Effect Of Anti-Retroviral Therapy On Cutaneous Anergy In Aids

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A. Introduction

Abnormal cell mediated immunity (CMI) in advanced HIV disease results in suppressed delayed type hypersensitivity (DTH) reactions. The prevalence of cutaneous energy to challenge with common recall antigens by the Mantoux method is greater than 70% among patients with fewer than 200 CD4+ T cells(l). Anergy is a surrogate marker for abnormal CMI and limits identification of patients who have been exposed to Mycobacterium tuberculosis.

During the past two years a new paradigm for the treatment of HIV disease has emerged; one investigator has named it highly active anti-retroviral therapy (HAART)(2). This paradigm utilizes multi-drug regimens including the new protease inhibitors and monitoring treatment efficacy with viral burden assays. Initial investigations suggest that HAART results in marked improvement in CMI(2); however, the effect of HAART on the prevalence of cutaneous energy has not been evaluated systematically.

Previous studies have demonstrated significant discordance b initial and follow-up Mantoux testing in immunocompetent a patients(3). Inherent deficiencies of the Mantoux methods, th immune dysregulation in HIV disease and the booster phenomenon are possible mechanisms of this discordance. Anergy is more stable among advanced HIV disease. The spontaneous conversion rate from positivity among patients with less than 200 CD4+ T cells is

We propose to determine if HIV seropositive patients with fewer than 200 CD4+ T cells who are allergic at baseline testing are more likely than the historic control to convert to DTH positivity after one year of HAART.

B. Study design

A prospective cohort study compared to a historic control published in the literatures.

C. Study subjects

75 consecutive HIV seropositive patients at the CPMC infecti have less than 200 CD4+ T cells and cutaneous energy. Patients will be identified by their primary clinician prior to initiating HAART. Anergy is defined as 0-mm of induration to Mantoux testing with tuberculin, candida, or mumps antigen. Mantoux testing may be performed in the month preceding study entry. Patients may not have received any antiretroviral. therapy besides nucleoside monotherapy in the 6 months preceding study entry.

D. Methods

At study entry prior to initiating HAART, patients will have Mantoux testing with candida, mumps, tuberculin as described elsewhere along with measurement of T cells and viral burden. They will then be treated by HAART as deemed appropriate by their primary clinician. Follow-up Mantoux testing will be repeated when clinically indicated by their clinicians or in approximately one year if an endpoint has not been reached.

a. End-point

The primary endpoint of the study is loss of energy defined as greater than 1-mm of induration to Mantoux testing with any of the three antigens.

b. Data analysis

All data will be treated with intention to treat analysis. The proportion of patients in the study cohort who reach the primary endpoint will be compared to the historical control by chi-square analysis. The study is designed to have an 80% power to detect an improvement to 30% of subjects reaching the primary endpoint with a 5% type I error rate.

E. Risks and benefits to study subjects

There is no anticipated risk or benefit to study subjects as they will receive state of the art care as directed by their primary clinician at the infectious disease clinic. There will be no financial benefit to study subjects.

F. Limitations of study design

Possible non-compliance with anti-retroviral therapy and follow-up visits is the most likely difficulty of the study.

G. Inclusion of minority study subjects

The CPMC infectious disease clinic cares for a large number of patients who are members of ethnic and racial minorities;,therefore, we do not foresee any difficulty enrolling a sufficient number of minority patients.

H. Financing

We require no special financing for the study because it involves the use of routine clinical care.

I. Bibliography

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