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Antimicrobial Susceptibility Pattern of Microorganisms Involved in the Pathogenesis of Surgical Site Infection (SSI); A 1 Year of Surveillance

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Abstract: The aim of this study is to identify the antibiotic sensitivity pattern of pathogens involved in the process of surgical site infection, in surgical wards. Changes made in the pattern of antibiotic use will result in different microorganism susceptibility patterns, which needs correct determination for precise empiric antibiotic therapy. One thousand patients (62% men and 38% women, 18-74 years old, with mean age 43±8)) who underwent surgical treatment, in Alzahra University Hospital, Isfahan University of Medicine, Isfahan, Iran, were studied from 2005 to 2006. Surgical wound infections, based on the reported criteria, were aspirated for culturing within 1 plus gram staining of prepared smears. Minimum Inhibitory Concentrations (MICs) were determined for samples and all derived data were compared by SPSS 13 and WHO net 5 software. The prevalence of SSI was 13.3% with 150 positive cultures, totally. Of 150 bacteria, isolated from surgical site infections *Staphylococcus aureus* had most frequency (43%). Resistance of isolated organisms was 41.7% in amikacin, 65 and 78.6% in ceftazidime, 85.7% in ceftriaxone, 61.5% in ciprofloxacin, 78.8% in gentamicine, 6.4% in imipenem, 13% in meropenem and 70.6% in trimethoprim/sulfamethoxazole, respectively. 78.9% of *Staphylococcus aureus* isolates were MRSA and vancomycine was the most effective antibiotic without any resistance. Among 10 isolates of coagulase negative *Staphylococcus*, no vancomycine resistance was seen, but in contrast all cases were resistant to oxacillin. The most common gram negative organism was *Klebsiella* (18 isolates) in which 100 and 80% were sensitive to imipenem and meropenem, respectively. Seventeen cases were *E. coli*, in which the most sensitivity was to meropenem (80%) and imipenem (77.8%). Thirteen cases of *Pseudomonas* were detected, in which 16.7% were resistant to imipenem and 8.3% to meropenem. Our results demonstrated that the total antibiotic resistance is increasing among SSIs, with an up sloping pattern, which will contact with a constant empiric antibiotic therapy. So, precise up to date antibiogram tantalize us toward balancing the rate of total antibiotic resistance to SSIs.

Key words: Surgical site infection, antibiotic susceptibility, antibiotic resistance

INTRODUCTION

Surgical-site infections (SSI) are the most common hospital-acquired infection among surgical patients and the third most frequent hospital-acquired infection in the general hospital population (Poulakou and Giamarellou, 2007). They cause significant postoperative morbidity, mortality and prolong hospital stay (Bratzler, 2006).

However, incorrect use of antibiotics occurs in 25 to 50% of operations (Bedouch *et al*., 2004; Pons-Busom *et al*., 2004). Inappropriate use of broad spectrum antibiotics or prolonged courses of prophylactic antibiotics, disposes all patients at even greater infection risk because of the development of antibiotic-resistant pathogens (Dahms *et al*., 1998). According to data from the National Nosocomial Infections Surveillance System (NNIS), there has been little change in the incidence and distribution of the pathogens isolated from infections during the last decade.

So, the aim of this study is to identify the antibiotic sensitivity pattern of pathogens involved in the process of surgical site infection, in surgical wards.

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MATERIALS AND METHODS

During the 12 month period from 2005 to 2006 we studied 1000 patients (62% men and 38% women, 18-74 years old, with mean age 43±8) who underwent surgical treatment (abdominal, vascular, orthopedic and reparative surgery), in Alzahra University Hospital, Isfahan University of Medicine, Isfahan, Iran. A wound infection was identified by the presence of purulent discharge from the incision with erythematous cellulitis, induration or pain and demonstrable fluid collection noted on ultrasound after surgery. Purulent exudates were obtained from the open discharging wounds with a sterile cotton swab. Aspirates were obtained by preparing the wound area with alcohol, inserting a sterile needle through the healing incision and aspirating fluid into a sterile syringe. Culturing was done within 1 h using standard bacteriological inoculation techniques. For the isolation of anaerobes, specimens were inoculated onto Columbia blood agar plates enriched with hemin and menadione, incubated in an anaerobic chamber at 37°C and examined at 48 and 96 h. Any growth was subsequently identified by standard microbiological methods. Gram stains were also performed and recorded at the time of culturing. Microscopic examination of gram stained slides and subsequent identification of bacterial isolates were done by an experienced senior microbiologist.

