Integrated Approach In Management Of HIV Patients

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INTRODUCTION

The recent advances in our understanding of the human immune apparatus have brought to fore the dynamic interplay that exists between host factors including genetic predisposition & antigen specific immune response, pathogen factors like virulence of the infecting pathogen & frequency of mutations, and drug factors like intrinsic anti-pathogen potency & the development of drug resistance which together determine outcome of the therapeutic interventions.

The cytokine microenvironment has been shown to differentially regulate HIV replication. Studies have demonstrated that HIV infection suppresses multi-lineage hematopoiesis before effects on thymopoiesis are observed and appears to have profound negative effects on systems of T-cell production. Thus the progressive fall in the CD4 cell counts & repetoire is largely due to the HIV mediated suppression of the bone marrow-thymus axis whereby the generation of new CD4 cells to replace the cells that are destroyed is suppressed. HIV infection of the CD4 cells also contributes to accelerated destruction of CD4 bearing immune cells. The progressive fall the circulating CD4 cell numbers and the resulting immune deficiency is more a reflection of the summation of the two mechanisms.

The huge success of modern chemotherapeutics in overcoming infectious diseases, wherein life cycles of various pathogens have been successfully inhibited, has resulted in focusing efforts on the similar lines in HIV therapeutics as well. Thus efforts have being focused on inhibiting the HIV life cycle with the use of ARV. However a combination of host & viral factors including the phenomenal rates of viral replication in the order of 10^9 new virions being generated each day in a chronically infected person, the development of long lived reservoirs of HIV early during primary infection & the inability of total viral suppression, have resulted in a cure being elusive with the use of ARV drugs alone. The focus has therefore shifted from a curable to treatable chronic infection. However the use of ARV has substantially improved the survival rates with reduction in morbidity & mortality.

It is now recognized that host factors together with viral factors determine the pathogenesis of HIV disease - the complex events that lead to the destruction of an HIV infected person's immune system. This realization that "host factors" including the specific immune response to the virus, non-specific factors and the individuals genetic make-up are as important to the HIV disease process as the intrinsic virulence of the virus itself. This has opened up the possibilities of manipulating these host factors in favor of the host and against the HIV in an attempt to impede HIV disease progression, and forms the basis of immune based and immune modulating therapies in the management of HIV disease.

Traditional Indian system of medicine describes a number of drugs of herbal origin which have now been documented to have immunomodulating & immunopotentiating activities in peer reviewed journals of modern medicine. Thus Withania somnifera is reported to increase the bone marrow cellularity and stimulate the proliferation of the pluripotent stem cells. Angelica galuca, Tinospora cordifolia & Astralagus membranacaus have been shown to increase the secretion of various hematopoetic growth factors like Epo, GM-CSF, & ILs, especially IL-2 which is the T-cell growth factor. Allium sativum, Curcuma longa & Glycerrhiza glabra enhance the production of cytokines like IL-10 which interferes with HIV replication, or enhance production and biological effects of beneficial cytokines like γ–INF & IL-2. These drugs also decrease the production & biological effects of harmful cytokines like IL-1 & TNF-α.

OBJECTIVES:

To study aims at integrating therapeutic options available in India so inhibit viral replication and at the same time bolster host immune responses as to be effective, durable, affordable, tolerable, facilitate compliance & adherence

METHODS:

