Serum Immunogllobulin G Levels in Graves' Disease Patients at Various Stages of Antithyroid Therapy

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Thirty six patients with Graves' disease (GD), diagnosed on the basis of clinical examination and appropriate laboratory tests were classified into three groups (A-C): Group A: twelve newly diagnosed Graves' disease patients; Group B: twelve hyperthyroid Graves' disease patients on antithyroid drug therapy and Group C: twelve Graves' disease patients who had been rendered euthyroid with antithyroid drug (ATD) therapy. Serum IgG was determined by radial immunodiffusion method using commercially available kits (The Binding Site UK). The mean IgG in newly diagnosed patients with GD (Group A) was 18.78±1.81. It was 22.75±1.89 in hyperthyroid GD patients on drug therapy (Group B), 14.3±0.8 in GD patients who were rendered euthyroid with drug therapy (Group C) and 11.85±0.72 in normal controls. The IgG level of group A patients were not significantly different from those of group B. However, the levels of IgG and IgA were significantly low in group C Graves' disease patients as compared to group A patients. A significant reduction in IgG level in Graves' disease patients who were rendered euthyroid after antithyroid drug therapy as compared to newly diagnosed Graves' disease patients indicate the immunosuppressive effect of antithyroid drug therapy.

Key words:Graves disease, antithyroid therapy

Endocrine autoimmunity is characterised by the appearance of strictly organ specific or even cell-specific autoantibodies in the serum, reacting with apparently normal constituents of the affected gland[1]. Autoantibodies to thyroid stimulating hormone (TSH) receptor on the surface of thyroid epithelial cells, which mimic the action of TSH but without negative feedback control are believed to be the direct cause of hyperthyroid state in Graves' disease[2,3].

Graves' disease is an organ specific autoimmune diseass[4] It is a multisystem disorder characterized by one or more of three pathognomonic clinical entities: hyperthyroidism with diffuse goiter, infiltrative ophthalmopathy and occasionally infiltrative dermopathy[5] Synonyms include Exophthalmic goiter, Toxic diffuse goiter, Basedow's disease, Parry's disease. It is hypothesized that the basic defect necessary for the development of Graves' disease is genetically induced, organ specific defect in suppressor T lymphocytes function which allows the immune response to occur[7]. Thyroid stimulating hormone receptor autoantibodies (TSHRAb) which stimulate the thyroid are found almost exclusively in patients with Graves' disease[8]. Furthermore if TSHRAb persist in circulation of patient during a course of antithyroid drug therapy, discontinuation of therapy almost invariably leads to relapse of the hyperthyroidism. It has been demonstrated that they mostly belong to IgG class[9]. Therefore all of these autoantibodies may contribute to raised serum IgG level. These TSHRAb have been proved to be IgG in nature[10]. Weetman et al[11] demonstrated that all of 11 serum tested showed thyroid stimulating activity restricted to IgG1. Furthermore light chain type was found to be lambda in about 99%[11] and of Kappa in 99.5% of the patients with GD[13], supporting the idea that GD may be the result of oligo or possibly monoclonal responses at the B cell levels.

A total number of fifty one subjects, thirty six patients with Graves' disease (GD) and fifteen normal controls, were included in this study. They were classified into the following groups.

Group A: It consisted of twelve newly diagnosed GD patients.

Group B: It comprised twelve GD patients who were on atnithyroid drug treatment but yet not rendered euthyroid.

Group C: It included twelve GD patients who had been rendered euthyroid with the antithyroid drug therapy.

Group D: Fifteen normal controls, age, sex and socioeconomical status matched, not suffering from any endocrine disease or systemic ailment were included in this group.

The GD patients were selected from the Thyroid Clinic Mayo Hospital and Institute of Nuclear Medicine and Oncology, Lahore. Diagnosis of GD based on history and clinical findings (Appendix I), was confirmed by appropriate laboratory tests serum thyroxine (T_4) measurement by radioimmunoassay (RIA), serum tri-iodothyronine (T_3) measurement by RIA and serum thyroid stimulating hormone (TSH) by RIA.

