A Study of Infectious Endocarditis in Ribeirão Preto, SP - Brazil. Analysis of Cases Occurring Between 1992 and 1997

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Objective *- To analyze the epidemiology, diagnosis, clinical aspects causes and evolution of infectious endocarditis.*

Methods *- The patients analyzed were treated at the University Hospital of the Faculdade de Medicina of Ribeirão Preto-USP and had a diagnosis of infectious endocarditis defined by Duke's criteria, which classifies infectious endocarditis as native, prosthetic valve or that occurring in intravenous drug users.*

Results *- One hundred and eighty episodes of infectious endocarditis in 168 patients were observed. Echocardiograms in 132 (73.3%) provided a diagnosis of infectious endocarditis in 111 (84%) patients; mitral valves were affected in 55 (30.5%), tricuspid valves in 30 (16.6%) and the aortic valve in 28 (15.5%) patients. Hemocultures were performed in 148 (93.8%) episodes of IE. The most commonly isolated infectious organisms were Staphylococcus aureus in 46 (27.2%) patients and Streptococcus viridans in 27 (15.9%). Complications occurred in 116 (64.4%) patients and 73 (40.5%) of the patients died.*

Conclusion *– The general profile of the observed infectious endocarditis was similar to that reported in studies performed in other countries and included users of intravenous drugs. The high degree of mortality observed is not compatible with progress in diagnosis and treatment of infectious endocarditis and is probably due to the absence of diagnostic suspicion. The high frequency of fatal cases of septicemia (45.1% of deaths) in the patients studied indicates that unnoticed cases of infectious endocarditis had only been diagnosed at necropsy.*

Key words: infectious endocarditis, endocarditis in Brazil, bacterial endocarditis.

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Infectious endocarditis (IE) is a serious disease whose mortality rate is currently being reduced; in the 1990s it reached values between 19 and 23% [1-3]. The profile of the disease throughout the world has undergone modifications in recent decades due to multiple factors, including increased life expectancy coinciding with the appearance of IE in the aged; earlier diagnosis and treatment of IE leading to better prognosis; increased occurrence of the disease in persons indiscriminately using intravenous drugs, with IE affecting mainly the right side of the heart; the presence of a large number of immune compromised IE patients, in particular those with AIDS, whose prognosis is worsened by their basal disease; present use of several endoscopic medical procedures, catheters and surgeries that mobilize bacteria from the flora of the skin or the digestive apparatus towards the intravascular system, propitiating endocarditic infection; and extensive use of antimicrobial agents. Cardiac surgery used for insertion of prostheses, as well as in cases of congenital cardiopathies, is a much used therapeutic measure in IE and improves prognosis. However, such prostheses are also a preferred site for infection leading to IE [1,4].

In spite of progress in complementary examinations, the diagnosis of IE remains a challenge. In view of the great difficulty in making this diagnosis uniform, criteria taking clinical and pathological aspects of IE into account have been established. Duke's criteria (developed at Duke University, USA) are the most widely used throughout the world, among other reasons, for calling for complementary examinations and for classifying several aspects of the disease attributing different values to them [2, 5-8]. Duke's criteria are considered to possess adequate sensitivity and sufficient specificity to permit their use in epidemiological works [1,5,7,8].

Studies of IE have been scant in Brazil, especially during the past decade. Gonçalves et al. [9], described 20 cases of IE with, neurological thromboembolic manifestations, formation of aneurysms and subarachnoid hemorrhages. Tiossi and collaborators [10] analyzed 20 IE patients who died. Mansur et al. [11] analyzed 300 cases in the city of São Paulo.

The present study had as its objective the study of patients affected by IE, in order to increase awareness of the

present situation of the disease as it currently exists. To achieve this aim, epidemiological factors, risk factors, clinical presentation, etiology, complicating factors, diagnostic methods, treatment and evolution of cases diagnosed as IE at the Clinics Hospital of the Medical School of Ribeirão Preto of the University of São Paulo (HCFMRP-USP) between 1992 and 1997 were analyzed.

Methods

The files of 198 individuals diagnosed as having infectious endocarditis, collected between 1992 and 1997 at the HCFMRP-USP, a general hospital belonging to the SUS chain, serving the entire Ribeirão Preto region, part of the State of São Paulo and the southern part of the State of Minas Gerais, were retrospectively analyzed.

