

The Utilization of Antibiotics in the Management of Acute Pancreatitis – Experience from One Transitional Country University Hospital

Srećko Marušić, Mario Sičaja, Milan Kujundžić, Marko Banić, Ozren Jakšić and Hrvoje Vražić

Department of Internal Medicine, University Hospital »Dubrava«, Zagreb, Croatia

ABSTRACT

The aim of the study was to analyze the evidence-based use of antibiotic therapy in the treatment of acute pancreatitis and to identify factors influencing the introduction of antibiotic therapy in the setting of transitional country clinical hospital. This retrospective study was conducted at Department of Internal Medicine at University Hospital Dubrava in Zagreb, Croatia. Data were collected from hospital records of patients treated for acute pancreatitis from January 1st, 2005 till December 31st, 2005. Data collected from patients' histories were compared with indications for antibiotic treatment and antibiotics with demonstrated therapeutic efficacy in acute pancreatitis which were obtained from published literature. Logistic regression was used to identify factors with a significant impact on deciding on the introduction of antibiotic therapy, and multivariate analysis was used to identify factors with a significant impact on the cost of treatment. Statistical significance was set at $p < 0.05$. Antibiotic therapy was used in 67.7% of patients with acute pancreatitis. Combination of amoxicillin plus clavulanic acid was most frequently administered, either as monotherapy or in combination with metronidazole and/or gentamicin (37.3%), followed by cefuroxime (32.8%) and cefoperazone (26.9%). The choice of antibiotic was appropriate in 35.8% of study patients; however in 29.9% of patients who were administered antibiotics had no indication for this therapy; and 46.9% of patients who had indications for receiving antibiotic therapy didn't receive it. In the groups of patients treated with antibiotics, the cost of treatment was significantly higher compared to groups of patients who were not treated with antibiotics ($p = 0.0035$; $p = 0.0026$). In addition to antibiotic therapy, the cost of treatment was significantly influenced by the length of hospital stay and treatment at intensive care unit. The use of antibiotics in the setting of transitional country university hospital in patients with acute pancreatitis is not evidence-based. Decision on the introduction of antibiotic therapy is not based on objective parameters of disease severity or evidence of therapeutic efficacy of particular antibiotics. The cost of treatment is significantly increased by the use of antibiotic therapy.

Key words: pancreatitis, antibiotics, evidence-based medicine, Croatia, treatment costs

Introduction

Acute pancreatitis is a common disease with an increasing prevalence worldwide. It is estimated that 210,000 patients are hospitalized for acute pancreatitis per year in USA¹. In Great Britain, the incidence of acute pancreatitis was 21 per million in the mid-1970s, increasing to 242 per million by the mid-1980s. The cause of this growing tendency has not been fully clarified; however, it has been postulated to be due to the increasing alcohol intake and improved disease diagnosis².

In most cases, acute pancreatitis is a mild disease with a mortality rate less than 1%. However, 20% of pa-

tients develop a severe form of the disease with pancreatic necrosis. Infection of the pancreas as a major cause of mortality and morbidity occurs in 40–70% of patients with acute necrotizing pancreatitis. In these patients, mortality rises to 10% and 25–40% in case of sterile and infected pancreatic necrosis, respectively^{1,3}. Therefore, attempts to prevent infection and reduce mortality in patients with necrotizing pancreatitis are quite reasonable. The earliest studies published some 30 years ago regarding antibiotic prophylaxis in acute pancreatitis failed to demonstrate favourable effects of ampicillin on the course

of acute pancreatitis⁴. In 1993, Pederzoli *et al.* published results of a randomized clinical trial demonstrating imipenem to significantly reduce the incidence of septic complications in patients with acute pancreatitis, but with no effect on mortality⁵. Similar results have been reported by Røkke *et al.* in 2007⁶. Pancreatic concentration of imipenem is bactericidal for most bacteria causing infectious complications². In 2003, Manes *et al.* reported results of a randomized clinical trial demonstrating meropenem to be as efficacious as imipenem in patients with pancreatic necrosis⁷.

