Endocarditis: a new reality

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Abstract

Despite a stable incidence of endocarditis (END) in recent years, the epidemiological features have changed. An increased incidence of right-sided heart diseases has emerged, associated with an increasing incidence of intravenous drug use.

Objective: a retrospective study in patients with endocarditis, diagnosed using the Duke endocarditis service (DES) criteria was carried out. Clinical and echocardiographic parameters were evaluated.

Population and methods: during the period from May 1992 to December 1995, 32 patients (25 men and 7 female, with an average age of 32.5 years), had a definite diagnostic criteria of END by DES. The clinical course and echocardiographic exams were evaluated. Epidemiological aspects, presentation, aetiological agents, evolution of the disease during hospital admission, complications and echocardiographic aspects were analyzed.

Results: all patients, except one were admitted with fever; 28 patients (27.5%) demonstrated no structural cardiac problem, 2 had congenital cardiac defects and 2 rheumatic valvular disease; 22 patients (68% were intravenous (IV) drug users. Staphylococcus aureus was the responsible aetiological agent in 16 cases.

Eight patients experienced septic embolic complications (4 pulmonary, 2 splenic, 1 digital and 1 cerebral), all patients were IV drug users.

The endocarditis was localized in the tricuspid valve in 20 patients (63%), aortic valve in 8, mitral valve in 6 and the pulmonary valve in 1 patient. The majority had involvement of one cardiac whilst only, three cases involved multiple valves. Vegetation was singular in 21 patients (66%) and multiple in 7 patients. There were five cases of major valve regurgitation: 3 aortic, 1 mitral, 1 tricuspid and 1 aortic abscess with a shunt from the left ventricle to the right atrium. Five patients (16%) required surgical correction, with good post-operative of outcomes. There was one operative mortality.

TTE was diagnosed in 31 patients (97%) and TEE was necessary in 4 patients for further evaluation namely persistent fever or haemodynamic compromise.

Conclusions: 1) – This study revealed the predominance of the right-sided endocarditis in young IV drug users without pre-existence tricuspid valvular disease, with a 25% incidence of septic embolization. Staphylococcus aureus was the predominant bacterium cultured.

2) – The initial TTE was diagnostic in all but one case, TEE was important for further information in patients with haemodynamic compromise or uncontrolled infection.

Keywords: endocarditis, Duke endocarditis service, echocardiography.

Introduction

Infectious endocarditis (IE) is a disease that affects multi-organ systems, and an early diagnosis requires a high level of clinical suspicion.[1]

The need to identify this pathology at an early stage should be emphasized as this is the only way to improve the prognosis of the disease, which when not treated, results in mortality in 100% of the cases. With the administration of a correct, prolonged antibiotherapy in hospital, mortality is around 30%.[2] Currently, despite the advances in the field of antibiotherapy and improvements in surgery in patients with IE, the overall mortality rates remain alarmingly high. The first detailed descriptions of patients with IE, reported by Osler and Horten, date back to the beginning of the century. It was only in 1981 that Von Reyn and colleagues wrote a set of clinical, laboratory and histological parameters with the purpose of identifying diagnostic categories, as clinical criteria were non-existent at that time. The acceptance of echocardiogram as a very important technique for the identification of vegetations added a new parameter to the diagnostic criteria of IE defined by DES, which are currently the most widely accepted by a vast majority of authors (*Table 1*).[3] Although the incidence of endocarditis has not increased in the recent years, its epidemiological and clinical aspects have changed

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TABLE I

Diagnostic criteria for infectious endocarditis - modified DES

***Major* criteria**
- positive blood cultures:
- most common microorganisms
- persistent bacteraemia
- evidence of endocardial involvement:
- positive echocardigram:
· vegetation;
· or abscess;
· or partial dehiscence of prosthetic valve
- new valvular regurgitation or change to a pre-existing murmur.
***Minor* criteria**
- predisposing factors:
· pre-existing heart conditions;
· use of IV drugs;
- fever
- vascular events
- immunological events
- microbiological evidence
- echocardiogram: suggestive of infectious endocarditis
Diagnosis: 2 major criteria, or 1 major and 3 minor, or 5 minor

with the emergence of a new group of patients: drug dependent patients.[4] Endocarditis in these patients has its own clinical behavior, mostly affecting the right heart, involving different etiological and infectious agents that are responsible for the infection, and clinical manifestations, complications and prognoses that are different from those of left heart endocarditis, providing a new perspective on this pathology.

The diagnostic decision of IE in an iv drug dependent patient is the responsibility of the internist, who usually treats these patients. When IE is appropriately treated, the mortality rate is significantly lower than that observed in cases of IE involving the left heart or patients with prosthetic valve.