IE cases were defined according to Duke's criteria, respectively, as definitive, possible or rejected [5]. Possible cases had clinical and complementary examination data insufficient for a definitive diagnosis, but clearly did not qualify for rejection. Eighteen cases were rejected and not included in the study.

Episodes of IE were classified into four groups as follows: (I) patients without a history of intravenous use of drugs presenting with attacked native valves; (II) users of intravenously applied drugs; (III) carriers of a recently placed prosthetic valve (in which IE had developed within 60 days after valve replacement); (IV) carriers of pre-existing (old) prosthetic valves (in which endocarditis had developed 60 days or more after valve replacement).

Data were compiled and analyzed using the computer program Epi-Info 6.0 (CDC, USA). Statistical calculations were made by the bicaudal Fisher's exact test, and considered significant when $P<0.05$, using the Graph Pad program in Stat (Graph Pad Software Inc., San Diego, USA)

Results

One hundred and eighty episodes of infectious endocarditis occurred in 168 patients over a period of six years. As shown in table I, according to Duke's criteria, 142 (79%) were definitive cases and 38 (21%) were classified as possible cases. Among the 180 occurrences, 12 individuals had more than one episode. Table I also shows the occurrence of 121 episodes of IE in the native valve of patients without a history of the use of intravenous drugs, in 37 users of such drugs, in 3 cases of recent and in 20 cases of old prosthetic valves.

Table II shows sex, age and predisposing factors of the 168 IE patients. Male individuals (68.4%) predominated over females, especially in the group of intravenous drug users. Patient ages fell between 2 months and 106 years (mean age, 38 years). Cardiac diseases predisposing to IE were observed in 41 patients with affected native valves who did not use intravenous drugs, and in 12 intravenous drug users. Twenty-six (86.6%) of the patients using intravenous drugs were HIV-infected. Conditions predisposing towards bacteremia were found in 14 nonusers of intravenous drugs presenting with endocarditis in normal valves, and in one patient with an old prosthetic valve. Among patients presenting with endocarditis in native valves and nonusers of intravenous drugs, 9 (7.4%) had undergone dental procedures, and 5 (4.1%) had an infectious focus in the respiratory tract prior to the appearance of IE. In the group of intravenous drug users, 1 (2.5%) case of pulmonary infection as a risk factor over and above the risk inherent to drug addiction, was noted. Among patients with an old prosthetic valve, 1 (5.8%), related the existence of a predisposing dental focus.

Based on the duration of signs and symptoms, the time of infection preceding the IE diagnosis in the 180 episodes varied between one and 150 days (table III). Regarding the clinical picture the majority (87.2%) of the patients was febrile and prostrated (78.8%). Other frequent symptoms were loss of weight (44.4%) and myalgia (20.5%). Cardiac murmurs were detected in 73.3%; hemorrhagic phenomena either in the skin the mucosa, or both were found in 21.6%. Hepatomegaly was observed in 39.4% and splenomegaly in 27.7%. Complementary examinations showed anemia in 47.7% and leukocyte levels over 11,000/mm^3 in 47.2% of the patients. Proteinuria (31.6%), hematuria (27.7%) and increased levels of serum creatinine (25.5%) were also observed.

Echocardiograms were performed in 73.3% of the patients. The preferred site of attack of IE in native valves of nonusers of intravenous drugs was the mitral and aortic valves; this was also found in carriers of old prosthetic valves. The tricuspid valve was more frequently attacked (48.3%) in intravenous drug users. The site of IE was not found in 53 (29.4%) episodes (table III).

Table I – Episodes of infectious endocarditis (IE), identified by Duke's criteria in the four groups of patients studied.

Classification of IE according to Duke	NV	IVDU	RPV	OPV
Definite IE diagnosis	102	28	2	10
According to 2 major criteria	25	18	1	3
1 major and 3 minor criteria	8	4	0	2
5 minor criteria	1	0	0	0
Confirmed by anatomopathological examination	68	7*	1	5
Possible IE	19	11	1	7
Total	121	37	3	20

IE - infectious endocarditis; NV native valve; RPV - recente prosthetic valve; OPV - old prosthetic valve; IVDU - intravenous drug users. * Event selected by clinical criteria and confirmed by anatomophathological examination.

