ORIGINAL ARTICLE

Role of Immunoglobulins for the Prevention of Serious Infections in Adults with Human Immunodeficiency Virus Infection

K. C. Mohanty, R. M. Sundrani, A. P. Lale

Abstract

Present study was conducted on eighteen HIV infected adult patients to assess the efficacy of intravenous immunoglobulins (IVIG) therapy in preventing infections in a prospective randomized out-patient clinical trial. Intravenous immunoglobulin therapy was instituted for a period of one year. Results of the therapy showed remarkable reduction in frequency of serious infections, better quality of life by reducing number of days with fever and frequency of diarrhoea, frequency and duration of hospitalization also markedly reduced.

Introduction

The depletion of $CD4^+$ helper / inducer lymphocytes is closely associated with recurrent and frequent episodes of opportunistic infections in Human Immuno–deficiency Virus (HIV) infected persons. The most frequently acquired infection is Pneumocystis Carinii pneumonia (PCP). But due to effective prophylaxis for P. carinii pneumonias, the incidence of other infections is increasing (1). The frequency of serious systemic illness with common encapsulated bacteria in HIV infected adults is increased. The increased rates of invasive disease due to streptococcus pneumoniae have been reported and recurrent episodes of pneumonia, often without an identified origin, also cause morbidity in HIV infected patients (2).

However, HIV infected patients also show dysfunction of B lymphocytes. Polyclonal hypergammaglobulinemia, which is observed in these patients, concerns the IgG and IgM production. Therefore, it is a hint for a disturbed control of immunoglobulin synthesis (3).

An ideal intravenous immunoglogulin preparation would contain structurally and functionally intact immunoglobulin molecules with normal biological half–life and a normal proportion of immunoglobulin subclasses. The preparation should contain high levels of antibody or antibodies relevant to its proposed use and there should be no contamination with vasomotor peptides, endoxin or infectious agents particularly viruses (4).

This outpatient trial was initiated to get more information about the role of intravenous immunoglobulin in prevention of bacterial infections (other than M. tuberculosis), episodes of diarrhoea,

From the Deptt. of Tuberculosis & Respiratory Diseases, Grant Medical College & Sir J. J. Group of Hospitals, Byculla, Mumbai.
Correspondence to : Director Professor K. C. Mohanty, Head of Department, Tuberculosis & Respiratory Diseases, Grant Medical College and Sir J. J. Group of Hospitals, Byculla, Mumbai 400 008.

duration and frequency of hospitalizaion and tuberculin status in adult HIV patients.

Material and Methods

The study was open, randomized out-patient clinical trial. Adult patients (older than 18 years) who had evidence of HIV infection that met criteria B and C according to definition of Centres for Disease Control and Prevention (CDC) were included in this study. Patients underwent screening of serum electrolytes, aminotransferase, creatinine, uric acid, urea, haematocrit, platelet and WBC count and erythrocyte sedimentation rate (ESR).

Patients who were enrolled in study were given 50 mg and 20 mg immunoglubulins per kg body weight initially and every 21 days thereafter respectively. The maximal infusion rates were those recommended by the manufacturers. All patients were tested before giving immunoglobulin for its hypersensitivity reaction.

All patients were closely observed during the study period. Tuberculin status was assessed at the interval of 0, 2, 6 and 12 months.

Diarrhoea was defined as 3 stools per day that lasted for more than 3 days and hospitalization for short term was defined as period of hospitalization that lasted for more than one day.

Results

The study period was from 31st January, 1996 to 31st January, 1997. The total number of patients included were 36 out of which 18 were given immunoglobulin and rest were observed as a control. Those 18 patients receiving immunoglobulin were from high income gr or whose treatment was reimbursable by employer

The patients baseline characteristics are liste Table 1. The groups were comparable with regard t and sex. Age group of both control and treatment g was suggestive of being comparable to each o alongwith distribution of males and females among th There was no difference concerning the transmissi HIV in treatment and control group. Further, there no significant difference related to Hb level, thrombo count and ESR.

All patients from treatment group were rece sulfamethoxazole–trimethoprim (TMP-SMX) thera

Table 1 – Baseline characteristics of study populatio

Characteristics	Control Group	IVIG Group
Sex : male/female ratio	12/6	15/3
Age group 18 to 25	4/3	4/2
Age group 26 to 35	7/2	9/1
Age group 36 to 45	1/1	2/0
Transmission of HIV		
No. of patients		
Heterosexual	13	11
Homosexual	1	1
Blood products	0	4
IV drugs	4	2
Sulfamethoxazole-Trimethoprim therapy defaulters	2/18	0/18
Median haemoglobin levels, gm per dl (range)	11.2 (15.6 to 7.3)	11.4 (16.8 to 7
Median platelet count $\times 10^9$/L (range)	121 (222 to 31)	132 (438 to 54)
Erythrocyte sedimentation rate, mm at the end of one hour	56 (121 to 10)	42 (78 to 6)

and control group also received it except two patients [illegible] them

The overall incidence of infections in study patients is given in Table 2.