Objective - A retrospective trial involving patients with endocarditis according to the DES definitive diagnostic criteria, with assessment of the epidemiological, clinical and echocardiographic parameters of patients admitted to the Medicine Service of Desterro Hospital.

Material and methods

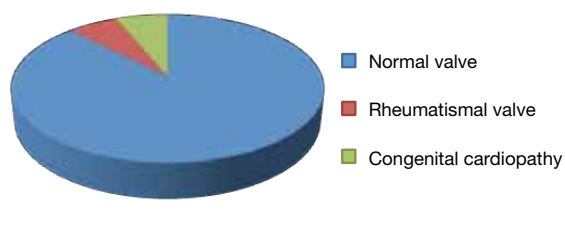
The medical records and echocardiograms of patients diagnosed with endocarditis discharged from hospital from May 1992 to December 1995 were analyzed retrospectively.

Data collection and analysis were performed based on a previously elaborated protocol, which included the following parameters: predisposing factors, form of presentation, isolated etiological agents, evolution, complications and echocardiographic aspects. M-mode and two-dimensional transthoracic echocardiograms were performed using a market Aloka SSD 725 ultrasound system, with 3 MHZ transducer, at the Medicine Service of Desterro Hospital. All the exams were performed and reviewed by two different reviewers. Whenever Doppler or transoesophageal echocardiogram was required, a Toshiba Powervision device was used, with a multi-frequency transthoracic probe and a multi-plan transoesophageal probe, carried out at the Cardiology Service of Pulido Valente Hospital. The presence of vegetation observed on the echocardiogram was defined as a distinct echogenic mass, associated with the valve or subvalvular apparatus with independent valve movement.

Results

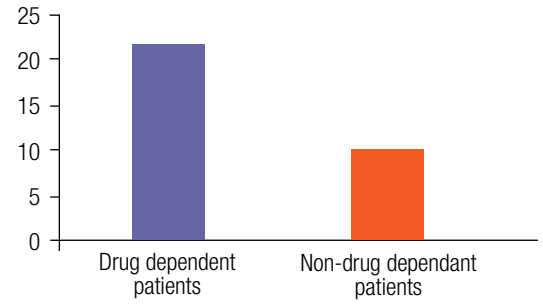
Of the 32 patients with a definitive diagnosis of endocarditis, 25 were male and 7 female, with an average age of 32.5 years.

Twenty-eight patients (87.5%) did not have any associated structural cardiopathy (there were two cases of lupus and one case of colon neoplasm), and of the four remaining patients, two had rheumatismal cardiopathy and two, congenital cardiopathy (hypertrophic cardiomyopathy and bicuspid aortic valve) (*Fig. 1*).



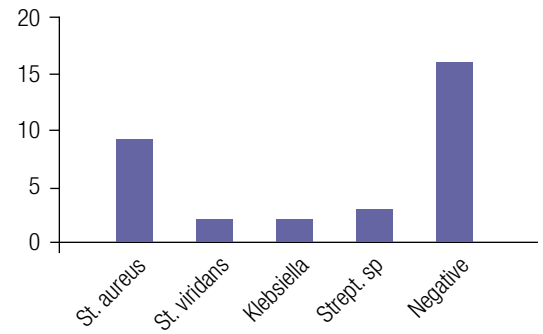
Predisposing factors I - Structural cardiopathy.

FIG. 1



Predisposing factors II - Drug dependence.

FIG. 2



Etiological agents.

FIG. 3

The main predisposing factor found was drug dependence in 22 patients - 68.7% (*Fig. 2*).

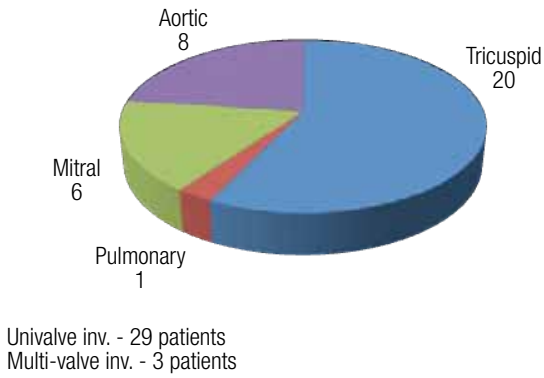
All patients were hospitalized due to febrile syndrome, except one patient who had nonbacterial thrombotic endocarditis in the context of colon neoplasm.

In half of the cases (16 patients), the isolated etiological agent was St. aureus, found exclusively in the drug dependent population; Strep viridians was found in 3 patients, Klebsiella in 2 patients, and Strep species in 2 patients. The percentage of negative blood cultures was 28% (*Fig. 3*).