Table II – Information about the 168 patients who had IE, including predisposing factors, in the four groups of patients studied.

Patient information	NV	IVDU	RPV	OPV	Total
Nº. of patients	119	30	3	16	168
Sex (Males/Females)	75:44	28* : 2	2:1	10:6	115:53 (68.4%:31.6%)
Mean age (years)	35	29	56	43	38
Previous cardiac disease*	41	12	3	16	72(42.8%)
Previous cardiac disease	15	1	0	7	23(13.6%)
Congenital cardiopathy	14	0	0	1	15(8.9%)
Previous IE	6	10**	0	4	20(11.9%)
Mitral valve prolapse	2	1	0	0	3(1.7%)
Aortic valve stenosis	1	0	0	0	1(0.5%)
Aortic valve insufficiency	1	0	0	0	1(0,5%)
Other cardiopathies	1	0	3	4	8(4.7%)
HIV infection	4	26***	NIA[#]	NIA	30 (17.8%)
Probable foci of bacteremia	Dental 9 Pulmonary 5	Pulmonary 1	NIA	Dental 1	Dental 10(5.9%) Pulmão 6 (3.5%)

IE- infectious endocarditis; NV- native valve; RPV- recent prosthetic valve; OPV- old prosthetic valve; IVDU- intravenous drug users. *Significantly higher proportion (P=0.0009) of male individuals among IVDU compared with the sum of the other groups. ** Significantly higher proportion (P=0.0003) of patients with a history of previous IE in IVDU compared with the sum of the other groups. *** Significantly higher proportion (P<0.0001) of HIV $^{+}$ in IVDU compared with the sum of the other groups. [#] NIA – no information available.

Table III– Clinical, laboratory and diagnostic aspects of the 180 episodes of Infectious endocarditis of the four groups of patients studied.

Clinical, laboratory and diagnostic	IE	NV	IVDU	RPV	Total
Beginning of symptoms/diagnosis of IE*	21,2	25,5	7	20,3	
General condition	56	11	1	10	78(43.3%)
Regular	51	20	1	6	78(43.3%)
Poor	13	7	0	0	20(11.1%)
Fever	111	30	1	15	157(87.2%)
Prostration	97	30	2	13	142(78.8%)
Cardiac murmurs	87	29	3	13	132(73.3%)
Weight loss	56	22	0	2	80(44.4%)
Hepatomegaly	39	25	0	7	71(39.4%)
Splenomegaly	32	13	0	5	50(27.7%)
Hemorrhagic phenomena	29	8	0	2	39(21.5%)
Myalgia	22	13	0	2	37(20.5%)
Artralgia	18	8	0	0	26(14.4%)
Serum hemoglobin <10mg/100ml	59	20	20	7	86(47.7%)
Leukocytes >11000/ mm^3	59	20	2	4	85(47.2%)
Proteinuria >3,5g/dia	36	14	0	7	57(31.6%)
Hematuria	27	14	0	9	50(27.7%)
Serum creatinine >1,5mg/100ml	32	9	1	4	46(25.5%)
Serum AST >40mUI/ml	16	10	0	3	29(16.1%)
Echocardiogram/IE diagnosis	84 / 71	31/ 26	2 / 2	15 / 12	132/111 (73.3%/84%)
Endocardic attack at:					
Mitral valve	41	6	2	6	55(30.5%)
Aortic valve	19	3	1	5	28(15.5%)
Tricuspid valve	15	15***	0	0	30(16.6%)
Mitral and aortic valves	5	0	0	1	6(3%)
Mitral and tricuspid valves	1	1	0	0	2(1.1%)
Aortic and tricuspid valves	3	0	0	0	3(1.5%)
Pulmonary valve	1	0	0	0	1(0.5%)
Pulmonary artery	1	0	0	0	1(0.5%)
Membranous septum	1	0	0	0	1(0.5%)
Unknown	36	14	0	5	53(29.4%)

IE- infectious endocarditis; NV- native valve; RPV- recent prosthetic valve; OPV- old prosthetic valve; IVDU- intravenous drug users. *Average of time period (days) between the beginning of symptoms and the diagnosis of IE. ** Echocardiogram/IE diagnosis – relation between the number of patients who made the echocardiogram and the number of patients in which the examination confirmed the diagnosis. *** Significantly greater (P=0.0002) proportion of event in the IVDU group attacking the tricuspid valve-compared with the sum of the other groups.