Because of their favourable pharmacokinetic profile, fluoroquinolones have been postulated to be effective in preventing infection in severe acute pancreatitis. In a controlled randomized clinical trial, pefloxacin proved to be less efficacious than imipenem in patients with acute necrotizing pancreatitis⁸. Results of a randomized double-blind clinical trial comparing a combination of ciprofloxacin and metronidazole with placebo in patients with necrotizing pancreatitis were published in 2004. There was no significant difference in the incidence of necrotic pancreatic tissue infection, morbidity and mortality⁹. »Sainio *et al.* reported results of their randomized clinical trial demonstrating cefuroxime to significantly reduce mortality in patients with necrotizing pancreatitis of alcohol aetiology as compared with placebo. Cefuroxime was chosen because the most common causes of sepsis were sensitive to it 10«.

According to the published therapeutic guidelines, the use of imipenem or cefuroxime is most commonly recommended for the treatment of patients with acute pancreatitis^{11–15}.

Antibiotic prophylaxis is not indicated in all patients with acute pancreatitis. First meta-analyses of prospective studies on the prophylactic effect of antibiotics on the course of acute pancreatitis suggest that antibiotic prophylaxis can reduce mortality and morbidity only in patients with severe form of the disease. This refers to patients with score ≥ 3 according to Ranson-Imrie criteria for assessment of the acute pancreatitis severity or with pancreatic necrosis verified by computed tomography (CT)^{4,15}. According to the results of the most recent meta-analysis the use of prophylactic antibiotics is severely challenged and the authors claim that antibiotics cannot reduce infected pancreatic necrosis and mortality in patients with acute necrotizing pancreatitis¹⁷. Nevertheless, majority of therapeutic guidelines recommend antibiotic prophylaxis in patients with severe acute pancreatitis^{10–14}. The risk of developing acute necrotizing pancreatitis can be assessed according to plasma concentration of C-reactive protein (CRP). The risk is low and antibiotic prophylaxis is not justified in patients with plasma CRP concentration lower than 110 mg/L¹⁸. In our country Croatia, which is still undergoing the process of transition there are no formal guidelines regarding the management of acute pancreatitis.

The aim of our study was to assess the rate of evidence-based usage of antibiotics in acute pancreatitis and to identify the factors that influence decision on the

introduction of antibiotic therapy in the setting of transitional country university hospital.

Methods

This retrospective study was conducted at Department of Internal Medicine, University Hospital Dubrava in Zagreb, Croatia. Data were collected from hospital records on patients of both genders treated for acute pancreatitis from January 1st 2005 till December 31st 2005.

Establishing the diagnosis of acute pancreatitis was defined by two criteria that had to be met: presence of abdominal pain; and serum amylase concentration increased at least threefold normal values.

Patients with other conditions requiring antibiotic therapy such as acute cholecystitis, cholangitis, pneumonia, urinary tract infection were not included. Data on patient age and gender, pancreatitis aetiology, length of hospital stay, cost of treatment, CRP concentration and disease outcome were collected for all study patients.

Disease severity was evaluated according to Ranson-Imrie criteria on admission and 48h of admission to hospital¹⁸. According to the severity of acute pancreatitis, patients were divided into three groups: mild (Ranson-Imrie criteria score < 3), moderate (Ranson-Imrie criteria score ≥ 3 to ≤ 5) and severe (Ranson-Imrie criteria score > 5).

During hospital stay, all patients underwent ultrasonography of the abdomen. When ultrasonography of the abdomen or clinical course of the disease raised suspicion of pancreatic necrosis, CT of the abdomen was obtained in order to confirm the diagnosis of necrotizing pancreatitis.

Data on antibiotics received during inpatient treatment were collected for all study patients.

Indications for the use of antibiotics were determined from literature data^{4,14–16}. Antibiotics were considered to be indicated if at least one of the following criteria was met: pancreatic necrosis verified by CT of the abdomen, Ranson-Imrie criteria score ≥ 3 and plasma CRP concentration > 110 mg/L.

According to literature data, imipenem, meropenem and cefuroxime were considered the antibiotics of choice^{5–7,12–15}.

Study patients were classified into four groups according to the presence of indications for antibiotic therapy and use of antibiotic therapy. The cost of treatment was compared between the groups of patients with indications for antibiotic therapy who were and were not administered antibiotics. The cost of treatment was also compared between the groups of patients without indications for antibiotic therapy who were and were not administered antibiotics.

