Study of 42 cases of infective endocarditis in the HAART era in Spain

Acute infection, often associated with bacteremia, accounts for more than 50% of hospital admissions of intravenous drug abusers (IVDAs). Infective endocarditis (IE) is responsible for an estimated 5–8% of theses admissions. Moreover, in Spain, IVDAs comprise the most important risk group for acquiring HIV and hepatitis C virus (HCV), and developing IE [1,2].

In a previous study from the pre-HAART era, during a 7-year period (1986–92) [3] we diagnosed 164 episodes of IE in 136 patients, and only 21 were HIV-negative patients. Most of the HIV-infected patients had no symptoms related to their HIV (54%), and only 22% had AIDS. The onset was acute for 97% with HIV infection and 81% without HIV, fever and respiratory symptoms being the main complaints in both of them. The vegetation originated mainly on the tricuspid valve, and *Staphylococcus aureus* was recovered from most blood cultures in both groups. In HIV-infected subjects, the chest X-ray was normal in only 19%, and septic emboli were observed in 56%. The mortality rates were similar (6% in HIV-positive patients and 5% in HIV-negative patients).

The epidemiology and natural history of IE in patients with HIV infection have undergone a striking change, and the total number of cases has recently diminished. However, the symptoms, underlying conditions and etiologic organisms have not changed [4,5]. The outcome in these patients is similar to that for the general population, but those with $CD4^+$ lymphocyte counts lower than 200 mm^3 and with mixed or left-sided involvement may have a worse survival rate [6,7].

In the present study, we did a retrospective analysis of 42 cases of IE diagnosed in 36 patients during the previous 5 years (1996–2001). IE was defined according to the Durack criteria (1994) [8], and only the probable and definite IE episodes were evaluated. Data were collected with regard to the clinical, laboratory and demographic characteristics of patients, as well as results of blood cultures and data on clinical outcome. Afterwards, the influence of HIV was evaluated and the results compared with the 164 IE cases previously evaluated.

We used Student's *t*-test and Pearson chi-square to compare the patients with HIV infection and IE seen before and after the use of HAART. The statistical tests were two-tailed, and a *P*-value of less than 0.05 was considered to indicate statistical significance.

Only one of the 36 patients was not an IVDA, and most of them (81%) were men. The mean age was 31 years (range: 20–49 years), and 15 (36%) had had a previous episode of IE.

Thirty-three patients were infected with HIV (78.5%); 13 of them had AIDS, and the mean $CD4^+$ count was 226/mm^3 (range: 56–592). Only five (15%) were receiving HAART, and 97% also had HCV infection.

The onset was acute in 26 cases (62%). All the patients were febrile, 33 (78%) had respiratory symptoms (dyspnea, cough, and pleuritic pain), and 23 (55%) had a cardiac murmur. The chest X-ray was normal in only three cases (7%), and septic emboli were observed in 17 (41%), alveolar consolidation in 20 (49%), pleural effusion in 10, (25%) and heart enlargement in seven (17%). The vegetations were detected by two-dimensional echocardiography, and the tricuspid was the most frequently affected valve (34 cases, 83%). Mitral valve endocarditis was diagnosed in four cases (9.7%)—aortic in one (2.4%), and pulmonary in three (7.3%). Other findings were pericardial effusion in seven cases (16.6%), dysfunction of the left ventricle in four (9.5%), and valvular insufficiency of the affected valve in more than 50% (23 cases). Blood culture was negative in 22 patients (52.3%); there were two cases of polymicrobial IE (one *Pseudomonas putida* plus *Streptococcus viridans*, and *Streptococcus mitis* plus *Staphylococcus epidermidis*), and *Staphylococcus aureus* was the most frequently isolated organism (11 cases, 26.1%).

Patients were treated with antibiotics for 2–4 weeks, but two needed treatment for 6 weeks. Therapy was dependent on the organism's susceptibility, but initially the subjects were empirically treated with cloxacillin with or without tobramycin. Five patients died (12%). All of them had HIV, and all deaths were due to IE-related causes.

Table 1 Clinical, laboratory and demographic characteristics as well as results of blood cultures and data on clinical outcome of patients with HIV infection seen during 1986–92 compared to 1996–2001

	1986–92 143 episodes	**1996–2001 33 episodes**
No. of episodes per year[a]	20.4	6.6
Men/Women	88 (76%)/55 (24%)	26 (80%)/7 (20%)
Mean age (years)	27 (17–45)	30 (20–38)
Intravenous drug addict	143 (100%)	33 (100%)
$CD4^+$ lymphocyte count	201 ± 47 mm^3	226 ± 38 mm^3
AIDS[a]	26 (22%)	13 (39%)
Affected valve		
Tricuspid	133 (92%)	31 (93%)
Pulmonary[a]	1 (0.7%)	2 (6%)
Mitral	11 (8%)	3 (9%)
Aortic	3 (3%)	1 (3%)
Blood culture		
Negative[a]	52 (36%)	17 (51%)
Staphylococcus aureus[a]	68 (48%)	11 (33%)
Polymicrobial	7 (5%)	1 (3%)
Others	16 (11%)	4 (12%)
Favorable outcome	130 (90%)	28 (84%)
Deaths[a]	8 (6%)	5 (15%)

[a]$P < 0.05$.

There was a significant decrease in the number of episodes of IE compared to the findings of previous studies [3], probably due to a reduction in the number of IVDAs who need hospitalization. However, mortality was more elevated in the HAART era, but we have no explanation, because the proportion of left-side endocarditis, usually related to worse prognosis, was similar in both groups. The epidemiologic, clinical, radiologic and echocardiographic data were also similar. The significant increase in the proportion of negative blood cultures is also difficult to explain, but is probably due to an increase in the use of antibiotics by outpatients.

Table 1 shows data on HIV-infected patients and IE obtained during the pre-HAART and the HAART eras. Few patients are not infected by HIV in this series, so it is difficult to compare the groups.

The frequency of IE in the HAART era has diminished in HIV-positive subjects, and most of the cases are seen in patients without HAART, probably because IE is more related to drug abuse than to HIV, CD4 lymphocyte count, or HAART use. It is usually reported in the early stages, and apparently HIV has no influence on clinical manifestations, but mortality is more elevated in this group [9,10]. For these reasons, in the HAART era, IE may be an important disease with an elevated mortality rate in patients with HIV infection, although overall they will probably be active IVDAs not receiving antiviral treatment.

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