



ROLE OF IMMUNOLOGICAL MONITORING IN BURNS PATIENTS

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SUMMARY : *The immunological parameters of 30 patients admitted within 6 hours of burns injury were compared with those of controls. Serum levels of immunoglobulins (IgG, IgA, IgM), complements (C3 & C4) and proteins (total & albumin) were estimated on admission and two weeks later in surviving patients. The aim of this prospective study was to find out the clinical importance of immunological monitoring in burns patients. It was observed that the initial fall and rebound increase in C3 and C4 levels were found to be highly significant.*

We conclude that IgA, IgG, C3 and C4 monitoring can help in predicting prognosis of burns patients. Based on the immunological parameters initially in nonsurvivors and two weeks later in surviving patients we can say hypothetically that prophylactic or therapeutic administration of immunoglobulins for their general or specific role could bring hopes for burns patients in future.

INTRODUCTION

The very high incidence of infectious episodes in cases of polytrauma, major burns or major surgery in spite of the continuous development of new broad spectrum antibiotics and appropriate intensive care management, indicates that a severe injury leads to acquired immunological deficiencies¹.

In burns, besides the destruction of the mechanical barrier of skin, depression of immunoglobulin and complement component levels in the early postburn period aggravate the chances of infection².

A rebound of humoral factors to levels above normal characteristically occurs in patients with uncomplicated burns, but secondary depression is commonly observed in patients who develop infections subsequently³. Periodic monitoring of immunological parameters of a patient therefore can be very informative.

The aim of the present study was to assess the role of immunological monitoring of burns patients in predicting the risks of specific complications and overall prognosis. This information in turn can indicate therapeutic or prophylactic immunotherapy to prevent or minimise septic complications in burns.

MATERIALS AND METHODS

This prospective study was carried out between September 1990 and February 1991 in 30 patients

admitted within 6 hours of burn injury, at Kasturba Medical College Hospital Burns Centre at Manipal. The study group comprised of 19 female and 11 male patients, ranging from 4 to 55 years of age. The burns were due to flame (20), scalds (4) and other causes (6). The control group consisted of 10 healthy volunteers between 20 to 40 years of age.

10 ml of blood was taken from each of the control and study group, for estimation of IgG, IgA, IgM, C3, C4, Total Protein and Albumin levels. For the study group, these values were estimated first on admission prior to any treatment, and then again in the second week, for the survivors.

Immunoglobulins and complement components were estimated by Radial Immuno Diffusion (RID) and proteins by Biuret's method. All values were standardised for a hematocrit of 45%, tabulated and statistically analysed by students "t" test.

Blood samples of all the 30 patients in the study group were studied on admission, prior to any therapy, but for the purpose of analysis, samples of those 10 patients who died before completion of two weeks were grouped as A1, and the 20 who survived as A2. For the surviving patients, blood samples were collected again after two weeks, and grouped as B. Controls were grouped as C.

OBSERVATIONS

Table 1 shows the patient-profile. Of the 10 patients who died, 7 had >60% Total Burn Surface Area

(TBSA) and 3 belonged to the 31-60% TBSA group. Table 2 shows the values of immunological parameters in controls.

Table 1

Patient Profile

% TBSA	No. of Pts	Died
10-30%	15	0
31-60%	8	3
>60%	7	7
Total	30	10

Table 2

Immunological Parameters in Control Cases

Parameter	Mean Value (mg/dl)	± S.D.
Ig G	1452.54	± 91.23
Ig A	264.43	± 79.19
Ig M	189.91	± 53.22
C3	94.30	± 15.30
C4	28.90	± 4.67
T. Protein *	6.58	± 0.97
S. Albumin *	4.63	± 0.40

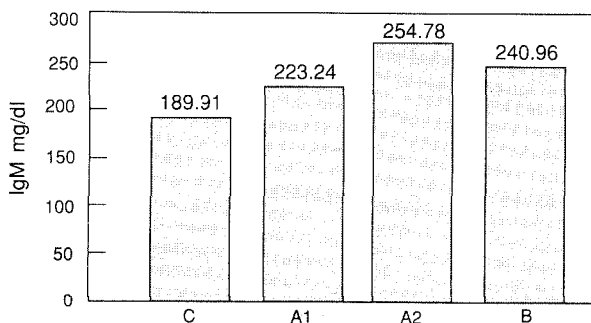
(n=10) * levels in gm/dl

The immunological parameters in the study group patients (A1, A2 & B) are compared with control values in Figs. 1-5. Important observations made in the present study as per their statistical significance are as follows:

1. The difference in IgM values of all the groups (A1, A2, B & C) in comparison to each other is not significant (Fig.1).