Statistical analysis: Mann-Whitney U test was used to compare continuous variables and χ^2 analysis (or Fisher exact test) was used to analyze differences between categorical variables. Logistic regression was used to determine relative importance of factors with impact on the decision to introduce antibiotic therapy, while multi-

varate analyses of associations with the cost of treatment were assessed using multiple regression. Statistical significance was inferred at $p < 0.05$. The variables that did not follow normal distribution were logarithmized for logistic regression and multivariate analysis. Statistical analyses were done using Statistica for Windows, Version 5.5.

Results

The study included 99 patients. Data on patient age and gender, disease aetiology, length and cost of hospital stay, parameters of disease severity and disease outcome are shown in Table 1.

TABLE 1
DEMOGRAPHIC AND CLINICAL DATA OF STUDY PATIENTS – PATIENTS TREATED FOR ACUTE PANCREATITIS FROM JANUARY 1ST 2005 TILL DECEMBER 31ST 2005, DEPARTMENT OF INTERNAL MEDICINE, UNIVERSITY HOSPITAL DUBRAVA, ZAGREB, CROATIA

Number of patients	99
Gender	
Male	59 (59.6%)
Female	40 (40.4%)
Age, yrs (median, minimum-maximum)	61 (22–89)
Aetiology	
Gallstones	54 (54.5%)
Alcohol	27 (27.3%)
Alcohol + gallstones	4 (4.0%)
Triglycerides	2 (2.0%)
Post-ERCP	2 (2.0%)
Idiopathic	10 (10.1%)
Length of hospital stay, days (median, minimum-maximum)	11 (1–32)
Cost, EUR (median, minimum-maximum)	963 (187–4938)
Severity, Ranson-Imrie criteria	
Mild (0–2)	45 (45.5%)
Moderate (3–5)	47 (47.5%)
Severe (6–9)	7 (7.0%)
CRP, mg/L (median, minimum-maximum)	68.7 (0.6–422)
Death	6 (6.1%)

Out of 99 study patients, 67.7% were administered antibiotic therapy. Amoxicillin plus clavulanic acid was most frequently used, either as monotherapy or in combination with metronidazole and/or gentamicin, being received by 37.3% of study patients. Cefuroxime was administered as monotherapy or in combination with metronidazole and/or gentamicin in 32.8%, cefoperazone in 26.9%, and a carbapenem as monotherapy or in combination with metronidazole and/or gentamicin in 3% of study patients. Appropriate choice of antibiotics was recorded in 35.8% of patients.

Antibiotics were administered in 75% of patients with acute pancreatitis caused by gallstones or secondary to endoscopic retrograde cholangiopancreatography (ERCP). In this group, the leading antibiotic was cefoperazone (33.3%), followed by amoxicillin plus clavulanic acid and cefuroxime (31% each), and imipenem (4.7%) administered as monotherapy or in combination with metronidazole and/or gentamicin.

Antibiotics were received by 59% of patients with acute pancreatitis caused by excessive alcohol consumption. In this group, the leading antibiotic was amoxicillin plus clavulanic acid (50%), followed by cefuroxime (43.7%) and cefoperazone (6.3%) as monotherapy or in combination with metronidazole and/or gentamicin.

Antibiotic therapy was used in 56.3% of the remaining 16 patients. The leading antibiotic was amoxicillin with clavulanic acid (44.4%), followed by cefoperazone (33.3%) and cefuroxime (22.2%) as monotherapy or in combination with metronidazole and/or gentamicin (Table 2).

Indications for the use of antibiotics were present in 70.1% and absent in 29.9% of 67 patients administered antibiotic therapy. Indications for the use of antibiotics were present in 46.9% and absent in 53.1% of 32 patients that were not administered antibiotic therapy.