Hemocultures were performed in 168 episodes of IE (table IV). Microorganisms were isolated in 102 cases; in five of them, more than one bacterial species was isolated. The most frequent causal agent was *Staphylococcus aureus* in 27.2% of the cases, followed by *Streptococcus viridans* in 15.9%. IE caused by gram-negative rods occurred in 5.9% of the episodes.

Complications observed in the 180 episodes of IE were: embolisms in 36.1%, septicemia in 18.3% and serious heart failure in 18.3%, respectively. Surgical replacement or repair of valves was performed in 40 (22.2%) patients. The most frequent indication for surgical treatment was serious heart failure in 36.5% of the cases; in 40% surgery was aimed at the replacement of the mitral valve, and in 35.5 % of the aortic valve. Replacement of the tricuspid valve was performed only in users of intravenous drugs (table V).

The mortality observed in the 180 episodes of IE was 40.5% (73 deaths). Deaths occurred in 42.9% of cases of IE in native valves in the absence of intravenous drug addiction, in 37% of users of intravenous drugs, in 66.5% of those with recent prosthetic valves and in 25% of those with old prosthetic valves. The main cause of death among the patients was septicemia, followed respectively by, embolic phenomena and serious cardiac insufficiency (table VI).

Discussion

Cases of infectious endocarditis (IE) were divided into four groups: those in which native valves were affected in patients without a history of the use of intravenous drugs; those in users of such drugs; those affecting patients' recent prosthetic valves and those affecting patients' old prosthetic valves. This division was based on clinical and etiological differences observed among these patients [3,6]. However, because only three cases of IE in recent prostheses were observed, the analysis of this group was rendered imprecise. In our study, 2/3 of the patients with IE were males, in agreement with an evaluation of 300 cases of IE during the 1980s in the city of São Paulo. In the United Kingdom, an analysis of 118 cases of IE [6] and in Canada a study of 135 cases [3] also showed a predominance of male patients.

The average age of our IE patients was 38 years. Mansur et al. [11] observed that the majority of their patients were between 21 and 30 years old. Cecchi et al. [12] in Italy noted an average age of 40 years of their IE patients; in Sweden, Hogevik et al.[2] found it to be 69 years. Our results, compared with those of the earlier Brazilian study in the 1980s, shows the average age of IE patients to have risen; this was also noted in other countries according to the European sources cited.

Cardiopathies prior to the onset of IE were observed in 42.8% of the cases, rheumatic causes being the most prevalent among them (table II). A higher percentage of cardiopathies occurring prior to IE have been reported [11]; Sandre et al.[3] reported 35% prior cardiopathies. Hogevik et al.[2] observed rheumatic cardiopathies prior to IE in 18% of their cases.

Foci of possible bacteremia, of dental or pulmonary origin, which could have caused IE, were reported by 9.5% of the patients. Hogevik et al. [2] described dental and gum diseases capable of producing bacteremia due to *S. viridans* in 45.4% of IE patients. In our study, bacterial foci and procedures capable of evoking bacteremia had not been properly identified.

The average time periods between beginning symptoms of IE and diagnosis were of 20-25 days (table III); this period is shorter than the one previously reported in the city

Table IV - Positivity of hemoculture and cause of the 180 cases of IE in the four groups of patients studied.

Etiologic diagnosis of IE cases	NV	IVDU	RPV	OPV	Total
Hemoculture/microorganism detection*	113/67	37/28	1/0	17/7	168/102 93.3%/60.7%
Etiological agent isolated					
Staphylococcus aureus	26	18*	0	2	46(27.2%)
Staphylococcus of the *viridans* group	17	8	0	2	27(15.9%)
Staphylococcus epidermis	6	1	0	0	7(4.1%)
Streptococci of group D					
Enterococcus	5	3	0	0	8(4.7%)
Non *enterococcus*	1	0	0	0	1(0.5%)
Other *streptococci*	4	1	0	0	5(2.9%)
Corynebacterium SP	2	0	0	0	2(1.1%)
Serratia marcescen	1	0	0	1	2(1.1%)
Hemophilus influenzae type B	1	1	0	0	2(1.1%)
Pseudomonas aeruginosa	0	1	0	0	1(0.5%)
Acinetobacter anitratus	1	0	0	0	1(0.5%)
Enterobacter cloacae	1	0	0	0	1(0.5%)
Escherichia coli	0	0	0	1	1(0.5%)
Micrococcus SP	1	0	0	0	1(0.5%)
Unidentified bacteria	0	0	0	1	1(0.5%)
Histoplasma capsulatum	1	0	0	0	1(0.5%)