Minimum Inhibitory Concentrations (MICs) were determined by Mueller Hinton plates containing 2% NaCl which inoculated with a direct colony suspension equivalent to a 0.5 MacFarland standard in accordance with the National Committee for Clinical Laboratory Standards. The breakpoints mentioned in the last edition of CLSI (Clinical and Laboratory Standards Institute) tables M_7A_6 was used to determine susceptibility and resistance. The plates were incubated at 35°C for 24 h MIC of 9 antibiotics on isolated bacteria was determined by gradient concentration method (E-Test®; AB BIODISK Co. Sweden). Quality control was tested by *E. coli* ATCC25922 and *Staphylococcus* ATCC29213. Data was analyzed by SPSS 13 and WHO net 5 software.

RESULTS

The prevalence of SSI was 13.3% with 150 positive cultures, totally. Of 150 bacteria, isolated from surgical site infections, 65 (43%) were *Staphylococcus aureus*, 27 (18%) were *E. coli*, 32 (21%) were *Klebsiella* sp., 20 (13%) were *Pseudomonas* sp., 15 (10%) were *Staphylococcus* coagulase negative, 8 (5%) were *Acinetobacter* spp., 8 (5%) were *Enterobacter*, 2 (1.3%) were *Serratia*, 1 (0.6%) was *Enterococcus*, 2 (1.3%) were *Citrobacter* and 0% of anaerobic or mixed isolates. According to break point used for susceptibility meet CLSI M7-A6 (Clinical and Laboratory Standard Institute) criteria, resistance of isolated organisms was 41.7% in amikacin, 65 and 78.6% in ceftazidime, 85.7% in ceftriaxone, 61.5% in ciprofloxacin, 78.8% in gentamicine, 6.4% in imipenem, 13% in meropenem, 70.6% in trimethoprim/sulfamethoxazole respectively. 78.9% of *Staphylococcus aureus* isolates were MRSA (MIC of oxacillin >4) and vancomycine was the most effective antibiotic without any resistance (97.1% sensitivity). The susceptibility of staphylococcus aureus isolates in rifampin was 85.2% but we could not use this agent against *Staphylococcus* alone because of rapidly production resistance to it. Amikacin and gentamicine resistance were 66.7% and then due to this high rate of resistance, they should be in combination with other drugs for synergistic effect. Clindamycin was a relatively nice antibiotic for this organism too (41.4% sensitivity) but should be used only after antibiogram detection. Fleurocinolones were not a good choice in our study, hence ofloxacine resistance was 77.8% and ciprofloxacin resistance rate was 62.5% in isolates (Table 1). Among 10 isolates of coagulase negative *Staphylococcus*, no vancomycine resistance was seen, but in contrast all cases were resistant to oxacillin. A relative rifampin resistance (40%) and a high clindamycin (60%) were also seen (Table 2). The most common gram negative organism was *Klebsiella* (18 isolates) in which 100 and 80% were sensitive to imipenem and meropenem, respectively. 85.7% of them were resistant to gentamicine. Among cephalosporins, resistant rate to cefepime, ceftazidime and

Table 1: Antibiotic susceptibility pattern of *Staphylococcus aureus* in surgical site infections

Antibiotic name	Breakpoints		R (%)	I (%)	S (%)	MIC_{50}	MIC_{90}
Amikacin	S≤16	R≥64	66.7	0.0	33.3	256.0	256.0
Cefepime	S≤8	R≥32	81.8	9.1	9.1	256.0	256.0
Cephalothin	S≤8	R≥32	53.6	7.1	39.3	48.0	256.0
Ciprofloxacin	S≤1	R≥4	62.5	0.0	37.5	8.0	32.0
Clindamycin	S≤0.5	R≥4	48.3	10.3	41.4	2.0	256.0
Gentamicine	S≤4	R≥16	66.7	3.7	29.6	96.0	256.0
Ofloxacine	S≤1	R≥4	77.8	0.0	22.2	32.0	32.0
Oxacillin	S≤2	R≥4	78.9	0.0	21.1	256.0	256.0
Rifampin	S≤1	R≥4	7.4	7.4	85.2	0.016	2.0
Vancomycine	S≤4	R≥32	0.0	2.9	97.1	1.5	3.0

Table 2: Antibiotic susceptibility pattern of coagulase negative *Staphylococcus* in surgical site infections

Antibiotic name	Breakpoints		R (%)	I (%)	S (%)	MIC_{50}	MIC_{90}
Cephalothin	S≤8	R≥32	66.7	11.1	22.2	256.0	256.0
Clindamycin	S≤0.5	R≥4	60.0	0.0	400.0	32.0	256.0
Gentamicine	S≤4	R≥16	83.3	0.0	16.7	96.0	256.0
Oxacillin	S≤0.25	R≥.5	100.0	0.0	0.0	256.0	256.0
Rifampin	S≤1	R≥4	40.0	20.0	40.0	1.5	32.0
Vancomycine	S≤4	R≥32	0.0	11.1	88.8	8.0	256.0