Logistic regression identified indication for CT of the abdomen as the only parameter showing a statistically significant correlation with the decision on antibiotic therapy introduction (Table 3). Comparison of patient groups with indications for antibiotic therapy showed the cost of treatment to be statistically significantly higher in the group of patients administered antibiotic

TABLE 2
CHOICE OF ANTIBIOTICS ACCORDING TO DISEASE AETIOLOGY – PATIENTS TREATED FOR ACUTE PANCREATITIS FROM JANUARY 1ST 2005 TILL DECEMBER 31ST 2005, DEPARTMENT OF INTERNAL MEDICINE, UNIVERSITY HOSPITAL DUBRAVA, ZAGREB, CROATIA

Antibiotic	Number of patients (n=67)	Choice of antibiotic according to disease aetiology		
		Alcohol (n=16)	Gallstones + post-ERCP (n=42)	Other (n=9)
Amoxicillin plus clavulanic acid*	37.3% (n=25)	50% (n=8)	31% (n=13)	44.4% (n=4)
Cefuroxime*	32.8% (n=22)	43.7% (n=7)	31% (n=13)	22.2% (n=2)
Cefoperazone*	26.9% (n=18)	6.3% (n=1)	33.3% (n=14)	33.3% (n=3)
Carbapenems (imipenem or meropenem)*	3% (n=2)	0%	4.7% (n=2)	0%

* monotherapy or combination with metronidazole and/or gentamicin

TABLE 3

LOGISTIC REGRESSION FOR THE USE OF ANTIBIOTICS – PATIENTS TREATED FOR ACUTE PANCREATITIS FROM JANUARY 1ST 2005 TILL DECEMBER 31ST 2005, DEPARTMENT OF INTERNAL MEDICINE, UNIVERSITY HOSPITAL DUBRAVA, ZAGREB, CROATIA

	OR (95%CI)	P
Gender	0.347 (0.11–1.091)	n.s.
Age	1.009 (0.971–1.048)	n.s.
Biliary aetiology + post-ERCP	2.16 (0.90–5.14)	n.s.
Alcohol etiology	0.60 (0.236–1.521)	n.s.
Ranson-Imrie criteria	1.188 (0.70–2.016)	n.s.
Leukocytosis >16000/mL	0.969 (0.211–4.441)	n.s.
Necrosis on ultrasonography	2.373 (0.206–27.39)	n.s.
Indication for CT scan	5.36 (1.45–19.83)	0.012
Treatment at ICU	2.445 (0.502–11.910)	n.s.
Serum CRP	1.147 (0.85–1.547)	n.s.
Serum amylases	1.00 (0.999–1.001)	n.s.
Serum LDH >400 IU/L	0.603 (0.148–2.46)	n.s.

n.s. – not significant

therapy than in those that did not receive it (Figure 1). Pancreatic necrosis was verified by CT of the abdomen in six patients from the group administered antibiotic therapy and none from the group without antibiotic therapy. As a severe course of the disease associated with a significant increase in the cost of treatment can be expected in patients with pancreatic necrosis verified by CT of the abdomen, these patients were excluded from comparison studies.

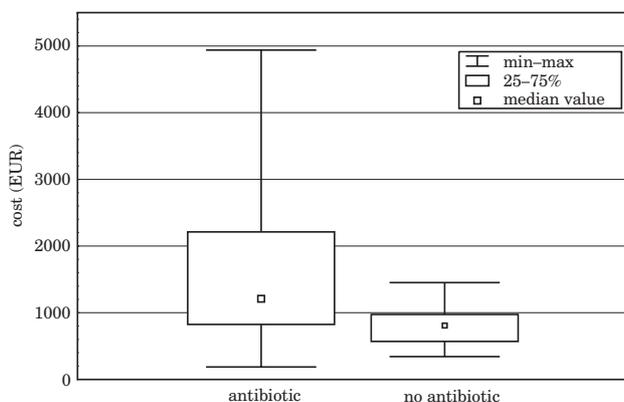


Fig. 1. Cost of treatment in patient groups with indications for antibiotic therapy.

Comparison of patient groups without indications for antibiotic therapy showed the cost of treatment to be statistically significantly higher in the group of patients administered antibiotic therapy than in those that did not receive it (Figure 2).