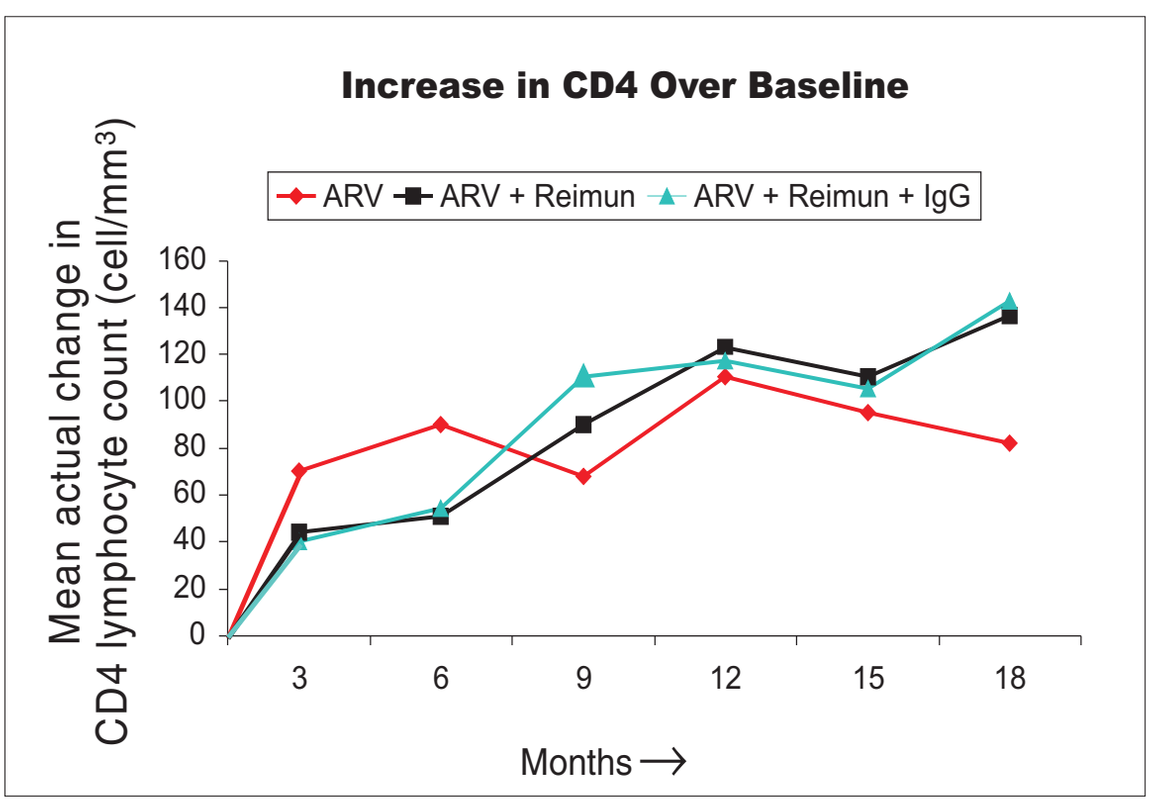
Design : Sequential Open labeled
Setting: K J Somaiya Medical College Hospital
Study period: 18 months
No. of patients: 95
Inclusion criteria: Symptomatic HIV +ve patients, CD4 < 300, Mantoux ve
Assessments: At baseline Clinical examination, Hematocrit, KFC, LFT, MT, HbsAg, X-ray chest, Sputum AFB/ PCP/ Candida, CD4 lymphocyte enumeration, Monthly Clinical examination, CBC, Quarterly MT, CD4 lymphocyte enumeration

Study Groups & Treatment Regimen

Group A(n=38) - ARV (AZT 300 mg + 3Tc 150 mg) b.i.d
Group B(n=36) - ARV (AZT 300 mg + 3Tc 150 mg) b.i.d + Herbal Immune Potentiator (Reimun)
Group C(n=21) - ARV (AZT 300 mg + 3Tc 150 mg) b.i.d + Herbal Immune Potentiator (Reimun) + IgG i.v. 0.5 gm once a week x 1 month, once in 2 weeks x 2 months, once a month

Outcome measures :Included Survival rates, Recovery period, Impact on clinical status of the patients (Karnofsky Performance Score, Weight gain, Appetite, Frequency of hospitalization), Impact on immunological status (Serially enumerated CD4 lymphocyte counts, Effect on MT, Control of secondary infections & Incidence of newer opportunistic infections), Tolerability of regimens, ADRs, Durability of improvement

RESULTS



Parameters	ARV	ARV + Reimun	ARV + Reimun + IgG
Wt. Gain	1.7 kg	8.5 kg	8.5 kg
Control of sec infec .	45 days	30 days	23 days
Recovery period	>3 mths	61 days	47 days
ADRs	2	–	–
Intolerance/ withdrawal	2	–	–
Rehospitalization	2	–	–
Death	3	–	–

Mantoux Test:
Increase in induration in mm

	0	3	6	12
ARV	-ve	1 mm	2 mm	5 mm
ARV+ Reimun	-ve	3 mm	7 mm	9 mm
ARV+ Reimun + IgG	-ve	3 mm	7 mm	9 mm

In conclusion the results of this study indicate that, while administration of ARV therapy alone Improves both the clinical status & immune status, however the durability of improvement especially with dual NRTIs is shorter. In addition ADRs & intolerance (which force withdrawal / therapy interruption) become severe limitations in the long term control of HIV disease progression.with ARV alone.

Concomitant use of herbal immune potentiator (Reimun) & IgG significantly enhance, both clinically & immunologically the durability & quantum of improvement as indicated by significant & durable increase in serially enumerated CD4 lymphocyte counts as well as significantly increased induration in the Montaux test At the same time the ARV related toxicity as well as the treatment failure rates are substantially reduced with faster control of HIV related diseases.