Infections occurred in nine (50%) patients from immunoglobulin group, while thirteen (72.2%) from control group. Bacterial and viral are common opportunistic infections. We were able to isolate the bacterial organisms from both groups. The commonest organisms isolated from both groups were streptococci followed by staphylococci. In control group Pseudomonas was isolated from one patient. One case from treatment group and two cases from control group were diagnosed as Pneumocystis carinii pneumonia. Diagnosis was confirmed by bronchoalveolar lavage.

The response to treatment was very surprising in both groups. Fever with chills was present in five patients (38%) after one week in control group and none in treatment group. Respiratory signs were present in nine patients (69%) after one week in control group while in four patients (44%) in treatment group. Radiological features of consolidation were persistent more than six weeks in six patients (46%) in control group while in three patients (33%) in treatment group. Five patients (55%) were cured with two weeks of anti-microbial therapy in treatment group, while only three patients (23%) in control group. Six patients (46%) required prolonged treatment more than three weeks in control group while two (22%) in treatment group.

Table 3 indicates episodes of diarrhoea in a year and hospitalization for the same. Eleven (61%) patients from treatment group had episodes of diarrhoea less than five times while only two (11%) from control group. There were four (22%) patients from control group with more

Table 2 – Etiology of infection and response to treatment

Characteristics	IVIG Group	Control Group
Etiology of consolidation		
Streptococcus	4/9	5/13
Staphylococcus	2/9	2/13
Pseudomonas	–	1/13
PCP	1/9	2/13
Unknown	2/9	3/13
Response to treatment		
Fever with chills		
Third day	6	3
Fifth day	3	5
More than 1 week	–	5
Respiratory signs		
First week	5	4
Second week	2	3
More than 2 weeks	2	6
Persistent radiological features		
Four weeks	4	2
Six weeks	2	5
More than six weeks	3	6
Duration of treatment		
Two weeks	5	3
Three weeks	2	4
More than three weeks	2	6

Table 3- Episodes of Diarrhoea in one year and Hospitalization

Characteristics	IVIG Group	Control Group
Diarrhoeal episodes		
Less than 5	11	2
Five to 10	7	12
More than 10	–	4
Hospitalization		
Nil	12	6
Twice	4	4
Four times	2	5
More than four times	–	3

than ten diarrhoeal episodes while none from treatment group. The most important feature is hospitalization. Twelve (66%) patients were managed as out-patient basis for their diarrhoeal episodes from treatment group while six (33%) from control group. Three (16%) patients from control group required hospitalization more than four times while none from treatment group.

Table 4 shows tuberculin status of both groups. At the beginning of the study both groups were tuberculin positive. After two months of treatment, none from treatment group was tuberculin negative but 4 (22%) from control group lost tuberculin positivity. At the end of one year, 2 (11%) from treatment group were tuberculin negative while 8 (44%) from control group were tuberculin negative.

Table 4 – Tuberculin Status

Characteristic	IVIG Group		Control Group	
Tuberculin	Positive	Negative	Positive	Negative
0 month	18	0	18	0
2 month	18	0	4	4
6 month	17	1	13	5
12 month	16	2	10	8

Discussion

Studies on HIV infected children suggest that high dose of immunoglobulin therapy might be beneficial in reducing the episodes of recurrent infections. In adults, there is no such study available in India and only few studies are available from western countries, *so this is first time we are coming up with our results of treatment group who received immunoglobulins for one year.*

In our study maximum patients were from age group of 26 to 35 in both treatment and control group. A study done by Kiehl *et. al.* also showed that median age for treatment group was 31 while it was 32 for control group. In this study patients were accepted from 19 years to 48 years of age (1).

In our study, major route of transmission of HIV in both treatment and control group was hetero-sexual while study of Kiehl *et. al.* showed maximum patients from homosexual group (1). A study done by NICHD in which route of transmission in majority of children was vertical transmission with minor group of them were contact by repeated blood transfusions (6).

Kiehl *et. al.* showed Pneumocystis carinii pneumon prophylaxis in 19/57 in control group while 13/70 treatment group. In our study Pneumocystis cari pneumonia prophylaxis was comparatively mo satisfactory, no one defaulted in treatment group wh two patients defaulted in control group.

Study of Spector et al showed in children wi advanced HIV infection who received immunoglobuli 46/81 from treatment group were regular on TMP-SM prophylaxis while 28/81 from control group (7).

It is obviously seen from table 2 that in response treatment, the treatment group showed 5/9 fast recove particularly in duration of treatment compared to contr group 3/13 after two weeks.

We have documented three cases of Pneumocyst carinii pneumonia, one from treatment group and tw from control group. Inspite of patient taking TMP-SM prophylaxis, one treatment group patient develope Pneumocystis carinii pneumonia.

Our findings from table 3 confirmed the results Kiehl *et. al.* who demonstrated in randomized trial (4 adult outpatients) and Brunkhorst *et. al.* (40 adu outpatients) that the prophylactic immunglobulin thera

had no influence on the incidence of opportunistic infections while the number of serious infections and the mean time of hospitalization could be significantly reduced (1, 8). Table 4 suggests that only two patients became tuberculin negative at the end of one year from treatment group while 8 from control group.

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