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Extended Abstract

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Cardiology- 2018- Infective Endocarditis in Chronic Hemodialysis Patients: A Review Article for Assessment and Treatment- Oyku Gulmez- Baskent University Istanbul Medical and Research Center- Turkey

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Introduction

Keywords: Infective endocarditis; End-stage renal disease; Hemodialysis Introduction Cardiovascular Disease (CVD) represents the first cause of death (almost half of the total mortality) and morbidity in patients with end stage renal disease (ESRD), whereas infection represents the second cause of death with an incidence ranging from 12% to 22% [1,2]. Infective endocarditis (IE) is a life-threating condition associated with high morbidity and mortality. Furthermore, it is significantly more common in patients with ESRD receiving chronic hemodialysis (HD). Therefore, health-care-associated and HD-associated IE is proposed to be added as a fifth category to the historical categorical classification of IE which are native valve IE, prosthetic valve IE, IE in e.v. drug users, nosocomial IE. The current review summaries the epidemiology, pathogenesis and microbiological profile, clinical presentation and diagnosis, prognosis and management of IE in HD patients. Epidemiology The first case of IE in a HD patient was reported in 1966 [3]. Retrospective studies reported the incidence of IE in HD patients as 6% [4]. In US population, the incidence of IE in HD patients has been estimated to be approximately 308 cases/100,000 patient-years, an age-adjusted incidence ratio of 17.9 for HD patients compared with the general population (1.7-6.2 cases/100,000 patient-years). A 1 year IE French Survey found the incidence of IE in HD patients 50-60 times higher than the overall incidence of IE in France [6]. Moreover, in a study using Taiwan National Health Insurance Research Database, the incidence of IE was 201.4/100000 person-years [2]. Of note, the frequency of IE in patients receiving peritoneal dialysis (PD) is not higher when compared with the general population. However, HD is associated with a 42% higher risk of IE when compared with PD [2,5]. Pathogenesis and microbiological profile Patients with ESRD have impaired immune system because of uremia, biochemical abnormalities, malnutrition, elderly, and comorbid conditions such as diabetes mellitus and underlying systemic disease which increase the bacteremia risk [2,3]. The other risk factor for bacteremia causing IE is the presence of vascular access. Patients with ESRD receiving HD are prone to metastatic bloodstream infections due to tunneled catheters with one of the most common form as IE. Although, native arteriovenous fistula has been recommended as the preferred vascular access by National Kidney Foundation clinical guidelines, 28% of patients continue to undergo HD via central venous catheter [7]. Recurrent bacteremia because of vascular access infection during HD occurs with a rate of one episode per 100 patient-months of which IE develop in 1-12% of them [3,8,9]. Moreover, the incidence of HD access-related bacteremia is reported to be from the highest to the lowest as: patients with temporary catheter, patients with permanent central venous catheter, patients with arteriovenous grafts, and patients with native arteriovenous fistula [10]. The sources of bacteremia can be endogenous (patient's own cutaneous flora) or exogenous (hands of personnel, contaminated equipment) [3]. The prominent role of recurrent bacteremia because of vascular-access in HD patients may explain the reason of unincreased frequency of IE among PD patients when compared with general population. Left-sided endocarditis is predominant and occurs twice as often as right-sided endocarditis in HD patients. Mitral valve is more frequently affected than the aortic valve (up to 40% of cases), reaching a frequency

Prognosis Although the prognosis of IE in PD patients is significantly better than those of HD patients, mortality still remains high with reported rates ranging from 30% to 50% and have changed only a little