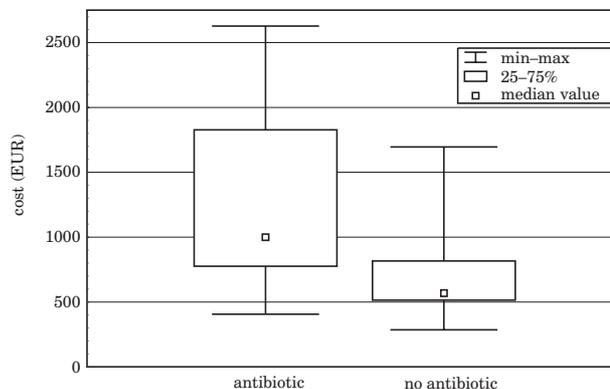


Fig. 2. Cost of treatment in patient groups without indications for antibiotic therapy.

Multivariate analysis identified the length of hospital stay, treatment at intensive care unit (ICU) and use of antibiotics as the parameters that statistically significantly influenced the cost of treatment (Table 4).

The length of hospital stay was longer and the proportion of patients treated at ICU greater in the groups of patients administered antibiotic therapy as compared with the groups of patients without antibiotic therapy, however, the difference did not reach statistical significance. Six patients died, all of them with indications for antibiotic therapy. Five of these six patients were administered antibiotics, whereas one patient did not receive antibiotic therapy. Mortality difference was not statistically significant.

TABLE 4

MULTIVARIATE MODEL FOR TREATMENT COST – PATIENTS TREATED FOR ACUTE PANCREATITIS FROM JANUARY 1ST 2005 TILL DECEMBER 31ST 2005, DEPARTMENT OF INTERNAL MEDICINE, UNIVERSITY HOSPITAL DUBRAVA, ZAGREB, CROATIA

	Regression coefficient	P
Hospital stay, days	100	<0.0001
Treatment at ICU	754	<0.0001
Antibiotic therapy	275	<0.008
CT scan	122	n.s.
Necrosis on US	153	n.s.
Ranson-Imrie criteria	18	n.s.
Age	-1.5	n.s.

Multiple $r = 0.90$; $F = 37.526$; $p < 0.0001$

Discussion

Study results showed that the majority of study patients (67.7%) were administered antibiotic therapy. Yet, an appropriate choice of antibiotics was recorded in only 35.8% of patients, whereas the rest of patients were administered antibiotics without evidence of therapeutic efficacy in acute pancreatitis.

Most patients (37.3%) received a combination of amoxicillin and clavulanic acid. This antibiotic has for years been the most widely prescribed and unjustifiably over-used antibiotic in Croatia, mainly due to intensive marketing factors and long-standing presence of the drug on the market. This has entailed prescribing of the antibiotic out of custom, also for indications that lack any evidence for its efficacy and in conditions that may require antibiotics of a considerably narrower antimicrobial spectrum.

Cefuroxime was the second leading antibiotic, administered in 32.8% of study patients. As cefuroxime is much less expensive than carbapenems and there is evidence for its therapeutic efficacy, it could be considered optimal antibiotic for the treatment of patients with acute pancreatitis in our circumstances. However, it should be preceded by comprehensive information on the most common agents causing infection in patients with acute pancreatitis and their sensitivity to cefuroxime.

The next most common antibiotic was cefoperazone, received by 26.9% of study patients. This antibiotic was most frequently used in patients with acute pancreatitis due to gallstones or secondary to ERCP. As cefoperazone is mostly excreted *via* biliary tract, in our hospital it has mostly been used in the management of patients with biliary tract infection. However, there is no evidence for therapeutic efficacy of cefoperazone in this indication to be superior to therapeutic efficacy of other, less toxic and less expensive beta-lactam antibiotics such as cefotaxime and ceftriaxone^{19–22}. Such a high utilization of cefoperazone is not justified, the more so as patients with clinical, radiographic or laboratory signs of biliary tract infection were not included in the study.

Only 3% of study patients were administered a carbapenem (imipenem or meropenem). While the percentage of these patients was definitely too low, the use of this group of antibiotics is not likely to be justified in all patients with indications for antibiotic prophylaxis because of the high price of carbapenems and the potential risk of bacterial resistance induction.

Interestingly enough, none of the study patients received ciprofloxacin. At our hospital, the utilization of this antibiotic has increased by 160% in the past five years, which will certainly have unfavourable effect on bacterial resistance (unpublished results).

