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ORIGINAL ARTICLE

Comparing clinical and laboratory findings of infective endocarditis among intravenous drug users and non-drug users

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ABSTRACT

Background: Infective endocarditis (IE) is a serious complication of intravenous (IV) drug use. During the recent decades, its incidence has been increased. The present study was designed to compare the clinical and laboratory findings of IE among IV drug users and non-drug users.

Materials and methods: Totally, 40 IV drug users and 40 non-drug users were included and their medical files reviewed. Initial data including age, sex, fever, heart murmur, systemic emboli, cough, hemoptysis, pleuretic chest pain, abscess, and the possible organism were gathered by a questionnaire.

Results: IV drug users were younger and showed a male predominance. When compared with non-drug users, right-sided IE, abscess, and history of previous antibiotic therapy before admission were more commonly found among IV drug users. Staphylococci were the most prevalent causative organism among IV drug users, while among non-drug users, streptococci were the most common agents. Heart murmur was detected more frequently among non-drug users.

Conclusion: Infective endocarditis among IV drug users is a serious entity produced mainly by S. aureus, and affects preferentially the right-side cavity. Our results emphasized on the importance of clinical characteristics of IE among IV drug users.

Keywords: *Infective endocarditis, Intravenous drug use, Clinical findings.*
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INTRODUCTION

Annually, 200 millions of people worldwide are classified among intravenous (IV) drug users, of whom 78% are living in developing countries (1). IV drug users are usually hospitalized due to acute infections (60% of cases), of which, 5-15% entails the diagnosis of infective endocarditis (IE) (2). IE has an annual incidence of 1.5-3.3 patients per 1000 IV drug users (1,2). Systemic infections, S. aureus colonization and previous history of IE are well established predisposing factors for IE (3). Cocaine-addicted patients are more prone to IE. This may be in part explained by the vasoconstrictive effect of cocaine or further drug injections (2,4). Furthermore, HIV-infected patients have a unique propensity to develop IE.

Left-sided IE occurs more frequently among non-drug users, however, the clinical syndrome of IE differs in users of IV drug. Tricuspid valve infection is most common and S. aureus is the main infecting microorganism. The diagnosis of IE usually is firmly established on the basis of the

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vegetations on transesophageal echocardiography and the presence of emboli. Other most common complaints in IV drug users with IE are fever, cough, dyspnea, and pleuretic chest pain. Heart murmurs are infrequent, and the overall mortality rate is less than 5%. Left-sided IE are usually complicated by brain abscess and splenic abscess that may lead to septic emboli. On the other hand, nasal or skin colonization of S. aureus are more frequent among IV drug users (3,5,6). Furthermore, poor hygiene predisposes IV drug users to normal flora-associated infections. Prior investigators demonstrated that among IV drug users, frequent drug injections and non-sterile drugs are even more important than immune system malfunction (7,8).

Promoting physicians' knowledge and attitude towards the common problems of IV drug use, especially IE, could prevent irreversible complications. Therefore, the aim of the present case-control study was to ascertain the clinical and laboratory findings of IE among IV drug users and non-drug users.

PATIENTS and METHODS

During a 10-year period, 40 IV drug users (case group) and 40 non-drug users (control group) who had the diagnosis of IE were randomly selected. IE was verified based on echocardiographic features and Duke criteria for IE diagnosis. Then, initial data including age, sex, fever, heart murmur, infected valve, systemic or pulmonary emboli, cough, hemoptysis, pleuretic chest pain, abscess, duration of hospitalization and the infecting microorganism were gathered by a questionnaire. Data were analyzed by SPSS for Windows (version 13, SPSS Inc., USA) and chi square and Fischer's exact tests were used, when appropriate. For all tests, significance was defined as $p<0.05$.

The study protocol was approved by the Medical Ethics Committee of Tehran Medical Science University.

RESULTS

The study population included 40 IV drug users and 40 non-drug users with a mean age (± standard deviation) of 37±9 and 48±11 years, respectively ($p<0.001$). Totally, 39 (97.5%) cases and 22 (55%) controls were male, therefore, males are more likely to develop IE ($p<0.001$).

Body temperature was significantly higher among non-drug users (38.6±0.78 vs. 36.5±0.61°C, $p<0.0001$). However, the frequency of hemoptysis (5% vs. 2.5%), cough (12.5% vs. 5%) and pleuretic chest pain (7.5% vs. 2.5%) failed to show significant differences between cases and controls.

