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Brief Original Article

Bacterial pericarditis and antimicrobial resistance at the Tehran Heart Center, Iran

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Abstract

Introduction: When bacterial pericarditis is suspected, urgent pericardial drainage combined with intravenous antibacterial therapy is mandatory to avert devastating, life-threatening complications. There have been scanty results on antimicrobial susceptibility of common causative microorganisms of bacterial pericarditis; most studies had small sample sizes and were performed decades ago.

Methodology: This prospective study surveyed the causative bacteria in infectious pericardial effusions and their antimicrobial susceptibility among 320 consecutive cardiac patients who underwent pericardiocentesis at Tehran Heart Center between 2007 and 2012, using the European Society of Cardiology (ESC)'s criteria.

Results: *Staphylococcus* spp. (*S. epidermidis, S. aureus, S. haemolyticus*) were the main causative organisms isolated from cultures of pericardial effusion samples. Other causative organisms were *Streptococcus* spp., *Enterococcus faecium*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*. In the cultures studied, 35% methicillin-resistant *Staphylococcus epidermidis* (MRSE) and 42.9% methicillin-resistant *Staphylococcus aureus* (MRSA) were detected. The most effective antimicrobial agents in *S. epidermidis* were gentamicin, ciprofloxacin, and cefoxitin. Clindamycin was relatively effective. *S. aureus* was highly susceptible to clindamycin and erythromycin. In cases of *S. haemolyticus* infection, clindamycin, erythromycin, cefoxitin, and ciprofloxacin were effective antibiotics.

Conclusions: In order to diminish the nascence and extension of antimicrobial-resistant pathogens, logical and optimized antimicrobial usage and monitoring in hospitals are highly recommended. It is incumbent on healthcare systems to determine current local resistance patterns by which to guide empiric antimicrobial therapy for specific infections and microorganism types.

Key words: pericardial effusion; pericarditis; MRSE; MRSA.

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Introduction

Purulent pericarditis is present in a wide variety of pathological conditions with varying etiologies such as immunosuppression and chronic diseases (*e.g.*, alcohol abuse, rheumatoid arthritis), but is commonly secondary to injury, cardiac procedures, or insult to the pericardium [1-3]. There is considerable urgency to establish a correct diagnosis, because if left untreated, the combination of tamponade and sepsis results in a mortality rate approaching 100% [4-6]. When bacterial pericarditis is suspected, urgent pericardial drainage combined with intravenous antibacterial therapy is mandatory to avert devastating, life-threatening complications [7]. The incidence of purulent pericardial effusion has declined since the era of broad-spectrum antibiotics, but incidence of this disease has not been reported accurately. However, the worldwide incidence of antimicrobial resistance with a changing spectrum of causative organisms and underlying causes is increasing [8].

To the best of our knowledge, there have been scanty reports about antimicrobial susceptibility of common causative microorganisms of bacterial pericardial effusions, and most studies had small sample sizes and were performed decades ago, while other reports did not specify the exact type of microorganisms and type of antibiotic susceptibility and resistance. Indeed, many of these studies have been conducted in developed countries, and epidemiologic aspects of them are not well known in developing countries.

In Iran, the spread of antimicrobial resistance among bacterial pathogens has emerged as an important challenge for the Iranian medical

community. The emerging of resistance might relate to reactive oxygen species [9]. There are few data regarding bacterial resistance patterns in Iran. Therefore, it is essential to prospectively evaluate the distribution and susceptibility patterns of bacterial species. Hence, we conducted this study to investigate positive bacterial growth cultures of pericardial effusions and to determine causative organisms and their antimicrobial susceptibility in Tehran Heart Center.

Methodology

This prospective study surveyed the causative bacteria in infectious pericardial effusions and their antimicrobial susceptibility in 320 consecutive cardiac patients who underwent pericardiocentesis at Tehran Heart Center, a major referral and educational cardiac hospital affiliated with Tehran University of Medical Sciences, between 2007 and 2012. Detection of the infection was based on clinical findings as well as laboratory data and other tests based on the European Society of Cardiology (ESC)'s criteria [10].

The pericardiocentesis procedure was performed by cardiac surgeons or cardiologists on a sterile situation, and fluid samples were sent to the clinical and pathological laboratory. In order to conduct bacteriological studies, cultures were performed for both aerobic and anaerobic bacteria. All culture samples referred to the laboratory were qualified by quality control criteria; samples with the results of colonization or contamination were excluded. For determining transudate versus exudate, the chemistries in the pericardial fluids were compared to those in the blood, using Light's criteria (98% sensitivity, 72% specificity) [11]. Antimicrobial susceptibility testing was performed using the Kirby-Bauer disk diffusion method, in accordance with the Clinical and Laboratory Standards Institute (CLSI)'s guidelines [12]. Briefly, data were gathered using hospital information system and laboratory information system reports, as well as the hospital's surgery database, which was computerized and prospectively recorded clinical and pathological information on standardized forms during the in-hospital period and at follow-up.

