic antibiotic studies (Q=2.66; df=1; P=0.103).

Incidence of sepsis

Nonpancreatic infections include generalized infection, infection of the respiratory and urinary systems, and those of unknown origin. In our analysis, we examined only prevalence of generalized infection by toxin-producing bacteria confirmed by the results of a positive blood culture. Data regarding the prevalence of sepsis were available from seven studies. Three hundred seven patients had sepsis confirmed by the results of a positive blood culture: 90 in the treatment group and 217 in the control group. Overall antibiotic administration was associated with a significant reduction in the incidence of generalized sepsis (RR=0.42, 95% CI 0.327-0.548; P<0.0001). Forest plot of odds ratio (95% CI) for the incidence of sepsis is shown in Fig. 4. There was no significant heterogeneity among studies (Q=12.20; df=9; P=0.202) (Fig. 4). When stratified by type of the prophylactic antibiotic (carbapenems vs. other antibiotics), there was no positive effect in patients treated with "other" antibiotics (RR=0.63, 95% CI 0.358-1.120; P=0.117) (Fig. 4, Table 2). On the contrary, carbapenems significantly reduced the incidence of generalized sepsis (RR=0.38, 95% CI 0.299-0.474; P<0.0001) (Fig. 4, Table 2). There was no significant heterogeneity in either carbapenem studies (Q=3.14; df=5; P=0.677) or in



Fig. 3. Forest plot of odds ratio (95% CI) for need of surgery



Fig. 4. Forest plot of odds ratio (95% CI) for incidence of sepsis

other prophylactic antibiotic studies (Q=4.04; df=3; P=0.257).

Discussion

The present meta-analysis revealed significant reduction in the rates of infected necrosis, sepsis and need for surgical intervention, resulting from prophylactic use of parenteral antibiotics in patients with ANP (15, 17, 18, 21, 31). However, the following effect may be attributed to carbapenems only. Subgroup analysis demonstrated that prophylaxis with combination of fluoroquinolones or cephalosporins with metronidazole (or other alternative schemes) was not effective and did not influence any primary or secondary outcomes. The hypothesis that prophylactic antibiotics decrease morbidity in patients with ANP is partially supported by other recent meta-analysis, which showed that the length of hospital stay was significantly reduced in the antibiotic-treated group (32). Results of the present study are consistent with repots from other authors who found a statistically significant benefit of prophylactic antibiotic use for the prevention of infected necrosis, mortality, or both in patients with ANP. Experimental studies also showed that ciprofloxacin and imipenem significantly reduced the rate of infected necrosis, abscess formation, and mortality (33). Moreover, previous studies showed that antibiotics with greatest penetrance and bactericidal properties were carbapenems, fluoroquinolones, metronidazoles, and cephalosporins (12, 16, 18). Therefore, several published guidelines state that the use of prophylactic broad-spectrum antibiotics reduces the incidence of infected necrosis, but without any corresponding improvement in mortality (34, 35). Similar data were produced in our meta-analysis, which includes the most recent and the only randomized placebo-controlled double-blind clinical trial by Isenamann *et al.* (24).

Pooled data revealed decrease in mortality rates, associated with the use of prophylactic antibiotics (RR=0.76, 95% CI 0.586-0.976; P=0.032); however, the issue still remains controversial as subgroup analysis (carbapenems vs. other antibiotics) did not show any benefit in any of the groups. Several other studies also failed to demonstrate the reduction in mortality rates in patients receiving prophylactic antibiotics. This phenomenon could be attributed to several factors. First, none of the studies, included in this meta-analysis, distinguished among deaths occurring in the early or later phases of ANP. Mortality statistics therefore include a combination of deaths from infected necrosis and deaths from other causes during the early phase of the disease (systemic inflammatory response syndrome, multiorgan failure, etc.). There is also certain inconsistency among trials because of treatment variability, nutritional support, inclusion criteria, type and duration of antibiotic prophylaxis, and assessment of severity of the disease.