IE infectious endocarditis; NV- native valve; RPV- recent prosthetic valve; OPV- old prosthetic valve; IVDU-intravenous drug users. *Hemoculture/detection of microorganisms – Nº of patients in which hemocultures were made/Nº of positive hemocultures (a small No. of hemocultures were positive for more than one microbial species). # Significantly higher (P=0.0139) proportion of *S. aureus* isolated from patients of the IVDU group compared with the sum of the other groups.

Table V – Complicating factors, surgical treatment and mortality in the 180 cases of IE in the four groups of patients studied.

Groups of IE patients	NV	IVDU	RPV	OPV	Total
Most frequent complications					
Embolism	40	18	1	7	66(36.6%)
Cerebral	19	4	0	2	25(13.8%)
Pulmonar	9	9	0	2	20(11.1%)
Extremities	8	5	0	0	13(7.2%)
Other viscera	10	2	1	2	15(8.3%)
Septicemia	26	5	0	2	33(18.3%)
Cardiac insufficiency	24	6	0	3	33(18.3%)
Shock	16	2	0	2	20(11.1%)
Intracardiac abscess	1	0	0	0	1(0.5%)
Others	0	0	1	0	1(0.5%)
Total No. of cases with complications	84	23	2	7	116(64.4%)
Surgical treatment of IE	29	7	0	4	40 (22.2%)
Indication for surgical treatment					
Cardiac insufficiency	11	2	0	1	14(36.5%)
Persistent bacteremia	2	0	0	0	2(5%)
Recurrent embolism	2	0	0	0	2(5%)
No information available	14	5	0	3	22(55%)
Type of surgical treatment used **					
Mitral valve replacement	12	1	0	3	16(40%)
Aortic valve replacement	10	2	0	2	14(35%)
Tricuspid valve replacement	0	3	0	0	3(7.5%)
Mitral valvoplasty	3	0	0	0	3(7.5%)
Tricuspid valvoplasty	1	0	0	0	1(2.5%)
Pulmonary valvoplasty	1	0	0	0	1(2.5%)
Other	7	1	0	0	7(17.5%)

IE- infectious endocarditis; NV- native valve; RPV recent prosthetic valve; OPV- old prosthetic valve; IVDU- intravenous drug users.* Total cases with complications, some more than one. **Some patients underwent more than one surgical treatment.

Table VI – Mortality due to IE of the 180 patients, according to the four groups studied

Groups of patients with IE	NV	IVDU	RPV	OPV	Total (mortality)
Nº of deaths	52	14	2	5	73 (40.5%)
Causes of death					
Septicemia	19	7	1	1	28 (38.3%
Embolism	10	0	0	0	10 (13.6%)
Cardiac insufficiency	6	1	0	1	8 (10.9%)
Cardiac insufficiency plus septicemia	4	0	0	1	5 (6.8%)
Other causes	8	4	0	1	13 (17.8%)
Not determined	5	2	1	1	9 (12.3%)

IE- infectious endocarditis; NV- native valve; RPV- recent prosthetic valve; OPV- old prosthetic valve; IVDU- intravenous drug users.

of São Paulo [11], which was 30 days or more in half of the cases. Because our results refer to cases of IE obtained 10 years later than these, it appears probable that the shorter time periods noted by us are due to progress in diagnostic methods (echocardiogram) and greater access to medical facilities. Hogenik et al. [2] in 1995 in Sweden reported an average period between onset of symptoms and IE diagnosis of 13.5 days.