This study was approved by the research ethics committee of Tehran University of Medical Sciences. Informed written consent was obtained from all patients who underwent pericardiocentesis. The study was conducted in accordance with the principles of the Declaration of Helsinki, and patient confidentiality was maintained.

Results

A total of 320 hospitalized patients with pericardial effusion at Tehran Heart Center between 2007 and 2012 were enrolled in this study. The patients' mean age was 61.13 ± 16.09 years, and 58% of them were women. Positive bacterial growth cultures of pericardial effusions were detected in 35 (10.93%) cases (60% women, mean age 67.80 ± 14.27

Table 1. Antimicrobial susceptibility of *Staphylococcus* spp. isolated from pericardial fluid cultures between 2007 and 2012

Microorganisms	Antibiotics	Total No.	Susceptible	Intermediate	Resistant
Staphylococcus epidermidis		21			
	Erythromycin	19	6 (31.6%)	0	13 (68.4%)
	Cefoxitin	20	13 (65%)	0	7 (35%)
	Penicillin	18	4 (22.2%)	0	14 (77.8%)
	Ciprofloxacin	18	13 (72.2%)	0	5 (27.8%)
	Gentamicin	16	14 (87.5%)	1 (6.3%)	1 (6.3%)
	Clindamycin	21	12 (57.1%)	1 (4.8%)	8 (38.1%)
	Linezolid	2	2 (100%)	0	0
Staphylococcus aureus		8			
	Erythromycin	8	6 (75.0%)	0	2 (25.0%)
	Cefoxitin	7	3 (42.9%)	1 (14.3%)	3 (42.9%)
	Penicillin	2	0	0	2 (100%)
	Ciprofloxacin	3	1 (33.3%)	0	2 (66.7%)
	Gentamicin	2	0	0	2 (100%)
	Clindamycin	7	6 (85.7%)	0	1 (14.3%)
Staphylococcus haemolyticus		2			
	Erythromycin	2	2 (100%)	0	0
	Cefoxitin	2	2 (100%)	0	0
	Penicillin	1	0	0	1 (100%)
	Ciprofloxacin	1	1 (100%)	0	0
	Clindamycin	2	2 (100%)	0	0

years), and 94.28% of them were exudative. In the positive culture group, death occurred in 2 cases (5.71%); in the negative culture group, death occurred in 17 cases (5.96%).

The majority of pericardial fluid infections were caused by Gram-positive organisms (94.32%). The most common pathogens responsible for pericardial fluid infections included *S. epidermidis* (60%; 21/35), *S. aureus* (22%; 8/35), and *S. haemolyticus* (6%; 2/35). Other causative organisms were *Streptococcus* spp. (3%; 1/35), *Enterococcus faecium* (3%; 1/35), *Pseudomonas aeroginosa* (3%; 1/35), and *Acinetobacter baumannii* (3%; 1/35).

Antimicrobial susceptibility of *Staphylococcus* spp. isolated from pericardial fluid cultures is listed in Table 1. The most effective antibiotics on *S. epidermidis* strains were gentamicin ciprofloxacin, and cefoxitin, to which the susceptibility rates were 87.5%, 72.2%, and 65%, respectively. The greatest resistance was observed to penicillin (77.8%), erythromycin (68.4%), and clindamycin (38.1%).

Against *S. aureus* infections, clindamycin (85.7%) and erythromycin (75%) were the most effective antibiotics. The highest resistance rates were observed with penicillin (100%), gentamicin (100%), and ciprofloxacin (66.7%).

S. haemolyticus grew in two cultures, both of which were susceptible to erythromycin, cefoxitin, ciprofloxacin, and clindamycin, and were resistant to penicillin.

The rate of methicillin-resistant *S. epidermidis* (MRSE) was 35% (7/20), and that of methicillin-resistant *S. aureus* (MRSA) was 42.9% (3/7).

Acinetobacter baumannii as a nosocomial infection was resistant to gentamicin, imipenem, meropenem, cefepime, amikacin, and tobromycin. It was susceptible to ciprofloxacin and showed intermediate susceptibility to ceftazidime.

Streptococcus pneumonia was susceptible to gentamicin, vancomycin, and clindamycin, and showed resistance to erythromycin and penicillin.

Pseudomonas aeruginosa showed susceptibility to amikacin, gentamicin, ciprofloxacin, tobromycin, cefoxitin, and imipenem. It was resistant to ceftazidim and cefepime.

Enterococcus faecium was resistant to gentamicin, vancomycin, penicillin, and ampicillin.

Discussion

Antimicrobial resistance is generally increasing all over the world, but variations do exist among different countries, probably due to various antimicrobial patterns [13]. A number of factors contribute to this, including the severity of patient illness, predisposition to nosocomial infections, cross-transmission of pathogens characteristic of ward areas within the hospital, and the widespread use of prophylactic and therapeutic anti-infective agents. Appropriate therapy of these infections directed by local resistance data can have significant consequences for both patients and the healthcare system [14-16].