There are certain other limitations to this study as well as to majority published meta-analyses. The number of patients enrolled in each included study was relatively small, and the power to evaluate differences in clinical outcomes was not calculated. A large number of patients in the prophylactic antibiotic groups changed antibiotics during the course of the disease (e.g., 15 of the 41 in the study of Isenmann et al. and 20 of the 30 in that by Sainio et al.). There were a considerable number of patients in control groups in whom antibiotics were administered later during the course of the disease (e.g., 20 of the 35 in the study of Isenmann et al. and 23 of the 30 in that by Sainio et al.). There are some other issues that must be considered when evaluating antibiotic treatment for severe acute pancreatitis, which may have affected the data used in the present and previous meta-analyses. These include the optimal mode and timing of nutritional support, the timing of antibiotic administration, timing and indications for surgery, necessity of percutaneous drainage or laparoscopy, treatment of gallstone pancreatitis, and whether patients were monitored in an intensive care unit. On the other hand, inefficiency of antibiotics may be caused by the reduced uptake of antibiotics into the necrotic pancreatic tissue because of perfusion impairment and by delayed initiation of treatment (the average time between the onset of symptoms and admission to hospital is 2 to 5 days) (36). Currently

the timing of initiation of antimicrobial prophylaxis might be reasonably based on early markers of pancreatic necrosis (37). Moreover, consideration of the potential value of early markers of secondary pancreatic infection may better delineate the subgroup of patients who may benefit at most from timely administration of antibiotics (38). Based on our findings, we suggest that antibiotics with established efficacy in necrotic pancreatic tissues should be started in all patients in whom necrosis of the pancreas is proven or anticipated. However, further studies are required to provide adequate data to answer many questions and to define the role of antibiotic prophylaxis in patients with acute necrotizing pancreatitis.

Conclusions

Antibiotic prophylaxis is superior to antibiotic treatment on demand in acute necrotizing pancreatitis. Patients with proven pancreatic necrosis should receive antibiotic prophylaxis using carbapenems, since the combination of fluoroquinolones or cephalosporins with metronidazole was shown to be ineffective. However, the issue of antibiotics in acute necrotizing pancreatitis remains highly controversial and is a matter for further investigations and discussions. This evidence-based analysis highlights the need for further prospective clinical trials regarding the indications and timing of antibiotic prophylaxis in patients with acute necrotizing pancreatitis.

Metaanalizė: profilaktinis parenterinių antibiotikų vartojimas sergant ūminiu nekroziniu pankreatitu

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Raktažodžiai: ūminis nekrozinis pankreatitas, infekuota kasos nekrozė, profilaktinis antibiotikų vartojimas, metaanalizė.

Santrauka. Ūminis pankreatitas yra grėsminga būklė. Mirštamumas nuo šios ligos yra apie 10–15 proc. Apie 80 proc. sergančiųjų ūminiu pankreatitu mirčių yra susijusios su įvairiomis infekcinėmis komplikacijomis, todėl dabar plačiai diskutuojama, ar profilaktinis antibiotikų vartojimas turi įtakos infekcinių komplikacijų dažniui bei ligos baigčiai.

Mes atlikome išsamią duomenų paiešką "PubMed" sistemoje apie profilaktinio antibiotikų vartojimo reikšmę ūminiam pankreatitui gydyti. Statistinei analizei buvo naudotasi straipsniais, publikuotais anglų kalba nuo 1990 metų sausio iki 2006 metų gegužės mėn. Remiantis šia paieškos strategija, atrinkti 692 straipsniai, kuriuose analizuojami įvairūs antibakterinių medikamentų vartojimo, gydant ūminį pankreatitą, aspektai. Iš 692 buvo atrinkti 97 straipsniai, kuriuose aprašomi įvairūs klinikiniai tyrimai, iš jų statistinei analizei panaudota tik 10 straipsnių, kuriuose aprašomi atsitiktinių imčių klinikiniai tyrimai, kurių metu buvo įvertintas profilaktinis sergančiųjų ūminiu nekroziniu pankreatitu gydymas antibiotikais. Naudodami atsitiktinių veiksnių modelį, mes atlikome šių straipsnių metaanalizę, siekdami gauti moksliniais įrodymais pagrįstą įvertinimą, kiek profilaktinis antibiotikų vartojimas mažina infekuotos kasos nekrozės bei sepsio riziką, chirurginio gydymo poreikį bei bendrąjį mirštamumą. Pacientams, sergantiems ūminiu nekroziniu pankreatitu, profilaktiškai turėtų būti skiriama veiksmingų parenterinių antibiotikų (pvz., karbapenemų), nes jie mažina infekuotos kasos nekrozės ir sepsio riziką, taip pat chirurginio gydymo poreikį. Tačiau ši sisteminė analizė parodė, jog dar reikia atlikti atsitiktinių imčių kontroliuojamųjų klinikinių tyrimų siekiant geriau įvertinti profilaktinio gydymo antibiotikais svarbą bei nustatyti tikslias indikacijas antibakterinių medikamentų vartojimui gydant ūminį nekrozinį pankreatitą.

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Received 18 July 2006, accepted 5 April 2007 Straipsnis gautas 2006 07 18, priimtas 2007 04 05

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