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• BRIEF REPORTS •

Empirical antibiotic treatment with piperacillin-tazobactam in patients with microbiologically-documented biliary tract infections

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Abstract

AIM: To report our experience with empiric antimicrobial monotherapy (piperacillin/tazobactam, of which no data are available in such specific circumstances) in microbiologically-documented infections in patients with benign and malignant conditions of the biliary tract.

METHODS: Twenty-three patients, 10 with benign and 13 with malignant conditions affecting the biliary tree and microbiologically-documented infections were recruited and the efficacy of empirical antibiotic therapy was assessed.

RESULTS: The two groups featured similar demographic and clinical data. Overall, the infective episodes were most due to Gram negative agents, more than 60% of such episodes (mostly in malignant conditions) were preceded by invasive instrumental maneuvers. Empirical antibiotic therapy with a single agent (piperacillin/tazobactam) was effective in more than 80% of cases. No deaths were reported following infections.

CONCLUSION: An empiric therapeutic approach with piperacillin/tazobactam is highly effective in biliary tract infections due to benign or malignant conditions.

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INTRODUCTION

The common causes of intra-abdominal infections are those related to the biliary tract[1]. However, to obtain a microbiological diagnosis in biliary tract infections (BTI) is not easy, due to the difficulty of sampling bile and the low incidence of positive blood cultures. Therefore, antimicrobial therapy is often empirical[2], and the choice of an appropriate regimen depends on the knowledge of the most common causative bacteria and the reported efficacy of antimicrobial drugs in BTI. Moreover, the paucity of randomized clinical trials for BTI treatment probably justifies the fact that there is no standardized approach to these infections[2].

The present study was to report our experience with empirical single antibiotic treatment with piperacillin-tazobactam of BTI in patients with benign and malignant diseases of the biliary tract, since there are no specific data on this compound in the treatment of such infections.

MATERIALS AND METHODS

Twenty-three consecutive patients (15 men, 8 women, age range 22-88 years) with microbiologically documented BTI entered the study. Underlying disease and causative organisms were assessed. Empirical treatment (4.5 g t.i.d) was started immediately after obtaining samples (blood and/or bile) for microbiological cultures, and concordance with antibiogram and its efficacy were also evaluated. The treatment was judged effective when fever and clinical symptoms of infection resolved within 72 h, whereas the persistence of fever beyond 72 h from the start of treatment, the deterioration of clinical conditions or the death as a result of the primary infection was considered as failure.

RESULTS

Overall, records were obtained from 10 patients with benign and 13 patients with malignant conditions affecting the biliary tree. Table 1 shows the clinical characteristics of the two groups. In more than 60% of patients, BTI were preceded by an invasive procedure on the biliary tree, and this was less frequent in benign than in malignant conditions (50% *vs* 77%).

Table 1 Demographic and clinical variables of 23 patients with BTI

	Benign conditions	Malignant conditions
No (%)	10 / 23(43.5)	13 / 23(56.5)
Average duration of treatment (d)	7±1	10±1
Underlying condition (*No.*)	Choledocholitiasis (7)	Cholangiocarcinoma (6)
	Acute cholecystitis (2)	Pancreatic carcinoma (4)
	Iatrogenic stenosis (1)	Gallbladder carcinoma (2)
		Infiltrating hepatoma (1)
Previous instrumental invasive maneuvers (*No*)	None (5)	None (3)
	PTD (3)	PTD (10)
	ERCP (2)	

Abbreviations: BTI=biliary tract infections; ERCP=endoscopic retrograde cholangio-pancreatography; PTD=percutaneous transhepatic drainage.

