

Bacterial Profile and Antimicrobial Resistance to Commonly Used Antimicrobials in Intra-Abdominal Infections in Two Teaching Hospitals

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Abstract: Problem statement: Intra-abdominal infections are associated with significant morbidity and mortality. The resulting infection is typically polymicrobial and comprised of both aerobic and anaerobic microbes, which need systemic antimicrobial therapy. Since the bacteriology and antimicrobial susceptibility of postoperative intra abdominal infections were not determined in Iran, so this study was performed to evaluate the antimicrobial susceptibility patterns among aerobic bacteria isolated from post-operative intra-abdominal selected samples in 2 teaching hospitals in Kerman, Iran. **Approach:** the peritoneal sample of 174 patients which undergone abdominal surgery were cultured by routine microbiological methods for aerobic microorganisms. Antimicrobial susceptibility testing was performed to 4 commonly used antibacterials (Ampicillin, Cefazolin, Gentamicin and Ciprofloxacin) using disc diffusion method according to the NCCLS guidelines. **Results:** *Escherichia coli* (*E. coli*) was the most frequent microorganism which was isolated from 70.6% of peritoneal cultures, followed by *Klebsiella pneumonia* (13.7%), *Pseudomonas aeruginosa* (10.8%) and *Proteus mirabilis* (4.9%). *E. coli* which was the most common isolate was highly susceptible to ciprofloxacin (84.6%) and gentamicin (76.9%). The resistance rate of *E. coli* isolates to ampicillin was very high, i.e., 80.8% of *E. coli* isolates were resistant to ampicillin. The resistance rate for pseudomonas and *Klebsiella* spp. to commonly used antimicrobials varied from 25% to ciprofloxacin to 100% to ampicillin. **Conclusion:** *E. coli* was the most common isolate in post-operative peritoneal cultures. The results showed the relatively high resistance rate of the isolated microorganisms to commonly used antimicrobials, especially to ampicillin. So the choice of antimicrobial therapy must be based on the susceptibility tests and also take into account the risk of inadequate and in appropriate antimicrobial therapy and emergence of bacterial resistance to commonly used antimicrobials.

Key words: Intra-abdominal infections, antimicrobial resistance, abdominal surgery

INTRODUCTION

Abdominal infections are associated with significant morbidity and mortality. Nearly all bacteria causing abdominal infections are derived from the endogenous flora of the alimentary tract (Laterre *et al.*, 2006). The resulting infection is typically polymicrobial and comprised of both aerobic and anaerobic microbes. They can be classified by their severity as uncomplicated and complicated or by their origin as community or hospital acquired (Mazuski *et al.*, 2002a; Onderdonk *et al.*, 1990). Complicated infections are those that require both surgical or radiological drainage

procedures and antimicrobial therapy. Antibiotics play an important role in prevention and treatment of intra-abdominal infections (Blot and De Waele, 2005; Driscoll *et al.*, 2007; Dellinger *et al.*, 1994).

Intra-abdominal infections are common causes of hospitalization with approximately 2 million intra-abdominal procedures performed each year in the USA (Mazuski *et al.*, 1990).

The aerobes isolated include *E. coli*, usually the major isolate, enterococci, viridans streptococci, other Enterobacteriaceae, *Proteus* spp. and occasionally *Pseudomonas aeruginosa*, *Serratia* spp. and *Acinetobacter* spp. (the latter three are often associated

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with nosocomial infections). The anaerobes are predominantly the *Bacteroides* species and *Bifidobacterium* species (Laterre *et al.*, 2006; Goldstein and Snyderman, 2004; Pieracci and Barie, 2007a; Kroenke, 1985).

Antimicrobial therapy poses an important clinical challenge because of the diverse bacteriology of complicated intra-abdominal infections and the emergence of bacterial resistance. In general, selection of an empiric agent or combination regimen must be directed at providing reliable activity against *E. coli*, other gram negative facultative bacteria and *B. fragilis* (Mazuski *et al.*, 2002a; Guembe and 2008; Solomkin *et al.*, 2003; Marshall, 2004).