Pneumococcus is more commonly associated with contiguous spread from an intrathoracic site, while *S. aureus* is more often involved in hematogenous spread [7]. In the current study, *Staphylococcus* spp. (*S. epidermidis*, *S. aureus*, and *S. haemolyticus*) were the main causative organisms isolated from cultures of pericardial effusion samples in our hospital laboratory. From 1961 to 2000, *S. aureus*, *S. pneumoniae*, and *S. pyogenes* were the predominant isolates [17]. Though a wide variety of bacteria and fungi have been isolated as causative agents, streptococci and staphylococci were most commonly isolated [18]. Shailja *et al*., in a literature review, found that the main microorganisms isolated from pericardial fluid culture were *S. aureus* (36%), *S. Pneumonia* (21%), *H. influenza* (12%), *Streptococcus* (others) (5%), and *Neisseria. meningitides* (4%) [19]. Another study listed *Pneumococcus*, *Streptococcus*, and *Staphylococcus* as the most common microorganisms infecting the pericardium and pericardial space [20]. In 1955, at a time when bacterial pericarditis was more common, Deterling and Humphreys identified an infectious cause of pericarditis in 127 of 416 patients treated for pericarditis. A bacterial pathogen was identified in 59 of these 127 patients. *Pneumococcus* was the most common organism isolated from pericardial effusion, noted in 21 of the 59 patients [21]. The changes in the etiological diversity of pericarditis and pleural effusion were believed to be due to advances in medicine such as cardiac surgery, chemotherapy for cancer, organ transplantation, and antimicrobial therapy [22].

In the present study, MRSE and MRSA were detected in 35% and 42.9% of our cultures, respectively. The most effective antimicrobial agents against *S. epidermidis* were gentamicin, ciprofloxacin, and cefoxitin. Clindamycin was relatively effective. *S. aureus* was highly susceptible to clindamycin and erythromycin. In cases of *S. haemolyticus* infection, clindamycin, erythromycin, cefoxitin, and ciprofloxacin were effective antibiotics. In another study, the rates of MRSE and MRSA were reported to be 64% and 56%, respectively [18]. MRSA is a cause of concern in health systems all over the world, due to

its high incidence rates and associated undesirable outcomes. Treatment of staphylococcal infections is made difficult by the increasing emergence of resistance to beta-lactams and other antimicrobials, including reduced susceptibility to glycopeptides. Therapeutic alternatives exist, as *S. aureus* remains highly susceptible to vancomycin, teicoplanin, linezolid, and quinupristin/dalfopristin [23]. Mohr and Murray also asserted that vancomycin is as a safe drug and alternative agent for MRSA infections, as it has no drug-drug interactions, can be administered fairly infrequently through a peripheral vein, and is inexpensive [24]. Another study recommended that penicillin should be used for infrequent penicillin-susceptible isolates, that oxacillin and nafcillin are to be considered the major option for penicillin-resistant staphylococci, and that glycopeptides are the drugs of choice for infections caused by MRSA or MRSE. Co-trimoxazole, lincosamides, macrolides, tetracyclines, and fluoroquinolones are alternative agents, primarily in subjects allergic to beta-lactams. Newly introduced or experimental drugs, such as streptogramins (quinupristin-dalfopristin), oxazolidinones (linezolid), carbapenems (LY 333328), everninomicins (SCH 27899), and derivatives of tetracyclines (glycylcyclines), could be useful in therapy for infections caused by multi-resistant staphylococci [25].

In the intensive setting, *Acinetobacter*spp. increasingly causes nosocomial infections with mortality [26,27]. In the clinical samples, the most commonly encountered opportunistic pathogen is *Acinetobacter baumannii*. Because of its ability to colonize in the hospital setting and develop resistance, it leads to nosocomial infections that are difficult to treat [27,28]. We detected one case of *Acinetobacter baumannii* infection in purulent pericardial fluid, which could be of concern in critically ill patients.

Although infectious pericardial fluid is relatively rare in the current antibiotic era, it is a situation associated with excessive mortality (nearly 100% fatality rate) if the diagnosis is delayed. Thus, it requires high clinical surmise, early diagnosis, aggressive pericardial drainage (surgical or percutaneous), and appropriate antibiotic therapy. Furthermore, our report emphasizes the importance of physicians' insights in discerning resistant bacteria during treatment of patients and asserts the need for contriving a national strategy to control the spread of resistance in Iran. In fact, reports of updated susceptibility data from Iran are scarce. More studies are needed about the prevalence of positive bacterial growth culture in pericardial fluid and causative organisms and their frequency. Also, science needs to take further steps to resolve the experimental treatment. A limitation of our study is that we did not have access to the exact detail of underlying causes of pericarditis in all patients who had undergone cardiac surgery in Tehran Heart Center. Nevertheless, we investigated the information of all the patients who had undergone pericariocentesis due to pericardial effusion in our center using hospital information system and laboratory information system reports and the hospital surgery database.

There are few data regarding bacterial resistance patterns in Iran, and it is essential to prospectively evaluate the distribution of bacterial species isolated and their susceptibility patterns. We believe that our data, in conjunction with comprehensive surveillance data from all regions of Iran and the Middle East, will further amplify the reliability of ongoing global surveillance programs in developed countries and thus will enhance attempts to limit the spread of bacterial resistance worldwide.

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