Table 3: Antibiotic susceptibility pattern of *Klebsiella* in surgical site infections

Antibiotic name	Breakpoints		R (%)	I (%)	S (%)	MIC_{50}	MIC_{90}
Amikacin	S≤16	R≥64	47.1	11.8	41.2	32.0	256.0
Cefepime	S≤8	R≥32	69.2	7.7	23.1	256.0	256.0
Ceftazidime	S≤8	R≥32	85.7	7.1	7.1	256.0	256.0
Ceftriaxone	S≤8	R≥64	77.8	0.0	22.2	256.0	256.0
Ciprofloxacin	S≤1	R≥4	33.3	33.3	33.3	2.0	32.0
Gentamicine	S≤4	R≥16	85.7	0.0	14.3	128.0	256.0
Imipenem	S≤4	R≥16	0.0	0.0	100.0	0.5	1.5
Meropenem	S≤4	R≥16	13.3	6.7	80.0	0.19	12.0
Ofloxacine	S≤2	R≥8	66.7	0.0	33.3	32.0	32.0

Table 4: Antibiotic susceptibility pattern of *E. coli* in surgical site infections

Antibiotic name	Breakpoints		R (%)	I (%)	S (%)	MIC_{50}	MIC_{90}
Amikacin	S≤16	R≥64	26.7	0.0	73.3	4.0	256.0
Cefepime	S≤8	R≥32	76.5	0.0	23.5	256.0	256.0
Ceftazidime	S≤8	R≥32	80.0	10.0	10.0	256.0	256.0
Ceftriaxone	S≤8	R≥64	100.0	0.0	0.0	256.0	256.0
Ciprofloxacin	S≤1	R≥4	60.0	20.0	20.0	32.0	32.0
Gentamicine	S≤4	R≥16	90.0	0.0	10.0	32.0	64.0
Imipenem	S≤4	R≥16	11.1	11.1	77.8	0.5	32.0
Meropenem	S≤4	R≥16	10.0	10.0	80.0	0.19	8.0
Ofloxacine	S≤2	R≥8	71.4	0.0	28.6	32.0	32.0

Table 5: Antibiotic susceptibility pattern of *Pseudomonas* in surgical site infections

Antibiotic name	Breakpoints		R (%)	I (%)	S (%)	MIC_{50}	MIC_{90}
Amikacin	S≤16	R≥64	60.0	0.0	40.0	128.0	256.0
Cefepime	S≤8	R≥32	87.5	0.0	12.5	96.0	256.0
Ceftazidime	S≤8	R≥32	57.1	14.3	28.6	256.0	256.0
Ceftriaxone	S≤8	R≥64	88.9	11.1	0.0	256.0	256.0
Gentamicine	S≤4	R≥16	83.3	16.7	0.0	64.0	G256.0
Imipenem	S≤4	R≥16	16.7	0.0	83.3	1.0	32.0
Meropenem	S≤4	R≥16	8.3	25.0	66.7	0.75	8.0

R: Resistant, I: Intermediate, S: Susceptible, MIC: Minimal Inhibitory Concentration

ceftriaxone was 69.2, 85.7 and 77.8%, respectively. Ofloxacine resistance was more than ciprofloxacin (66.7 and 33.3%, respectively) (Table 3). 17 cases were *E. coli*, in which the most sensitivity was to meropenem (80%) and imipenem (77.8%). Amikacin was more effective than gentamicine (sensitivity rate 73.3 and 10%, respectively). Among cephalosporins, 23.5, 10 and 100% were resistant to cefepime, ceftazidime and ceftriaxone, respectively. Ofloxacine was more effective than ciprofloxacin (sensitivity rate 28.6 and 20%, respectively) (Table 4). 13 cases of *Pseudomonas* were detected, in which 16.7% were resistant to imipenem and 8.3% to meropenem. Amikacin resistance was less than gentamicine among them (60 and 83.3%, respectively). Cefepime resistance was very high (87.5%), ceftriaxone and ceftazidime resistance were 88.9 and 57.1%, respectively (Table 5). 100% of *Enterobacter* (8 cases) and *Acinetobacter* (8 cases) were sensitive to imipenem and meropenem. Cephalosporins were not effective antibiotic against them and resistance rate was great, but amikacin was an effective antibiotic against *Enterobacter* (83.3% sensitivity rate).

DISCUSSION

SSIs are increasingly becoming an institutional marker of quality assurance. These infections, representing a global threat, are associated with great complications (Hedrick *et al*., 2006). The most important ones for the patients who experience postoperative complications are increased hospital length of stay, readmission rates, mortality rates, costs of care, hospitals and payers (Bratzler, 2006) and most importantly emergence of multi-drug-resistant bacteria

(Poulakou and Giamarellou, 2007). Juristically, each of these complications has their own disadvantage per se and is related to each other somehow; increased hospital length will increase costs and emergence of MDR and vice versa: a vicious cycle. Thinking to global trends to decreasing the hospital length, we will encounter SSIs after hospital discharge. Then it seems reasonably that the diagnosis of SSIs is very important to decreased or prohibit the complications of late diagnosis hospitalized and post-discharge SSIs. Neglecting the origin of SSI advent, the problem of antibiotic resistant cases of SSI, is a catastrophe.