Only 11% of our patients were in poor general clinical condition. This observation, although of a subjective nature, suggests that duration of the disease and degree of toxemia caused by the infection were not important determining factors in most cases. Nevertheless, this finding is not correlated with the high degree of mortality observed in these patients. Fever, prostration and the presence of cardiac murmurs were noted in over of the cases, as has also been observed by others [1,2,4,6]. However, splenomegaly, which is related to the presence of prolonged bacteremia leading to a hypertrophied reticulo-endothelial system, occurred in 27.7% of the cases studied. Due to the increased frequency of acute infections by *S. aureus* and the reduction of the period between onset and diagnosis of IE, splenomegaly is being observed less and less. Earlier studies [11] showed splenomegaly in 47% of cases. However, studies in the 1990s in other countries relate the occurrence of splenomegaly in only 0 to 12% of the cases; such low values have been related to the acute form of the illness in patients in a higher age group [2,6,10].

Petechiae and other hemorrhagic phenomena in skin and mucosa were observed in 21.6% of the patients. Others [7,6] reported similar frequencies (22% and 33.3%, respectively).

Approximately half of our patients presented with leukocytosis and anemia (Table III). Leukocytosis is a frequent finding in acute IE; normochromic and normocytic anemia are described in up to 70% of the patients [13]. In the Canadian study [3], anemia was observed in 30% of the cases. Hematuria, described as having a high incidence in IE, was observed in of our patients.

Transthoracic echocardiography, an important method for the diagnosis of IE, was performed in 73.3% of our patients; its results suggested episodes of IE with, respectively, definitive, probable or possible vegetation in 84% (table III). In some cases, in which the transthoracic echocardiogram gave negative results, examination by the transesophageal approach showed vegetations. The percentage of patients who underwent echocardiography by us can be considered low in comparison with that in other countries, 93-100% [2,3,6,12]. The diagnostic efficiency of the echocardiogram was shown to be adequate, being equal to that observed by others [11,3] (83% and 83.9%, respectively).

The site of the endocarditic attack in our patients was predominantly the mitral valve (30.5%), followed by the tricuspid and the aortic valves in 16.6% and 15.5% of the cases, respectively. Our results show an increased effect on the tricuspid valve compared with those of others [14], who observed the mitral valve to be affected in 40% of the cases, aortic in 18% and tricuspid in 10.7%. The increased attack of the tricuspid valve is due to acute IE by *S. aureus* in patients using intravenous drugs, corresponding to 19.8% of all individuals studied.

Hemoculture is a fundamental examination for the differential diagnosis of IE. In our study, hemocultures were made in samples obtained from 93.8% of the IE cases, leading to the isolation of the microorganism in 60.7% (table IV). The percent positivity was slightly lower than that observed by others [12,] (65%). In another study [2], hemoculture positivity was 75%. We believe that a large part of our negative hemoculture results were due to the concomitant or previous use of antimicrobial agents by the patients.

The causal agents most frequently found in our patients were *S. aureus* in 27.2% and *S. viridans* in 15.9%. *Streptococcus faecalis (*group D *Streptococcus, Enterococcus*) was the third cause of IE, affecting 4.7% of the cases. Gram-negative rods caused 5.9% of the IE cases, while fungal endocarditis caused by *Histoplasma capsulatum* occurred in one case. These results differ from those of others [14] in which *S. viridans* predominated in about 31% of the episodes, *S. aureus* staying in second place with about 20%. IE by gram-negative rods and fungi was of low frequency [6], similar to that observed in our study. In the study by Hogevik et al. [2] IE by *Streptococci* predominated; in other studies, mainly those in which intravenous drug users participated, the predominant microorganism was *S. aureus* [3,6,12].

Establishing treatment for IE patients and determining their sensitivity to antimicrobial agents are aims of our further work, and are presently under development.

Complications occurred in 64.4% of the cases, most frequently embolisms (36.1%), mainly in the brain and lungs (table V). Heart failure and septicemia occurred in 18% of the cases, each. Other authors [3], observed embolism in 38.5% and heart failure in 37.7% of the cases.

Surgical treatment was used in 22.2% of the patients following indication of heart failure refractory to clinical treatment in 36.5% of the patients presenting with persistent bacteremia not relieved by antimicrobial therapy, and in 5% of patients with recurrent embolism (table V). Surgical treatment was more frequently used by us than by the Swedish workers (15%) [2]. It was however less frequent than in the Brazilian study of the 1980s (34%) [14] and the Canadian study [12] with 33% of the patients, respectively. In both the Brazilian and Canadian studies, the predominant indication for surgery was serious heart failure. Mitral valve and aortic valve replacement were employed in our study in 40% and 35% of the cases, respectively.