A high proportion of study patients (29.9%) were administered antibiotics without strict indications. Such inappropriate use of antibiotics is associated with the unnecessary risk of side effects, superinfection, induction of bacterial resistance, and increased cost of treatment^{4,13,15}.

REFERENCES

1. SWAROOP VS, CHARI ST, CLAIN JE, JAMA, 291 (2004) 2865. —
2. STEINBERG W, TENNER S, N Engl J Med, 330 (1994) 1198. —
3. BARON TH, MORGAN DE, N Engl J Med, 340 (1999) 1412. —
4. GOLUB R, SIDDIQI F, POHL D, J Gastrointest Surg, 2 (1998) 496. —
5. PEDERZOLI P, BASSI C, VESENTINI S, CAMPEDELLI A, Surg Gynecol Obstet, 176 (1993) 480. —
6. RØKKE O, HARBITZ TB, LILJEDAL J, PETTE-

The use of antibiotics without strict indications resulted in unnecessary expenses of about 8460 EUR, i.e. an amount that would cover treatment cost for 15 patients with a mild form of acute pancreatitis requiring no antibiotic therapy, or for 7 patients with a severe form of acute pancreatitis requiring antibiotic therapy. In contrast, 46.9% of patients from the group without antibiotic therapy had indications for antibiotic prophylaxis. Although a more severe course of the disease could be expected in this group of patients, there was no statistically significant mortality difference from the group of patients administered antibiotic therapy.

Study results revealed the lack of any objective parameters on making indications for antibiotic therapy. Logistic regression identified the indication for CT of the abdomen as the only parameter showing statistically significant correlation with the introduction of antibiotic therapy. Antibiotic therapy appears to be initiated exclusively on the basis of clinician's subjective assessment of the disease severity, thus influencing further diagnostic work-up.

Comparison of patient groups according to the cost of treatment revealed it to be statistically significantly higher in the groups administered antibiotics than in those without this therapy. It is generally believed that CT scanning significantly increases the cost of treatment; however, it was not confirmed in the present study.

Conclusion

In conclusion, the use of antibiotics in observed population of acute pancreatitis patients in University Hospital Dubrava is not evidence-based. Neither parameters of the disease severity nor evidence for therapeutic efficacy of particular antibiotics are considered on making indications for the introduction of antibiotic therapy. Therefore, antibiotic prophylaxis is not used in a large proportion of patients with proper indications, while being used in many patients without such indications. Inappropriate choice of antibiotics and use of antibiotics lacking evidence of therapeutic efficacy in acute pancreatitis were recorded in most patients. The cost of treatment is significantly increased with the introduction of antibiotic therapy, which is another reason to invest additional efforts to turn to appropriate use of antibiotics, and to introduce antibiotic prophylaxis only when indicated. The management of patients with acute pancreatitis could be significantly improved by the introduction of therapeutic guidelines strictly defining indications for antibiotic prophylaxis applicable to the local settings.

- RSEN T, FETVEDT T, HEEN LØ et al., Scand J Gastroenterol, 42 (2007) 771. —
7. MANES G, RABITTI PG, MENCHISE A, RICCIO E, BALZANO A, UOMO G, Pancreas, 27 (2003) 79. —
8. BASSI C, FALCONI M, TALAMINI G, UOMO G, PAPACCIO G, DERVENIS C et al., Gastroenterology, 115 (1998) 1513. —
9. ISENMANN R, RUNZI M, KRON M, KAHL S, KRAUS D, JUNG N et al., Gastroenterology, 126 (2004) 997. —
10. SAINIO

V, KEMPPAINEN E, PUOLAKKAINEN P, TAAVITSAINEN M, KIVISARI L, VALTONEN V, Lancet 346 (1995) 663. — 11. UOMO G, JOP, 1 (suppl 3) (2000) 130. — 12. GLAZER G, MANN DV, Gut, 42 (Suppl 2) (1998) S1. — 13. Royal College of Surgeons in Ireland. Management of Acute pancreatitis Clinical Guidelines. November 2003. Available from: <http://www.muh.ie/ed/handbook/Abdominal/GI/PancreatitisGuidelines-RCSINov2005.pdf>, Accessed: 10.12.2007. — 14. UHL W, WARSHAW A, IMRIE C, BASSI C, MCKAY CJ, LANKISCH PG et al., Pancreatology 2 (2002) 565. — 15. UK Working Party on Acute Pancreatitis, Gut, 54 (Suppl 3) (2005) 1. — 16. DA SILVEIRA EB, BARKIN JS, Am J Gastroenterol, 97 (2002) 1557. — 17. BAI Y, GAO J, ZOU D, LI Z, Am J Gastroenterol,

