

Prophylactic use of antibiotics and immunisations in patients with SLE

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Early diagnosis and treatment of infections in SLE is a challenge

Over the past several decades, medical research has improved our knowledge about the cause, recognition, and treatment of a variety of infectious diseases. Despite these advances, infections remain a major cause of morbidity and mortality in patients with systemic lupus erythematosus (SLE) throughout the world.¹⁻³ Almost two decades ago, the Lupus Survival Study Group examined the causes of death of 1103 patients with SLE. Infections accounted for 33% of the deaths, whereas active disease for 31%.⁴ Table 1 summarises more recent studies, demonstrating the discouraging fact that the percentage of deaths due to infection has changed little since the earlier reports.

Doctors caring for patients with SLE are left to answer the vexing question: how do we control the inflammation related to disease activity without increasing the infection rate? Considering that corticosteroids and other immunosuppressive agents used to control the underlying disease also increase the susceptibility to infections, this is indeed a difficult question.

POSSIBLE STRATEGIES

Several strategies may be helpful in decreasing the morbidity and mortality related to infections.

Simple hygiene

Perhaps the simplest strategy is to educate patients and their healthcare providers about the importance of simple hygienic measures such as hand washing in order to reduce the transmission of common infectious agents. In

addition, when possible, it is important to limit exposure to people with communicable illnesses.

Use of antimicrobial agents

The second important strategy is the prophylactic use of antimicrobial agents. In this issue of the *Annals of the Rheumatic Diseases*, Gaitonde and colleagues report their results with isoniazid (INH) prophylaxis in a group of patients with SLE in India.⁸ INH was started in all patients with SLE who were treated with "long term" corticosteroids. When compared with a similar historical cohort from some of the same researchers, the incidence of tuberculosis decreased from 11% to 2%.^{8,9}

This study had several limitations. One obvious limitation is the lack of generalisability of the benefit of INH prophylaxis in areas in which the prevalence of tuberculosis differs. In geographical areas such as the Philippines where the reported prevalence of tuberculosis in a cohort of patients with SLE was 13.7%¹⁰ or in Vietnam with a prevalence of 27% of clinical tuberculosis,¹¹ a similar strategy may be entertained. Obviously, in other areas with a high prevalence of tuberculosis, prophylaxis may also be very beneficial. On the other hand another study of 451 Greek patients with a variety of connective tissue disorders, including SLE, recommended that purified protein derivative screening with INH prophylaxis may not be necessary in patients with rheumatic syndromes who are receiving corticosteroids because of the low prevalence of tuberculosis in that cohort of patients.¹²

While there are only isolated cases of tuberculosis in patients with SLE in Western countries, tuberculosis is considered to be a growing public health hazard, especially in areas with a high prevalence of AIDS.¹³ Although prophylaxis with INH is not commonly practised, it is currently recommended in patients with positive tuberculin skin tests requiring high dose prednisone for SLE and other diseases.¹⁴ Risk factors for developing tuberculosis in patients with rheumatic diseases include the cumulative and mean daily dose of corticosteroids and a history of pulse corticosteroids treatment.¹⁵

A second limitation of the study by Gaitonde and colleagues is the lack of monitoring for liver toxicity in those patients who had no clinical symptoms suggestive of liver toxicity.⁸ With estimates of increased liver enzymes in 17% of patients taking isoniazid¹⁶ and the potential for progressive liver damage, this strategy of INH prophylaxis would not be acceptable in most Western countries.

"Infections are a major cause of mortality in SLE"

Obviously, the agents one considers using for prophylaxis are dependent on the prevalence of specific diseases in that particular group of patients. While prophylaxis against tuberculosis in Western countries may not be as much of a public health issue as in India, prophylaxis against a variety of other infectious agents is commonplace. Once previously thought to be unique to patients with AIDS, *Pneumocystis carinii* is being increasingly recognised in patients with SLE and other inflammatory disorders.¹⁷ Most patients who developed *Pneumocystis carinii* pneumonia were receiving corticosteroids and other cytotoxic agents and were lymphopenic at the time of their diagnosis.¹⁸ Strategies using a regimen of low dose trimethoprim/sulfamethoxazole three times weekly, or inhaled pentamidine monthly, should be considered in selected patients with active SLE being treated with immunosuppressive agents.^{18,19}

Table 1 Infection as a cause of death in patients with SLE

Author	Years covered	Patients (n)	Deaths (n)	Infection as primary cause of death (No (%))
Harvey <i>et al</i> , 1954 ⁵	1949-54	138	38	15 (39)
Ginzler <i>et al</i> , 1978 ⁶	1966-76	223	55	20 (36)
Rosner <i>et al</i> , 1982 ⁴	1965-78	1103	222	74 (33)
Pistiner <i>et al</i> , 1991 ²	1980-89	464	26	5 (19)
Janwityanuchit <i>et al</i> , 1993 ⁷	1980-89	537	77	23 (30)
Nossent, 1993 ³	1980-90	68	22	11 (50)

Certainly, patients with SLE who have valvular abnormalities should receive endocarditis prophylaxis before invasive dental or genitourinary procedures.²⁰ Although controversial, others have argued that because of the high percentage of patients with SLE who have endothelial damage to the heart valves (as high as 50%) in patients with SLE, antibiotic treatment should be considered in all patients with SLE who are undergoing procedures associated with transient bacteraemia in accordance with standard regimens suggested by the American Heart Association.²¹

Immunisations

The third important preventive measure is through the use of immunisations. Initially, there were reports of impaired immune response to pneumococcal vaccinations in patients with SLE,²² but more recent studies suggest that vaccinations are generally safe and effective.²³ Furthermore, antigenicity of the pneumococcus was not affected by concomitant immunosuppressive treatment.²⁴

"Pneumocystis carinii is increasingly found in patients with SLE"

For influenza vaccines, no differences in antibody response and safety were found when a group of healthy people were compared with patients with SLE.²⁵ A more recent study concluded that a protective immune response can be achieved safely in patients with SLE with both tetanus toxoid and *Haemophilus influenzae* type B in addition to pneumococcus.²³ Although vaccination in patients with SLE is felt to be safe, the presumed role of vaccine induced polyclonal B cell activation in causing or exacerbating rheumatic disease is unknown. Rheumatic syndromes temporally related to vaccination, especially hepatitis B, have been described, but a casual relationship has not been established.^{26, 27}

SUMMARY

Infections remain a serious and important cause of morbidity and mortality in patients with SLE.²⁸ Early diagnosis and treatment of infections in lupus patients is, and will remain, one of the most difficult challenges for doctors. Strategies to decrease the impact of these infections include:

- Simple hygienic measures and education aimed at both patients and doctors
- Antimicrobial prophylaxis in cohorts of patients with increased prevalence of certain infections, patients who receive heavy doses of immunosuppressive agents, or undergo procedures associated with temporary bacteraemia
- Immunisations similar to those available to the general population.

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