High mortality (40.5%) was observed in our patients. Its most frequent cause was septicemia (38.3%) accompanied by heart failure in 6.8% or embolism in 13.6% (Table VI). This mortality rate was higher than that observed in the São Paulo study [11] (27.1%) and much higher than that reported in recent studies from other countries (19-23%) [2,3,14]. Septicemia was the predominant cause of death, corroborating other observations [11], but differing from those [3] in which the major cause of death was heart failure.

Our 180 cases of IE had differences in the four groups of patients. In IE attacking native valves of patients without a history of drug use, a predominance of men with an average age of 35 years was observed. One third of the patients had a history of previous cardiac disease, echocardiograms made in 69.4% of the patients being positive in 84.5 of them, mitral and aortic valves being affected. Hemocultures in 93.3% of the cases, showed a 62.8% degree of positivity and the predominant isolation of S. *aureus* in 23% of the cases and of *S. viridans* in 15%.

Complicating factors, especially embolic episodes occurred in 69.4% of the cases; due to serious cardiac insufficiency, 23.9% of these patients underwent valve, mainly mitral, replacement. Mortality of IE cases affecting native valves of nondrug users was 43.6%, the second highest among the four groups studied; the main cause of death in these patients was septicemia.

Intravenous drug users were grouped separately in view of the well-known increased risk of endocarditic infection experienced by such individuals. In 37 episodes of IE observed in this group of patients, a peculiar finding was their low average age level, of less than 30 years, in agreement with the known fact that in a population of intravenous drug addicts, young persons predominate. There was a significantly larger number of men (93.3%) in this group, compared (P=0.0009), with the sum found for the other patient groups studied. The frequency of pre-existing endocarditis was also significantly higher (33.3%, P=0.0003) in

comparison with that found in other patients. It was also noted that 86.6% were infected with HIV, a proportion significantly higher (P<0.0001), than that in other patients with IE. It must be pointed out that these drug users, although infected with HIV, probably did not have AIDS because mortality in the group was lower than that of the average of the other patients, which in their majority were immunocompetent. Echocardiograms performed in 83.7% of the drug users demonstrated IE in 83.8% of patients, the tricuspid being the most affected valve (48.3%, P=0.0002) in these cases.

Association of IE in the right heart with the use of illicit intravenous drugs is known [3,6,12,13]. In 83.7% of our cases of IE in drug users, hemocultures were made; bacterial isolation was obtained in 83.8% of them. *S. aureus* predominated in 64.2% (P=0.0139) of the cases. A similar finding has been reported by others [3], *S. aureus* having been isolated in 40% of the drug users. In our study, embolism mainly at the pulmonary level occurred in 48% of cases of drug users. Surgery, predominantly replacement of the tricuspid valve, was performed in 18.9%. A 37.8% mortality rate observed in this group was mainly due to septicemia. It is interesting to note that although high and caused by *S. aureus* in patients infected with the HIV virus, this mortality ratio was lower than the average mortality ratio in all other cases. It is known that IE of the right heart causes a more efficient local immune response and has a better prognosis.

IE cases affecting old prosthetic valves were more frequent in older patients, of average age above 43 years: 25.5% of them had had previous episodes of IE. Echocardiography performed in 75% of the cases confirmed the diagnosis in 80%, in which mitral and aortic prostheses were most affected. Hemocultures made in 85% of these cases permitted bacterial isolation of predominantly S. *aureus* and *S. viridans* (28.6% each) in 41.4%. Gram-negative rods provided for 28.6% of the infections, demonstrating the sensitivity of valve prostheses to these germs. Embolism in 35% and heart failure in 15% were the most frequent complications in these cases. Surgical treatment was effected in 20%, with a mortality ratio of 25%, the lowest observed among the four groups, caused by septicemia or serious heart failure. Other authors [3] reported a mortality of 18% in these cases, having heart failure as their major cause.

Three cases of IE in recent valve prostheses occurred in older individuals, mean age of 56 years. These patients had the highest mortality rate observed in this study, 66.6%. Others [3] reported a mortality of only 14% in patients of mean age of 59 years, in such cases.