From the antecubital vein of each individual, approximately 2.5 ml of blood was collected aseptically using disposable syringes. The blood was allowed to clot and then centrifuged for 10 minutes at 2500 revolutions per minute. The serum thus obtained was separated in properly labelled sterilized vials and stored at -20oC till tested.

Estimation of immunoglobulins G

Serum IgG was determined by radial immunodiffusion

method using commercially available kits (The Binding Site - UK).

Preparation of a Standard Curve

One linear graph paper was used to construct standard curve for IgG. The square of diameters of precipitation rings obtained with three references sera of known concentrations were plotted on ordinate against the concentration of each standard (mg/L) on abscess. This showed a linear relationship (Fig.1).

the values of IgG (mg/L) of patient samples were determined by locating the square of diameters of precipitation ring of each sample on the related curve. This value was converted into g/L by dividing it by 1000.

Results

Table 1 shows the mean IgG±SE level in GD patients and normal controls. The mean IgG in newly diagnosed patients with GD (Group A) was 18.78ñ1.81. It was 22.75±1.89 in hyperthyroid GD patients on drug therapy (Group B), 14.3±0.8 in GD patients who were rendered euthyroid with drug therapy (Group C) and 11.85±0.72 in normal controls. There was no statistically significant difference in the mean value of IgG between group A and group B. There was statistically significant difference between groups A and C, between groups A and D, between groups B and C, between group B and D and between groups C and D.

Discussion

In the present study a significant difference in the level of IgG, between GD patients and normal controls was observed. Raised levels of IgG in GD have been reported by several other workers[14]. This may be due to the presence of autoantibodies, thyroidal as well as non thyroidal. The former includes TSHRAb, MSAb, TGAb, TGI and others while the latter may include antinuclear autoantibody, rheumatoid factor, autoantibodies to insuline. All of them are detected with high frequency in AITD[15]. It has been demonstrated that they mostly belong to IgG class[9] Therefore all of these autoantibodies may contribute to raised serum IgG level. The TSHRAb are definitely contributing factor, high levels of which has been observed in GD patients in the present study as has been discussed earlier. These TSHRAb have been proved to be IgG in nature[10].

There was no significant difference in the levels of IgG in newly diagnosed GD patients and hyperthyrooid GD paients on drug therapy. Zosin et al[(14)] has also demonstrated no significant difference in the levels of serum IgG after short-term antithyroid drug therapy. A significant difference was observed in GD patients who were rendered euthyroid as compared to newly diagnosed GD patients in this study. This reflects the immunosuppressive effect of ATD.

It was concluded from this study that long term therapy is needed in Graves' disease. This finding is supported by Allanic et al[16] who are also of the opinion to use long term (more than 6 months) drug treatment for Graves' hyperthyroidism to achieve the desired immunological effect.

Table 1. Serum IgG levels in GD patients and normal controls

Group	Serum IgG Levels (G/L)		
	Male	Female	All subjects
A	19.4±4.6 (n=4)	18.47±1.76 (n=8)	18.78±1.81 (n=12)
B	18.74±2.16 (n=5)	25.77±2.41 (n=7)	22.75±1.89 (n=12)
C	13.12ñ±.72 (n=5)	15.14±0.59 (n=7)	14.3±0.8 (n=12)
D	11.5±1.56 (n=6)	12.08±0.7 (n=9)	11.85±0.72 (n=15)

Statistical Analysis

A vs B = NS, A vs C = S, A vs D = S, B vs C = S B vs D = S, C vs D = S

S = Significant NS= Not significant

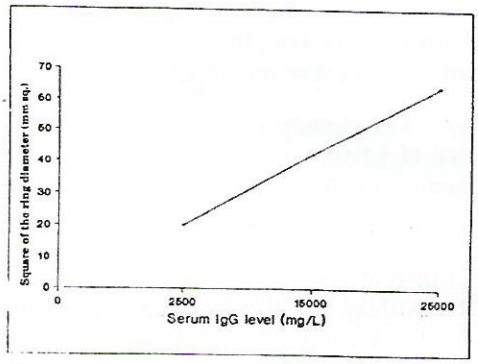

Fig. 1. Standard curve for immunoglobulin G

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