Transthoracic echocardiogram was the method used in all the cases, except one.

Involvement of the tricuspid valve was prevalent in 20 patients (62.5%), followed by the aortic valve in 8 patients, the mitral valve in 6 patients and the pulmonary valve in 1 patient (*Fig. 4*).

Univalve involvement was observed in 29 patients



Valvular involvement.

FIG. 4

(91%) and only 3 patients had multi-valve involvement. The majority of vegetations were isolated in 21 patients (66%), while multiple vegetations were observed in 7 patients; vegetations with a diameter greater than 10 mm were observed in 1/3 of the patients.

The complications were divided into septic embolism and haemodynamic. The embolic events were observed only in the drug dependent population, and corresponded to the cases of larger vegetations. Four cases of septic pulmonary embolism, two of splenic emboli, one of digital emboli, and one of cerebral embolism were identified (*Fig. 5*).

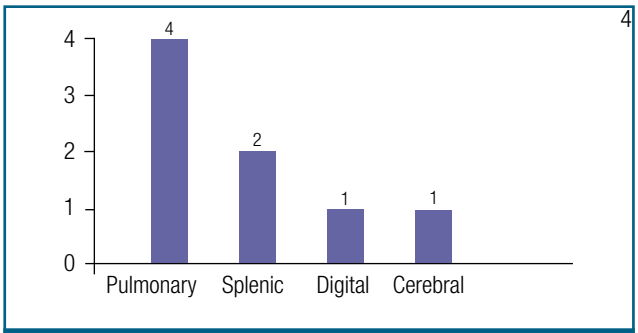
Haemodynamic complications were observed in 6 patients (18.7%), as well as 5 cases of major regurgitation with predominant involvement of the aortic valve (I.Ao-3, IM-1, IT-1) and one case of abscess of the aortic valve with a left ventricular chamber — right atrium shunt (*Fig. 6*).

Transoesophageal echogram was required in four cases in which patients had persistent fever or signs of haemodynamic involvement.

Therapy was effective for most of the patients, and heart surgery was required in five patients, with one single case of mortality in the post-operative stage (I. major aorta and abscess of aortic valve with left ventricular chamber — right atrium shunt in a non-drug dependent patient with bicuspid aortic valve).

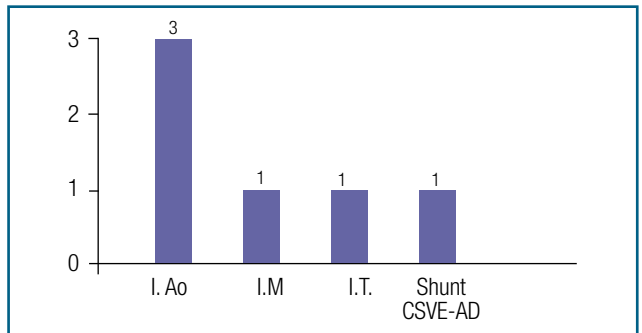
Comments

In recent years, a change in the epidemiology of IE has been observed. The control of rheumatic fever has



Septic embolic complications.

FIG. 5



Haemodynamic complications.

FIG. 5

led to a significant decrease in rheumatismal valve disease, and today an increased number of cases of IE have been seen in patients with prosthetic valves, which are treated in specialized medical and surgery cardiology institutions.

Drug dependence is currently considered one of the public health greatest problems, with important social and economic repercussions. Although it is still mostly observed in males and young individuals, drug dependence has been increasingly seen in older groups due to evolution and of the dependence and later adherence to drugs, and to the improvement in life expectancy of this population.[5] Our sample of 22 drug dependent patients is the same, showing a predominance of 19 male patients and ages ranging from 19 to 40 years (average age of 27 years). In this group, one of the reasons for hospitalization is the investigation of fever syndromes, which are sometimes a consequence of IE. The current incidence of IE in IV drug dependent patients is unknown, although a risk of 2% to 5% per year is estimated.[6] The non-specific nature of the clinical and laboratory symptoms are characteristic, with fever being the most common symptom,[7,8] as was observed in all our drug dependent patients.