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during the past decade despite the improvement in medical and surgical therapy in this population [2,4,8,9]. Impaired immune system, metabolic abnormalities, comorbid conditions such as diabetes mellitus are the conditions that alter the immune defence of HD patients and possible explanations of higher mortality. Heart failure, age, renal failure, stroke at the time of presentation and S. aureus bacteremia are classical risk factors of mortality in patients with IE [16]. Recently, the presence of persistent positive blood cultures after 48-72 h of appropriate antibiotic treatment is reported to be an independent risk factor for in-hospital mortality in general population [17]. Moreover, elevated troponin levels are associated with high risk for poor outcome such as higher mortality and surgery rates, central nervous system events, more extensive infection, and local invasion of the myocardium, coronary embolism and cardiac abscess in patients with IE [18]. Presence of persistent positive blood cultures and elevated baseline troponin levels may identify high-risk patients that need more aggressive treatment. The 2015 European Society of Cardiology (ESC) guideline of IE defines the predictors of poor outcome in patients with IE as: 1. Patient characteristics: Elderly, prosthetic valve IE, diabetes mellitus, comorbidity (renal or pulmonary disease, immunosuppression) 2. Clinical complications: Heart failure, renal failure, >moderate area of ischemic stroke, brain hemorrhage, septic shock 3. Microorganism: Staphylococcus aureus, Fungi, non- HACEK Gram negative bacilli 4. Echocardiographic findings: Periannular complications, severe left-sided endocarditis, low left ventricular ejection fraction, pulmonary hypertension, large vegetation, severe prosthetic valve dysfunction, premature mitral valve closure and other signs of elevated diastolic pressures. The mortality risk factors for IE in HD patients are less clear. Mitral valve involvement is strongly associated with in-hospital mortality which may be due to clinically significant septic emboli caused by larger sizes of mitral valve vegetation's. Lower gradient across the mitral valve might have allowed the lesions to attain a larger size [15]. The other factors that are associated with higher in-hospital mortality are septic embolism specifically embolus to the brain resulting stroke, IE related to drug resistant organisms such as MRSA and vancomycin-resistant Enterococcus sp [15]. The poor prognostic factors are defined as right sided endocarditis, large vegetation size, and diabetes mellitus [4]. Management Therapy of IE in HD patients, indications and timing of the surgery, or duration of the antimicrobial therapy, remains a clinical dilemma. Pathogen specific antibiotic treatment and duration as well as surgery in selected cases should be considered according to the guidelines on IE that can apply to both patients with and without ESRD. A minimum of two sets of blood cultures should be obtained from separate peripheral venipuncture sites in order to reduce the possibility of catheter infection before empiric antibiotic therapy started. Anti-staphylococcal penicillin or first generation cephalosporin should be selected for MSSA IE. Vancomycin should not be used for the treatment of MSSA IE as it has lower bactericidal activity when compared with oxacillin or cefazolin. Conversely, treatment of MRSA starts with vancomycin possibly in combination with rifampicilin. However, treatment of MRSA IE is a growing problem, both for to maintain a though plasma level of vancomycin about 15-20 mg/L without toxicity and for the rising incidence of S. aureus strains with increase vancomycin minimal inhibitory concentration. In such conditions alternative drugs such as linezolid and daptomycin can be preferred [3]. A minimum of 4-6 weeks of parenteral therapy is required to cure IE. The 2015 ESC guideline of IE defines candidates for surgery as: 1. Patients with heart failure refractory to medical therapy, 2. Uncontrolled infection (caused by fungi or multiresistant organisms), 3. Recurrent embolic events, 4. Enlarging vegetation or >10 mm vegetation, 5. Mechanical complications such as new heart block, 6. Valvular complications such as perivalvular or aortic abscess, fistula, and valvular perforation [19]. However, there is no study which examined the issue of whether the standard indications for surgery in general population can be applied to patients with ESRD receiving HD. The decision should be made after the benefits versus risks of operation complicated with the operative mortality and morbidity for this population as HD was shown to be an independent predictor of operative and long-term mortality.

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Although high perioperative mortality and morbidity related to a more advanced stage of the disease, 25-30 % of patients require surgery during the acute phase of infection which is consistent with reports from the general population. Moreover, appropriately timed valve surgery was showed to be independently associated with reduced mortality in left-sided endocarditis. The choice of type of prostheses used for valve replacement in HD patients with IE should be individualized. Risk factors for both bleeding and thrombotic complications, life expectancy (accelerated degeneration and calcification of bioprosthetic valves), suitability for long-term anticoagulant therapy and risk of prosthetic valve reinfection have great importance while decision making the type of prostheses. Because of the limited life expectancy and tendency for bleeding complications of HD patients, bioprosthetic valves should be considered in this population.

One important consideration relates to the decision making about the removal of HD catheters in patients with IE since the effectiveness is not clearly defined and data from controlled trials are scarce. While limited number of series suggest to remove and transfer the patient on PD, the others suggest to exchange the infected catheter with a new catheter.

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