Of 40 IV drug users, heart murmurs were auscultated in 9 (22.5%), of whom 5 were right- and 4 were left-sided. Surprisingly, 38 (95%) controls had heart murmurs, among whom 35 (92.5%) were left-sided. Thus, heart murmurs are more commonly found among non-drug users when compared with IV drug users ($p<0.001$). IV drug users developed IE in tricuspid valve (37.5%) followed by mitral and aortic valves (25% and 22.5%, respectively). Contrary, mitral valve was more commonly infected among non-drug users (40%) followed by aortic (15%) and tricuspid valves (10%) ($p<0.014$).

Among extracardiac manifestations, systemic emboli were suspected in 7 (17.5%) cases and 12 (30%) controls. Meanwhile, scattered abscesses (brain, spleen, valve ring, etc) were found in 13 (32.5%) cases and 6 (15%) controls. These differences did not reach a statistically significant level.

Totally, 10 (25%) IV drug users and 6 (15%) non-drug users had negative blood culture despite the clinical diagnosis of IE ($p<0.001$). Among IV drug users the infecting microorganisms were S. aureus (66.7%), gram-negative bacilli (13.3%), streptococci (10%), fungi (6.7%) and enterococcous (3.3%). However, the causative microorganisms of non-drug users were streptococci (58.8%), S. aureus (35.4%), gram-negative bacillus (2.9%) and enterococcous (2.9%).

A total of 18 subjects, including 12 cases (30%) and 6 controls (15%) had received antibiotic therapy in the proceeding weeks ($p<0.05$). This could explain the higher frequency of negative blood culture among IV drug users.

Finally, IV drug users had been hospitalized longer than non-drug users (15.9±5.3 vs. 12.4±3.4 days, $p<0.001$).

DISCUSSION

Infections, especially IE, are the major health concerns among IV drug users. The severity of clinical manifestations and the outcome of endocarditis in IV drug users are determined by several factors including the number of infected valves, valvular abscess, valvular rupture, the extent of valvular destruction, choice of antibiotic and metastatic involvement of other organs (2). These factors, in turn, are influenced by the nature of the causative organism and delays in diagnosis.

IE is a different entity among IV drug users. Classical peripheral manifestations including Osler's nodes and Janeway's lesions are less commonly occurred, while heart murmurs have been reported in 35% of cases at most (2,3,9).

Results revealed that younger men are more likely to develop IE. This is in agreement with prior studies (2,10,11). Similar to Chambers et al study, IV drug users may not experience fever during IE episodes, therefore, normal body temperature should not exclude the diagnosis of IE, especially among IV drug users (12). Furthermore, most of IV drug users who developed IE may not have heart murmur or they may have right-sided murmur (2).

In contrary to previous reports, our patients complained of pulmonary symptoms (cough, hemoptysis, pleuretic chest pain) less commonly. Hecht et al described the clinical features of IE among 34 IV drug users and reported fever in 97% and cough and pleuretic chest pain in more than 50% of their cases (11).

As noted earlier, the clinical picture of IE differs in IV drug users. Tricuspid valve is infected more frequently as compared to mitral valve in non-drug users (9,10,13). Levine et al detected tricuspid valve involvement either alone or in combination with other valves in 52.2% of their cases. Infection of aortic and mitral valve alone was reported in 18.5% and 10.8%, while 12.5% had developed IE of both aortic and mitral valve (9).

IE is the most common etiology of bacterimia among IV drug users. The bacterimia of IE is continuous and low grade, thus, in most instances (>80%), blood culture is positive. Five percent to 10% of patients with the clinical diagnosis of IE may have negative blood culture, usually because of previous antibiotic therapy. In our study, a total of 12 IV drug users and 6 non-drug users had received antibiotic therapy prior to their hospitalization. This could explain why more IV drug users revealed negative blood culture (25% vs. 15%). Indeed, 2 or 3 additional blood cultures should be obtained if the patients has received antibiotic in the preceding weeks and if initial blood cultures are negative.

Similar to prior reports, S. aureus was by far the most common infecting microorganism (66.7%) followed by gram-negative bacilli, streptococci, fungi and enterococcous (14-16), however, Netzer et al found Streptococcous viridens as the most frequent infecting microorganism in an analysis of 212 cases between 1980-1995 (17).

IV drug users had longer stay at hospital partly due to delays in diagnosis and further complications. The great majority of IV drug users with IE have valvular vegetations demonstrable by transesophageal echocardiography. Meanwhile, these patients may present with pleuretic chest pain caused by septic pulmonary emboli. Generally, septic complications occur more frequently among IV drug users, however, mortality rate is more or less the same as non-drug users (16,17).

In conclusion, the initial presentations of IE can be misleading among IV drug users: young adults may present with normal body temperature, negative blood culture and lack of heart murmur. The index of suspicion for IE, therefore, must be high, especially if the patient presents with scattered abscesses and right-sided heart involvement, and blood cultures should be obtained in these varied settings, particularly if antibiotic use is contemplated.

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