Many other factors influence the selection of an antimicrobial agent, including its potential to induce bacterial resistance, its risk of hypersensitivity, its overall tolerability, its dosing frequency and its cost. Accordingly, the search continues for an effective antimicrobial regimen that has activity against resistant pathogens, a minimal risk of side effects, a convenient dosing schedule and potential cost benefits (Bohnen *et al.*, 1992a; 1992b; Goldstein and Snyderman, 2004; Hasper *et al.*, 2009; Solomkin *et al.*, 2003; Pieracci and Barie, 2007b).

Several intravenous antibiotics have been investigated, as monotherapy or as part of a combination regimen, for the management of patients with intra-abdominal infections (Weigelt, 2007). The old standard of care involved double or triple-antimicrobial therapy (e.g., aminoglycoside/beta-lactam/clindamycin) to provide coverage against an array of potential pathogens (Weigelt, 2007). In recent years, monotherapy with imipenem/cilastatin (Primaxin) has become the new gold standard because of its broad spectrum of activity against anticipated pathogens and its relative safety and ease of use. In addition to imipenem/cilastatin contemporary agents with documented efficacy include ceftazidime, ampicillin/sulbactam, ticarcillin clavulanate (Timentin) and piperacillin/tazobactam (Zosyn) but the emergence of multidrug-resistant Enterobacteriaceae and other gram-negative bacilli have become a growing problem (Mazuski *et al.*, 2002a; Goldstein and Snyderman, 2004; Solomkin *et al.*, 2003; Weigelt, 2007; Mazuski *et al.*, 2002b).

Antibiotics are among the most misused drugs in Iran and are prescribed inappropriately for outpatients which causes the emergence of bacterial resistance to commonly used antimicrobials (Sepehri and Meimandi, 2005). Since the bacteriology and antimicrobial

susceptibility of postoperative intra abdominal infections were not determined in Iran, so this study was performed to evaluate the antimicrobial susceptibility patterns among aerobic bacteria isolated from post-operative intra-abdominal selected samples in 2 teaching hospitals in Kerman, Iran.

MATERIALS AND METHODS

This cross-sectional study was conducted in 2008 in two teaching hospitals of Kerman University of Medical Sciences. Kerman (the center of Kerman province) is situated 1,000 Km from Tehran in south of Iran having around 600,000 residents.

The peritoneal samples of 174 patients which undergone abdominal surgery were cultured by routine microbiological methods for aerobic microorganisms.

Samples were streaked on two plates that consist of blood agar supplemented with 5% defibrinated sheep blood and Eosin Methylene Blue (EMB) agar. Plates were incubated aerobically at 37°C for 48 h. Based on colony morphology, positive cultures were Gram stained and Gram-positive organisms were subcultured on blood agar plates (Padtan Teb Co, IRAN) Gram-negative rods were subcultured on MacConkey agar (Padtan Teb Co, IRAN). Organisms were identified using standard methods and API Identification System. Gram positive and gram-negative isolates bacterial sensitivity to commonly used antimicrobials (Ampicillin, Cefazolin, Gentamicin, Ciprofloxacin) were investigated by disk diffusion method using NCCLS guidelines (Ginocchio, 2002; Zapantis *et al.*, 2005).

Data were entered and analyzed by Stata v. 8. and results were reported as the type and percentage of microbial isolations and also the percentage of microbial susceptibility and resistance to commonly used antimicrobials.

