



LETTER TO THE EDITOR

Is there a place for corticosteroids in the therapy of infective endocarditis? Report of a case and review

**KEYWORDS**

Infective endocarditis;
Corticosteroids;
Enterococcus faecalis;
Immunotherapy

Infective endocarditis (IE) is a lethal infection even in the era of antibiotic therapy and cardiovascular surgery.¹ The clinical course of IE varies from an uncomplicated infection with minor valve damage to a fulminant life-threatening condition.¹ Although immunological phenomena are present in IE there is no clinical evidence on the use of immunomodulatory therapies. Is immunomodulation beneficial or harmful in IE? We present a case of a successful outcome of a patient with IE to whom corticosteroids were given along with antimicrobial treatment.

Case-report: A 42 year old man was diagnosed with IE by *Enterococcus faecalis* according to the DUKE criteria.² The patient had a history of Bentall type surgery three years ago because of acute aortic dissection in Marfan syndrome. Echocardiography detected a slight paravalvular leakage of the prosthetic aortic valve along with a 11mm zonular aortic vegetation that had prolapsed into the left ventricular outflow area (Figure 1). Pulmonary artery systolic pressure was 15mmHg and left ventricular cardiac ejection fraction was 60%. No immunological complications of IE were present. The patient was given ampicillin (12gr/24h) plus gentamicin 1mg/kg/24h. An initial partial remission of fever was achieved, but fever relapsed (39°C) on the 4th day of treatment. Simultaneously the patient developed a fulminant purpuric macular rash without demasquation or skin detachment that progressed from the trunk and the chest to the distal extremities. Peripheral blood

eosinophilia (14%) both with slightly elevated liver enzymes were detected. No RBC casts were found on urine analysis. Blood cultures at that time were sterile and no new sign or symptom compatible with IE was found. Because of the rapid onset and expansion of the skin reaction, the severity of clinical appearance and the organ involvement, the patient was given prednisolone at a dose of 1mg/kg/day. Amoxicillin was substituted by linezolid because of the probability of b-lactam allergy. Following corticosteroid administration, skin lesions resolved within fifteen days leaving a mild skin hyperpigmentation. Prednisolone was discontinued 30 days latter including dose tapering. On day 15, linezolid was substituted by vancomycin because of a relevant myelosuppression event. The patient completed a 6-week antimicrobial course and was discharged in good clinical condition. There were no complications from the use of corticosteroids. An echocardiography examination at discharge did not reveal vegetations but only a slight paravalvular regurgitation without valve insufficiency (Figure 2). A 32-months follow up did not evidenced IE relapse or any other cardiac sustained abnormality.

Discussion

There is no official guideline for the administration of corticosteroids in patients with IE, but sporadic reports on the successful outcome of patients with IE under corticosteroids. Methyl-prednisolone (0.5g daily for 3 days followed by 30, 20 and 10 mg for the consecutive 3 days) was correlated to normalization of serum inflammatory markers and restoration of renal insufficiency in a patient with IE-dependent glomerulonephritis.³ Successful administration of prednisone (60-80mg daily) in 3 patients with immune-mediated renal insufficiency⁴ and in 2 patients with Austrian syndrome was reported.⁵ The common denominator in all cases was the microbiological cure and the successful outcome of IE. Therefore, it is possible that corticosteroids influence the clinical course of IE, but how? Bacterial adherence to activated endothelial cells stimulate

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Figure 1 Echocardiographic detection of vegetation on aortic valve. Vegetation at diagnosis.

monocytes to produce cytokine like IL-6 and procoagulant factors, hereby forming the vegetation on the endocardium.^{1,6} Corticosteroids modulate cytokine production by inhibition of transcription factors as nuclear factor kB (NFkB) and activated protein 1, of inflammatory prostaglandins and of lymphocytes apoptosis.⁷ In a methicillin-resistant *Staphylococcus aureus* (MRSA) animal experimental IE model, a combination of vancomycin plus corticosteroids was associated with less severe histopathological valve lesions compared to treatment with vancomycin alone.⁸ In a methicillin-sensitive *Staphylococcus aureus* (MSSA) IE animal model, the addition of dexamethasone to antimicrobial therapy significantly reduced blood TNF-alpha levels compared to the control.⁹ Echocardiography and histology showed less valve damage and cardiac dysfunction in the combined group even after discontinuation of treatment which was attributed to the inhibition of collagen synthesis by dexamethasone.⁹ In an older streptococcal IE model affecting tricuspid valve, dexamethasone



Figure 2 Echocardiographic detection of vegetation on aortic valve. Vegetation disappeared in re-evaluation at the end of treatment.

also prevented valve damage.¹⁰ Mortality was not affected by the addition of dexamethasone in these experimental studies.^{8–10}

In conclusion, as randomized clinical trials are not available, information on the role of corticosteroids in IE are derived from experimental studies and case-studies. Well-designed multi-center international clinical trials are required in order to evaluate the use of corticosteroids in IE. This issue is important at the era of new manifestations of the disease, such as emerging implantable cardiac device IE.¹¹ Surgical treatment for IE is by all means essential in the majority of cases, as it improves survival.¹² Probably, corticosteroids in well-established doses could enhance the favorable outcome of patients operated for IE.

Conflict of interest

No author has any conflict of interest to disclose. No financial support was provided.

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