103 (2008) 104. — 18. BARAUSKAS G, SVAGZDYS S, MALECKAS A, Medicina (Kaunas), 40 (2004) 135. — 19. GREENBERGER NJ, TOSKES PP. Acute and Chronic Pancreatitis. IN: BRAUNWALD E, FAUCI AS, KASPER DL, HAUSER SL, LONGO DL, JAMESON JL (Eds.), Harrison's Principles of Internal Medicine Fifteenth Edition. (The McGraw-Hill Companies Inc, USA, 2001). — 20. FRIEDLENDER J, MEYER P, MARTI MC, ROHNER A, Chemotherapy, 34 (Suppl 1) (1988) 30. — 21. MULLER EL, PITT HA, THOMPSON JE JR, DOTY JE, MANN LL, MANCHESTER B, Surg Gynecol Obstet, 165 (1987) 285. — 22. TRAGER GM, WHITE GW, ZIMELIS VM, BRYK DA, PANWALKER AP, Chemotherapy, 27 (1981) 34.

S. Marušić

Department of Internal Medicine, University Hospital »Dubrava«, Av. Gojka Šuška 6, 10000 Zagreb, Croatia
e-mail: srmariusic@inet.hr

UPOTREBA ANTIBIOTIKA U LIJEČENJU AKUTNOG PANKREATITISA – ISKUSTVO IZ JEDNE KLINIČKE BOLNICE ZEMLJE U TRANZICIJI

SAŽETAK

»Ciljevi ove studije uključuju analizu upotrebe antibiotika u liječenju akutnog pankreatitisa u kliničkoj bolnici tranzicijske zemlje, usporedbu s publiciranim smjernicama, uz identifikaciju čimbenika koji utječu na odabir i uvođenje antibiotskog liječenja.« Ova retrospektivna studija provedena je na Klinici za internu medicinu Kliničke bolnice »Dubrava«, Zagreb, Hrvatska. Podaci su sakupljeni iz bolničkih arhiva pacijenata koji su liječeni radi akutnog pankreatitisa u razdoblju od 1.1.2005. do 31.12.2005. Tako sakupljeni podaci su uspoređeni sa publiciranim smjernicama za liječenje akutnog pankreatitisa. Logička regresija korištena je sa ciljem identifikacije statistički značajnih čimbenika koji utječu na odluku o uvođenju antibiotske terapije, a multivarijantna analiza je korištena sa ciljem identifikacije čimbenika koji imaju utjecaj na cijenu liječenja. Statistička značajnost zadana je za $p < 0,05$. Antibiotici su korišteni u 67,7% pacijenata koji su liječeni radi akutnog pankreatitisa. Kombinacija amoksicilina i klavulanske kiseline je najčešće propisivani antibiotik, samostalno ili u kombinaciji sa metronidazolom i/ili gentamicinom (37,3%), slijedi cefuroksim (32,8%) i cefoperazon (26,9%). Izbor antibiotika bio je ispravan u 35,8% slučajeva, međutim u 29,9% slučajeva nije bilo indikacije za antibiotskim liječenjem. U skupini pacijenata koji su liječeni antibiotikom, cijena liječenja je bila značajno viša u odnosu na skupinu koja nije bila liječena antibiotikom ($p = 0,0035$; $p = 0,0026$). Cijena liječenja je također bila uvjetovana dužinom intrahospitalnog boravka i liječenjem u jedinici intenzivnog liječenja. Upotreba antibiotika u okruženju kliničke bolnice zemlje u tranziciji nije temeljena na dokazima publiciranim u literaturi. Odluka o uvođenju antibiotika nije temeljena na objektivnim parametrima težine bolesti kako ni na terapijskoj učinkovitosti određenog antibiotika. Cijena liječenja značajno je uvjetovana korištenjem antibiotika.