RESULTS

A total of 174 patients were hospitalized for Intra-abdominal infections during the first 9 months of 2008 in two teaching hospitals in Kerman City. 96 (55.1%) of patients were men and 78 (44.9%) were women which showed significant difference ($p < 0.05$). The results of microbiological cultures showed that no aerobic microbial isolates was found in 41.4% of patients. Aerobic microorganisms were isolated in 102 (58.6%) patients. *Escherichia coli*

(*E. coli*) was the most commonly cultured microorganisms isolated from peritoneal samples (70.6%) followed by *Klebsiella pneumonia* (13.7%), *Pseudomonas aeruginosa* (10.8%) and *Proteus mirabilis* (4.9%) (Table1). The co-infection with two bacterial species (including *E. coli* and *Pseudomonas aeruginosa*) was seen in 7 (6.9%) of peritoneal samples. The resistance rates to commonly used antimicrobials in isolated bacteria from peritoneal samples varied from 15.4% for ciprofloxacin to 100% for ampicillin (Table 2). *E. coli* isolates were highly sensitive to ciprofloxacin (84.6%) but showed high resistance rate (80.8%) to ampicillin (Table 2).

Also *Pseudomonas aeruginosa* isolates showed high sensitivity to ciprofloxacin and gentamicin (75%) and high resistance rate to cefazolin (75%) and ampicillin (100%) (Table 2).

The resistance rate of *Klebsiella pneumonia* to commonly used antimicrobials varied from 40% to ciprofloxacin and gentamicin to 80% for ampicillin (Table 2). The results of this study showed that 64.3% of isolates were resistant to at least 2 antibiotics and 7.1% of isolates were resistant to all 4 used antimicrobials (Table 3).

Table 1: Type of microorganisms isolated from peritoneal samples in 174 patients with intra-abdominal operations in Kerman teaching hospitals in 2008, Kerman, Iran

Microbial agent	Number of isolates	Isolates (%)
<i>Escherichia coli</i>	72	70.6
<i>Klebsiella pneumonia</i>	14	13.7
<i>Pseudomonas aeruginosa</i>	11	10.8
<i>Proteus mirabilis</i>	5	4.9
Total	102	100.0
Mixed isolates	7	6.9

Table 2: Resistance rate to commonly used antimicrobials in 174 patients with intra-abdominal operations in Kerman teaching hospitals in 2008, Kerman, Iran

Antimicrobial	Resistance rate		
	<i>Escherichia coli</i> (n = 72)	<i>Kleb. Pneumonia</i> (n = 14)	<i>Pseudo. Aeruginosa</i> (n = 11)
Ciprofloxacin	15.4	40	25
Cefazolin	43.2	60	75
Ampicillin	80.8	80	100
Gentamicin	23.1	40	25

Table 3: Frequency of microbial isolates co- resistance to commonly used antimicrobials in 174 patients with intra-abdominal operations in Kerman teaching hospitals in 2008, Kerman, Iran

Co- resistance to antimicrobials	Resistant isolates (n)	Resistant isolates (%)
One	5	17.9
Two	18	64.3
Three	3	10.7
Four	2	7.1

DISCUSSION

The results of this study showed that *E. coli* was most frequent microorganism isolated from peritoneal samples in patients undergone abdominal surgery. Others also reported that *E. coli* is the most commonly isolated aerobic microorganism isolated from intra-abdominal infections (Snydman, 2004; Hasper *et al.*, 2009; Pieracci and Barie, 2007b; Weigelt, 2007).

Klebsiella pneumonia, *Pseudomonas aeruginosa* and *Proteus mirabilis* were other microorganisms which were isolated in a few percents of patients which are in complete agreement with other investigators reports (Snydman, 2004; Hasper *et al.*, 2009; Mazuski, 2007; Paterson *et al.*, 2005).

Pseudomonas aeruginosa isolation in intra-abdominal surgery patients which is one of the potential pathogens could be of important concern, because it is a major cause of nosocomial infections and this organism shows a remarkable capacity to resist antibiotics (Driscoll *et al.*, 2007; Montravers *et al.*, 2009; Obritsch *et al.*, 2005). Infection with *Pseudomonas aeruginosa* is typically observed in high-risk patients such as those with late-onset nosocomial infection and those who have received previous antimicrobial therapy, undergone recurrent surgeries, or both. In contrast, patients with early-onset health care-associated or community-acquired infections have a low prevalence of *Pseudomonas aeruginosa* (Mazuski *et al.*, 2002b; Weigelt, 2007; Mazuski, 2007; Hasper *et al.*, 2009).