Fig - 1

IgM Mean Values In C*, A1*, A2* and B* Groups

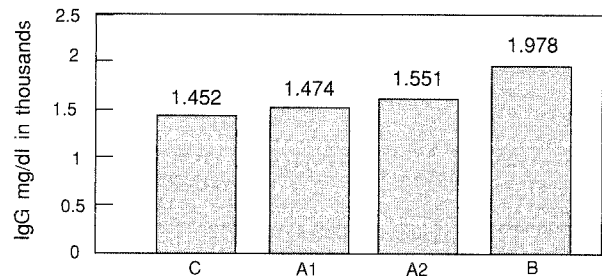


C* - Control; A1* - Day 1 sample of non-survivors; A2* - Day 1 sample of survivors; B* - Samples from survivors at two weeks

2. The change in IgG levels in all burns patients is not significant, but its increase at two weeks postburn, in surviving patients(B) is significant (Fig.2).

Fig - 2

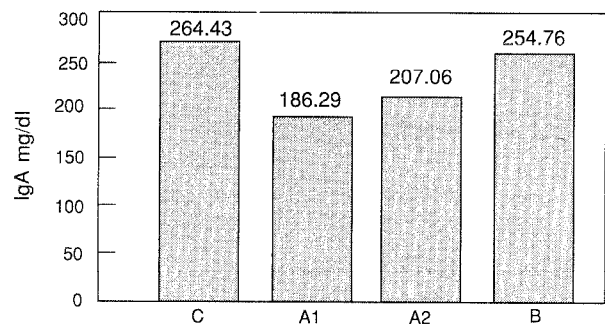
IgG Mean values in C*, A1*, A2* and B* Groups



3. The initial fall in IgA titres was highly significant in non-survivors (A1) but not significant in survivors (A2) (Fig. 3). However, at two weeks postburn (B), the rebound increase in IgA levels was highly significant (Table 3).

Fig - 3

IgA Mean Values In C*, A1*, A2* and B* Groups



4. All the changes in values of complement components C3 and C4, in the form of initial fall in all (A1 & A2) and rebound increase in survivors at two weeks postburn (B) were found to be highly significant (Fig. 4 and Table 3).

Fig - 4

C3 and C4 mean values in C*, A1*, A2* and B* Groups

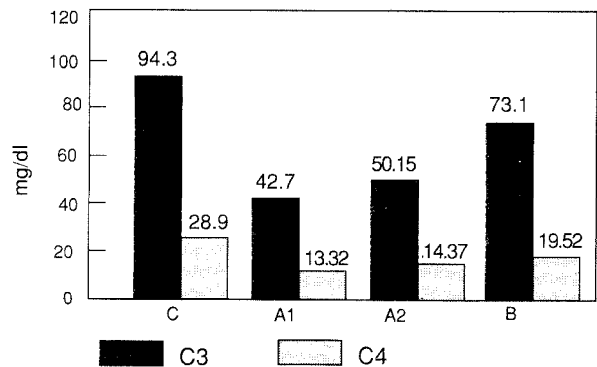


Table 3

Comparison of Immunological Parameters between Initial Values of Survivors (A2) and their Values at 2 weeks post burn(B)

Parameter	Mean values \pm S.D.	mg/dl	p value	Inference
	A2	B		
Ig G	1551.64 \pm 644.24	1978.07 \pm 546.45	0.050	S
Ig A	207.06 \pm 90.51	254.76 \pm 72.09	0.027	HS
Ig M	254.78 \pm 93.99	240.96 \pm 89.60	0.665	NS
C3	50.15 \pm 14.71	73.10 \pm 21.50	0.001	HS
C4	14.37 \pm 3.23	19.52 \pm 5.92	0.001	HS
T Prot*	5.78 \pm 1.05	5.95 \pm 1.11	0.616	NS
S Alb*	3.43 \pm 0.98	3.01 \pm 0.83	0.103	NS

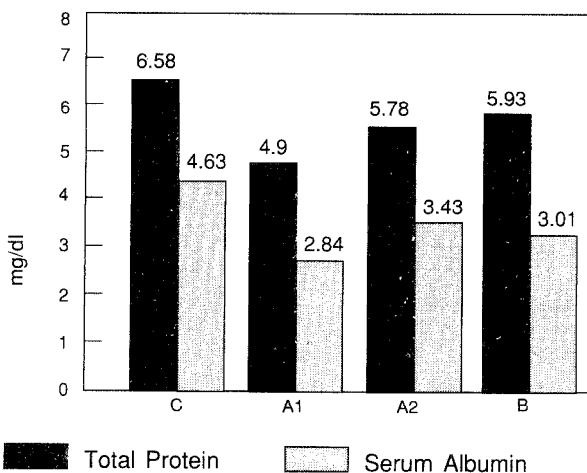
[NS = Not Significant ($p > 0.05$), S = Significant ($p = 0.05$)

HS = Highly Significant ($p < 0.05$)] * Levels in gm/dl

5. Initial fall in albumin levels in all burns patients (A1 & A2) was highly significant (Fig. 6), though its rebound increase was not significant at two weeks (Table 3). The only value found to be highly significant about total proteins was its initial fall in non-survivors (A1) (Fig. 5).