Although the right and left hearts can be affected in more or less equal measure, the tricuspid valve is the most frequently affected, corresponding to 55% of cases, followed by aortic valve in 35% and the mitral valve in 30%.[4] The higher involvement of the tricuspid valve in IV drug dependent patients has led to a new concept in the pathogenesis of IE. It is known that the bacteraemia alone does not result in the formation of vegetations if there is no previous endothelial lesion. The impurities contained in drugs administered intravenously cause lesions of the endothelial valve layers, either by a mechanical or immune process, which attracts bacteria and the development of IE. Although the tricuspid valve has a greater risk of infection by mechanical effects, the left valves can similarly be affected by small particles that are not filtered by the pulmonary barrier. Chronic iv drug dependence appears to be another important factor in the establishment of these changes, as well as the patient's individual response and the virulence of the microorganisms.[5]

The aspects described above are reflected in the etiological agents, whose origin and form of transmission depend on the geographical area, prevailing practices and type of drug used. [10]

St. aureus is increasingly the organism observed in IE — 20% of non-drug dependent patients and 57% of iv drug dependent patients.[1] Other agents were identified, such as Pseudomonas aeruginosa and Candida non albicans. At the best bacteriology institutes, laboratory techniques have enabled the identification of 90% of the organisms responsible,[11] and have found 5% to 15% negative blood cultures.[12]

Our results are significantly different, with a high percentage of negative blood cultures: 22.7% — which may be due to previous antibiotherapy, or laboratory difficulties.

Echocardiogram is the method of choice for the detection of vegetations. It is also important in the identification of structural and haemodynamic complications, and for monitoring the treatment of endocarditis. However, it is not a screening method for the

diagnosis of IE in non-selected patients with positive blood cultures or patients with undetermined febrile syndrome.[13] Nevertheless, echocardiogram should be performed in all patients who are clinically suspected of having IE, including patients with negative blood cultures.[14]

The higher sensitivity of the echocardiogram in the detection of vegetations is due to the improved resolution and technical advances in this technology: M-mode is less sensitive than the two-dimensional device, and TTE less sensitive than TEE. The later allows overcoming technical difficulties related to poor sound quality, and is the method of choice for the detection of small vegetations and periannular complications, and for the diagnosis of IE in patients with prosthetic valves or myxomatous degeneration of the mitral valve.

In a large trial involving patients with confirmed IE, the calculated TEE sensitivity was 90%, while the TTE sensitivity was 63%.[15,16] However, there is one important point: the TEE does not improve the diagnosis for the detection of vegetations of the right heart in iv drug dependent patients, when compared with TTE. It is not indicated as a routine test when IE of the right heart is suspected in these patients, except in cases of poor transthoracic sound quality, association with vegetations of the left heart and suspicion of abscesses, which is in fact a rare complication in IE of the right heart.[17]

In the patients we presented, all vegetations of the right heart of iv drug dependant patients were diagnosed by TTE.

It is important to point out that although echocardiogram enables excellent sensitivity, it does not provide a specific diagnosis, either with TTE or TEE.[18] The difficulties in differentiating between an active vegetation and an old vegetation or thrombus are known, or differentiating between an infectious vegetation and a nonbacterial thrombi lesion. It is always important to bear in mind that the cause-effect relation (vegetation - IE) involves clinical correlation or anatomical and microbiological confirmation.

Characterization of vegetations based on their dimensions, mobility and location has been used by some authors to classify the risk of embolism. Larger vegetations, particularly those located in the mitral valve and associated with infection by St. aureus, have been considered as predictive of embolic events.

More recently, the Duke group refuted this concept, demonstrating that vegetations with a diameter > 10 mm were associated with 50% of embolic events compared to 42% in vegetations with a diameter < 10 mm.[19]

The therapy used for IE is basically clinical and should be initiated as early as possible. Although appropriate treatment requires the etiological agent be known and the respective antimicrobial susceptibility, the results of which usually take a long time, in the initial phase antibiotic treatment is empirical and should be targeted at the most probable microorganism.[4] The suspicion of the etiological agent is based on epidemiological and clinical factors. In our cases, patients with acute IE were all IV drug dependent, suggesting a more virulent microorganism, such as St. aureus. Therapy with vancomycin and gentamicin was initiated, with good response, except in two cases, in which surgery was (successfully) performed, due to valvular dysfunction with haemodynamic involvement. Antibiotics against methicillin-sensitive strains were not used from the start, as there was a high percentage of resistant St. aureus in the iv drug dependent patients,[20] and due to the late results of the blood cultures and respective antibiogram.

Surgery should be always be performed when clinical therapy fails, and when embolic and haemodynamic complications occur. Indications for surgery are: development of CHF, aortic or myocardial abscesses, fungal endocarditis, unsuccessful control of the infection, Staphylococcus endocarditis in prosthetic valves and valvular dysfunction with haemodynamic involvement.[2]

Controversy still remains as to the best surgical procedure to treat IE in iv drug dependent patients.[21] Nevertheless, the importance of surgery is unquestionable, whatever the chosen technique, as recently proven in a published trial involving 80 patients who underwent surgery, with perioperative mortality of 7.5% and survival after 3 and 5 years of 74% and 70%, respectively.[22] ■

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