Perhaps, different risk factors are associated with different bacterial colonization of surgical site and therefore different antibiotic resistant orgamisms. For example, the great risk factor for SSI following urological operations is thought to be the presence of a preoperative urinary tract infection (UTI) (Hamasuna *et al*., 2004). The above matter attracts our minds toward this fact that different populations should decide discretely upon their most usual present risk factors (as obesity, pre-hospitalization ulcers and more). So, perhaps the presence of a unique preventive strategies for SSIs incidence and more importantly, antibiotic resistant SSIs, will be too helpful.

Treatment of infected patients depends on several factors including the severity of the infection, degree of antibiotic resistance pathogens, the sensitivity to alternative agents and the achievable concentration of antibiotic at the site of the infection. Outbreaks of infection have occurred and various control measures have been suggested in attempts to limit the spread of resistant strains (Gastmeier, 2007).

Staphylococci and *Enterococcus* are the most culprit pathogens in surgical-site (Taylor *et al*., 2000), so a small fraction of drug resistance among these gram-positive bacteria will impose great catastrophes to patients with SSIs. Methicillin/oxacillin resistant SA, continues to plague hospitals (Marshall *et al*., 2004), is prevalent in many of the country's most prestigious hospitals as demonstrated by adverse publicity (the superbug) and frequently observed in is often accompanied by multidrug resistance (Guyot and Layer, 2006). Vancomycine is usually the drug of choice for infections caused by MRSA, so the emergence of intermediate vancomycine resistant *S. aureus* is an important matter (Rapp, 2000). One strategy to combat the increasing rate of drug-resistant gram-positive pathogens seems to be prudent use of available antibiotics (Rapp, 2000). (SSIs), especially antibiotic-resistant ones, are a great concern for preoperative cares (Plonczynski, 2005). While administration of the correct antibiotic in its effective dose and in correct optimal time seems too helpful in preventing or reducing the occurrence of SSIs and also MDR cases (Plonczynski, 2005), but some important prophylactic measures are also needed (Chong and Sawyer, 2002): moving away from widespread antibiotic administration, surgical prophylaxis, new antibiotic guidelines and researches for antibiotic administration for each specific operation and new substitute for moderate to sever targets of resistance (which may only be a short-term answer).

We should also consider that when we decide to use some antibiotics to reduce the risk of the emergence of resistant to reserved powerful antibiotics, we may increase resistant to that antibiotic for the other species, for example use of third generation cephalosporins will decrease the emergence of VREs but will increase the emergence of MRSA. It's demonstrated by Engemann *et al*. (2003) that the 90-day mortality rate of patients infected with Methicillin-resistant *S. aureus* (MRSA) was greater than patients infected with Methicillin-susceptible *S. aureus*. Some simple prophylactic measures such as improved hand hygiene (Marshall *et al*., 2004), preoperative skin care (60 min before incision) (Dohmen, 2006), intranasal Mupirocin application (controversial) for staph. Carriers (Young and Winston, 2006), avoidance of antibiotic application after wound closure, appropriate preoperative prophylactic antibiotics (Zoumalan and Rosenberg, 2008), appropriate catheter application (O'Grady *et al*., 2002), screening patients for the presence of preoperative colonization or perhaps community-acquired MRSA especially when risk factors are present, decolonization of MRSA strains preoperatively (if present according to screening measures (Simor and Loeb, 2004) ,screening patients for the occurrence of post discharge SSIs (Oliveira and Carvalho, 2007) research for new drugs with the ability to get the depth of wounds with less concentration and so on.

An overview to the above measures, the rate of SSIs occurrence and sequentially MDR SSIs will be decreased. But it's apparent that the overall rates of SSIs have been slowly decreasing and drug-resistant species continue to become more prevalent. So, even best tries for decrease SSIs, won't be able totally to combat with ever-increasing rate of antibiotic resistance in nosocomial infections. This fact is associated with problems in empiric therapy based strategies. Although, risk factor assessment for the present catastrophes seem well, but some studies showed that the risk factors were similar to those reported from countries with more resources.

CONCLUSION

Present results demonstrated that the total antibiotic resistance is increasing among SSIs, with an up sloping pattern, which will contact with a constant empiric antibiotic therapy. So, precise up to date antibiogram tantalize us toward balancing the rate of total antibiotic resistance to SSIs.

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