Fig - 5

Total Protein and Serum Albumin mean values in C*, A1*, A2* and B* Groups



C* - Control; A1* - Day 1 sample of non-survivors; A2* - Day 1 sample of survivors; B* - Samples from survivors at two weeks

DISCUSSION

The importance of providing nutritional support and improving the immune status of burns patients for their survival are well understood. Enough literature is available on the fact that there is immunosuppression in the burnt patient^{2,4,6}.

However, very few studies from India have been reported^{7,8}. Mehdiratta and Singh⁷ included patients with extensive burns in their study, but have analysed the immunological parameters in relation to various types of burn wound infection. Menon et al⁸ had selected patients with 10%-40% TBSA burns, thus excluding extensive burns. However, they did suggest that IgG levels could be related to the prognosis of burns patients. The rise in IgG levels at two weeks postburn, in surviving patients in our study proves that monitoring of IgG values can be of prognostic importance. Munster⁹ observed that the immunological alterations in burns are dose-related i.e. with minor burns the alterations were minor and with major burns they were major. This finding was confirmed in our study too (Fig - 3-5).

Functions of different immunoglobulins in the body are highly specific. IgG provides the bulk of the immunity to most infective agents. The fact that there was a highly significant rise in IgG values ($p = 0.006$) in the surviving patients at two weeks postburn, indicates that raised IgG could have played an important role in fighting against infection and preventing fatal septicaemia.

Hershman et al¹⁰ suggested focussed immunotherapy such as specific replacement of these proteins to help combat infection. We strongly feel that periodic monitoring of IgG levels could guide the time and need for therapeutic IgG support.

IgA is a secretory immunoglobulin which keeps harmful pathogens out of the body. The harmful pathogens act as antigens and if they reach the respiratory system, IgA being the secretory antibody (present on the surface epithelium of the respiratory tract) combines with the antigen, to form nonabsorbable antigen-antibody complexes, which are disposed of by external secretory mechanisms. We observed that more the fall in IgA values, worse was the prognosis and a rebound rise in their values indicated better prognosis. The highly significant drop in initial IgA values in our patients, particularly of those who died of Adult Respiratory Distress Syndrome (ARDS) perhaps suggests that therapeutic administration of IgA could prevent fatal respiratory tract complications (like in patients with inhalation injury).

IgM was found to be of no significance in either the immediate postburn period or later. Since IgM is suggested to be the first line of defence capable of prompt antibody production against particulate antigens like bacteria, we feel, IgM levels would show alterations only in samples from patients with invasive wound sepsis or septicaemia.

The "complement system" plays an important role in defence reactions. Complement activation promotes acute inflammation, recruits leucocytes, and killing of pathogens by phagocytosis, lysis or release of toxic products¹¹. Absence or deficiency of the complement system reduces many inflammatory reactions. Robins² stated that chemotaxis and phagocytosis are dependent on complements, levels of which are reduced in a large burns wound. In this study, we observed a highly significant lowering of serum C3 and C4 levels ($p=0.000$) soon after burn injury in all patients. However, the initial fall in C3 and C4 levels was more in nonsurvivors (A1) than in survivors (A2). Therefore it appears that gross depletion of complement components in large burns could be responsible for compromised immune defence reactions of the body.

The rebound return of C3 and C4 to levels normal or above normal levels in surviving patients could be used as an indicator of favourable prognosis. Therefore, C3 and C4 levels should be routinely done for immunological monitoring of all burns patients.

A fall in total proteins was seen in all patients in this study, but this was statistically significant only in A1 group (nonsurvivors). Albumin levels, though significantly lower in all the three groups (A1, A2 and B), were lowest in the non-survivors (A1). Fall in total protein and albumin levels in A1 and A2 groups has been attributed to loss of protein, specifically albumin in the form of burn wound exudate. After two weeks, in surviving patients (B) albumin levels were still below normal, although total proteins had increased beyond initial levels (Table 3). Cell death anywhere in the body induces local cellular and vascular reactions, and messengers carried to the liver induce a shift in the metabolism of hepatocytes to synthesize lesser amounts of transport proteins (e.g. albumin) and more of protective proteins (globulins) thus reversing the A/G ratio. However the importance of total protein and albumin estimation as immunological parameters would be negligible, if direct assay of immunoglobulins and complement component levels is feasible.

CONCLUSIONS

We conclude that:

1. "Immunological monitoring" of burns patients should be routinely done if facilities exist because:-
 - a) Reduction in IgA, C3 & C4 levels in burns patients, in the immediate postburn period

indicates the degree of immunosuppression, and perhaps the need for therapeutic administration of immunoglobulins.

- b) Return of immunoglobulin and complement components to near normal or above normal levels at two weeks postburn indicates a favourable prognosis.
2. Total serum protein and albumin estimations may grossly reflect the status of immunoglobulin and complement functioning in the body, since they are basically proteins. This is important if facilities for immunoglobulin and complement assay are not available.
3. Hypothetically, we presume that therapeutic administration of a specific immunoglobulin as indicated by assays may help in improving the prognosis of burns patients.

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