Table 2 Microbiological variables in 23 patients with BTI

	Benign conditions (10 patients)	Malignant conditions (13 patients)
Insulation medium (No.)	Blood (7)	Blood (6)
	Bile (3)	Bile (7)
Polymicrobial infections	1 (4%)	7 (30%)
Isolated pathogens (No. cases)	*E.coli* (4)	Enterococcus spp (6)
	Enterococcus spp (3)	Staphylococcus spp (6)
	Pseudomonas spp (3)	Candida spp (5)
	Enterobacter spp (2)	*E.coli* (2)
	Streptococcus spp (2)	Pseudomonas spp (2)
	Klebsiella spp (1)	Proteus spp (1)
	Candida spp (1)	Enterobacter spp (1)
		Salmonella spp (1)

Table 2 shows the microbiological characteristics of the pathogens isolated in both groups. As expected, most infections were caused by Gram negative agents, and 30% of them (almost exclusively found in malignant conditions) were polymicrobial. *Candida spp* were always isolated from bile in polymicrobial infections. In 19(82.6%) patients there was no need of modifying the empiric therapeutic schedule, whereas in the remaining 4 the antibiotic regimen was modified according to the antibiogram showing resistance or insensitivity to piperacillin/tazobactam. In all patients with BTI due to benign conditions, decrease of fever and improvement of clinical conditions were observed within 3-18 h. A slower trend was observed in patients with BTI due to malignant conditions (improvement within 8-24 h), probably due to more polymicrobial infections and resistances to the empiric regimen. After the results from the antibiogram were obtained, these latter patients treated with more targeted antibiotic regimens, had the disappearance of fever and improvement of the clinical conditions. No deaths were reported attributable to BTI.

DISCUSSION

In this study, we reported our experience with an empiric antibiotic regimen in BTI, and showed that a monotherapy with piperacillin/tazobactam (that, to the best of our knowledge has still not been assessed in such circumstances) might be effective in more than 80% of cases. The organisms more commonly cultured in our patients, in both benign and malignant conditions, were Gram negative bacteria, the pathogens were more frequently associated with obstructive conditions of the biliary tree[3,4]. Several infective episodes followed invasive instrumental procedures, especially percutaneous drainage (that also gave a discrete yield for bile culture, as previously shown for this procedure[5]), and were mostly represented by polymicrobial infections.

A preferred therapeutic schedule for BTI, until recently, was usually a combination of a penicillin (usually ampicillin) and an aminoglycoside[6-9]. This combination had limited anaerobic coverage, frequent resistance (to ampicillin) of Gram negative bacteria, and the risks of renal damage (aminoglycoside, significantly increased in patients with cholestasis)[10]. However, other antibiotics (such as the ureidopenicillins) exhibited a broad spectrum of activity, that included many anaerobes, *enterococci* and *P.aeruginosa*, in addition to Gram negative bacilli[11], so that they may result in appealing for use as single agents. Actually, it has been shown that monotherapy with a ureidopenicillin (mezlocillin, piperacillin) is equally or more effective than the traditional approach with ampicillin/aminoglycoside for treatment of BTI[12-14], although in patients undergoing nonsurgical invasive procedure of the biliary tree and/or with suspected increased risk of *P.aeruginosa* the association of ureidopenicillin/aminoglycoside has been still justifiable[15,16]. On the other hand, the combination of piperacillin with the beta-lactamase inhibitor tazobactam (that displays a substantial elimination in bile[17,18]) might be a reasonable alternative when the local resistance pattern featured a high incidence of ureidopenicillin-resistant *E.coli* or *Klebsiella spp*[2,19], as also shown by its effectiveness as single empiric agent in high-risk, febrile neutropenic patients with cancer[20].

Experience with quinolones for treatment of BTI was still limited[2,21]. However, there is good evidence that monotherapy with these compounds might be as effective as combination therapy for treatment of BTI[22-24].

To date, the combination of piperacillin/tazobactam has been demonstrated clinically- and cost-effective in both uncomplicated and complicated intraabdominal infections[25-27], although no specific data on BTI are available. Therefore, we feel that our experience might be a useful adjunct to the therapeutic armamentarium.

In conclusion, empiric antibiotic treatment with piperacillin/tazobactam is frequently effective in BTI due to benign and malignant conditions. Of course, in such circumstances an early operative drainage of the biliary tree is always mandatory, regardless of the presence or absence of suppuration in the common bile duct[28], to prevent relapses and septic complications.

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