The analysis of the 180 episodes of IE of this study showed differences in the cause and site of cardiac attack, compared with results of studies performed in the 1980s [11,14] in Brazil. Such differences also appeared in results published in recent years in other countries, especially regarding intravenous drug users [3,11]. However, the high mortality ratios observed in our study, (40.5%) do not fit into the picture of recent progress in diagnosis and treatment of IE. Taking into consideration that IE is usually fatal when not adequately controlled by antimicrobial therapy, we believe that high mortality ratios result in part from the absence of correct diagnosis and adequate therapy. This is shown by the fact that in 26.7% of the cases in our files not even echocardiography had been performed [1,13]. The low mortality ratio observed in cases of affected old prosthetic valves indicates that in this group of patients known to be of high risk, IE diagnosis was always checked for. The low degree of positive responses of hemocultures in our studies is also worth pointing out. In 39.7% of the cases, no microorganism could be isolated. Either previous or inadequate use of antimicrobial agents or both or technical laboratory problems may explain this finding. Furthermore, the high frequency of septicemia as the cause of death (45.1%) renders it likely that in many cases endocarditis may have passed unnoticed, evolving into systemic infection.

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References

1. Scheld WN, Sande MA. Endocarditis and intravascular infections. In: Mandell GL, Bennett JE, Dolin R (eds). Mandell, Douglas and Bennett's Principles and Practice of Infectious Diseases. New York: Churchill Livingstone, 1995: 740.
2. Hogevik H, Olaison L, Andersson R, Lindberg J, Alestig K. Epidemiologic aspects of endocarditis in an urban population. Medicine 1995; 74: 324-38.
3. Sandre RM, Shafran SD. Infective endocarditis: review of 135 cases over 9 years. Clin Infect Dis 1996; 22: 276-86.
4. Levison ME. Endocardite Infecciosa. In: Bennett JC, Plumm MD (eds). Tratado de Medicina Interna, 6ª Ed. Rio de Janeiro: Guanabara Koogan, 1996: 1763.
5. Durack DT, Lukes AS, Bright DK. Duke endocarditis service. New criteria for active infective endocarditis: utilization of specific echocardiographic findings. Am J Med 1994; 96: 2000-9.
6. Lamas, CC, Eykyn SJ. Suggested modifications to the Duke Criteria for the clinical diagnosis of native and prosthetic valve endocarditis: analysis of 118 pathologically proven cases. Clin Infect Dis 1997; 25: 713-9.
7. Nettles RE, McCarty DE, Corey GR, Li J, Sexton DJ. An evaluation of the Duke criteria in 25 pathologically confirmed cases of prosthetic valve endocarditis. Clin Infect Dis 1997; 25: 1401-3.
8. Olaison L, Hogevik H. Comparison of the von reyn and Duke criteria for diagnosis of infective endocarditis: A critical analysis of 161 episodes. Scand J Infect Dis 1996; 28: 399-406.
9. Rios-Gonçalves AJ, Cunha RQ, Rozembaum R, et al. Endocardite infecciosa, aneurisma (s) micótico (s), hemorragia subaracnóidea e outras lesões neurológicas. Arq Bras Med 1991; 65: 559-71.
10. Tiossi CLD, Franken RA, Rivetti LA, Brasil SAB. Endocardite infecciosa. Análise de 20 casos de óbito na Santa Casa de São Paulo. Arq Bras Cardiol 1994; 62: 403-6.
11. Mansur AJ, Grinberg M, Gallucci SDD, Bellotti G, Jatene A, Pileggi. Endocardite infecciosa: análise de 300 episódios. Arq Bras Cardiol 1990; 54: 13-21.
12. Cecchi E, Parrini I, Chinaglia A, et al. New diagnostic criteria for infective endocarditis. A study of sensitivity and specificity. European Heart Journal 1997; 18: 1149-56.
13. Sohsten RV, Kaye D. Endocardite infecciosa. In: Veronesi R, Focaccia R (eds.). Tratado de Infectologia. São Paulo: Atheneu, 1996: 633.
14. Mansur AJ, Grinberg M, Bellotti G, Jatene A, Pileggi F. Infective endocarditis in the 1980s: experience at a heart hospital. Clin Cardiol 1990; 13: 623-30.