Anaerobic microorganisms, including Bacteroides (especially *Bacteroides fragilis*) are among the most commonly isolated microorganisms and are isolated in more than 80% of complicated intra-abdominal infections, however, in this study only the aerobic microorganisms were isolated and this is one of the limitations of present study (Guembe *et al.*, 2008; Baron *et al.*, 1992; Bennion *et al.*, 1990; Goldstein *et al.*, 2000).13,26-28

Also others reported the isolation of Enterobacter, *Staphylococcus aureus*, *Acinetobacter* in small portion of intra-abdominal samples (Hasper *et al.*, 2009; Guembe *et al.*, 2008; De Vera and Simmons, 1996; Smith *et al.*, 1999).

The prevalence of positive abdominal cultures in this study was about 58 percent which is in the range of other reported values (28.3% in uncomplicated intra-abdominal infections to 69% in complicated intra-abdominal infections) (Goldstein and Snydman, 2004).

The susceptibility to commonly used antimicrobials showed a relatively high resistance rate (80.8%) of *E. coli* to ampicillin which is clinically

important and may indicate inappropriate use of antimicrobials in teaching hospitals in Iran, however, *E. coli* was very sensitive to ciprofloxacin (84.6%) and gentamicin (76.9%) which is in agreement with the results of other investigators in other parts of the world (80-97%) (Goldstein and Snyderman, 2004; Goldstein and Snyderman, 2004; Paterson *et al.*, 2005).

Koksal *et al.* (2009) reported that the resistance rate to ciprofloxacin and gentamicin in Turkey was 57.6 and 38% respectively, which is much higher than the resistance rate in our study.

The *E. coli* sensitivity to cefazolin (56.8%) was significantly higher than other studies (Goldstein and Snyderman, 2004; Goldstein and Snyderman, 2004; Paterson *et al.*, 2005).

Klebsiella pneumonia was relatively resistant to commonly used antimicrobials used for treatment of intra-abdominal infections. Our data are in agreement with several studies in other parts of the world showing an increasing portion of resistant isolates of *Klebsiella pneumonia* (Koksal *et al.*, 2009; Jouini *et al.*, 2009; Schito *et al.*, 2009). *Klebsiella pneumonia* sensitivity to ciprofloxacin varied from 80.7% in Latin America to 91.4% in Europe countries which is comparable to the sensitivity rate in this study (75%), however, *Klebsiella pneumonia* sensitivity to ampicillin was 20% which much lower than the reported value in middle east (75.6%) and USA (91.3%) (Paterson *et al.*, 2005).

Pseudomonas aeruginosa isolates evaluated by this study showed very high resistance to beta lactam antibiotics (ampicillin and cefazolin). The best coverage against these isolates was obtained with ciprofloxacin and gentamicin. These data are in complete agreement with other studies which shows an increase in resistance rate to commonly used antimicrobials (Driscoll *et al.*, 2007, Montravers *et al.*, 2009; Obritsch *et al.*, 2005; De Francesco *et al.*, 2007; Mesaros *et al.*, 2007). Also the results of this study showed that 64.3% of isolates were resistant to at least 2 antibiotics and 7.1% of isolates were resistant to all 4 used antimicrobials.

CONCLUSION

In summary, the results of this study showed that *E. coli* was the most common isolate in post-operative peritoneal cultures. The sensitivity to commonly used antimicrobials varied and *E. coli* showed the highest sensitivity to ciprofloxacin and gentamicin and ampicillin showed the lowest antibacterial activity against microbial isolates from post-operative peritoneal cultures. The high antimicrobial resistance to

commonly used antimicrobials could profoundly affect the choice of therapeutic agents. So the choice of antimicrobial therapy must be based on culture growth and antibacterial sensitivity tests and also take into account the risk of inadequate and inappropriate antimicrobial therapy and emergence of bacterial resistance to commonly used antimicrobials.

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