IMMUNONEPHELOMETRY IN CYCLOSPORIN THERAPY

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INTRODUCTION

Cyclosporine is the most effective drug in human allogenic graft survival (1). Hypertrichosis, gingival hypertrophy, hypertension, hepatotoxicity have been observed (2-3) but nephrotoxicity seems to be the main problem (4-6).

Cyclosporine activity seems to be related with peripherical lymphocytes, intraocular levels in systemic administration are not effective (7), and topical treatment appears to be only useful in corneal disease (8-10).

Cyclosporine blood levels are important to evaluate intestinal absortion, as well as nephrotoxicity is related with blood levels (11).

Aqueous protein levels are related with inflammatory events in uveitis (12), and can be easily measured in diary clinic by computorized nephelometry; albumin can be a good reference of blood aqueous barrier «in vivo» (13) with α antitrypsin directly reflecting inflammatory activity (12).

Evaluation of cyclosporin therapy can be done with only one aqueous tap of 50-100 μl and measuring 5 proteins at least.

MATHERIAL AND METHODS

We selected six patients from our uveitis clinic 4 males and two females, age 43 ± 9,4 years with severe intermediate uveitis, corticosteroid resistant (14).

Common features of every patient were external quiet eyes, cystoid macular edema, cells and snowball opacities in vitreous cavity; typical pars plana snowbank in four patients (15).

Angiography was performed monthly to evaluate vasculitis and cystoid macular edema and also electroretinogram, electro-oculogram and visual fields were performed.

Patients were followed weekly by two different ophthalmologists and the examination included: neurologic study, best corrected visual acuity, biomicroscopy, direct and indirect ophthalmoscopy, Goldman lens and tonometry.

The following laboratory tests were performed: serum creatinine, serum glucose, angiotensin converting enzyme, lysozyme, R. F. test, complement fractions C_{3c} C_4 and C_{3pa} and CH_{50}) immunecomplexes (C_{1q}) class I histocompatibility antigens, protein electrophoresis, full blood count, E.S.R., serologic tests to syphilis, cytomegalovirus, toxoplasmosis, adenovirus, influenza A and B, H.I.V.; smooth muscle ANA, RNA, DNA and mitochondrial auto-antibodies.

Tuberculin skin test was performed and also X ray study of chest, skull and sacro iliac joints.

Aqueous taps were obtained with a 29 G gauge needle fitted to a 1 ml tuberculin syringe, and 5 $_{cm3}$ of blood from each patient before and after cyclosporine therapy (blood was centrifuged one hour 1500 g-4.º C).

Aqueous and serum samples were obtained from 16 otherwise healthy patients in cataract surgery 72 ± 12 years (range 41-89 years) 10 females 6 males. Aqueous and serum protein levels were evaluated by immunonephelometry Laser Behring with anti serum Behring.

Results were analysed by student T and Anova test.

Cyclosporine treatment was 5 mg/Kg/day and corticosteroids (prednisolone) were reduced to 0,5 mg/Kg/day, in every one.

RESULTS

Best corrected visual acuity in all patients are show in (table I) before and after one month of treatment with ciclosporine A.

Albumin aqueous mean level before 19,49 ± 16,87 mg/dl and after one month of therapy 21 ± 15,2 mg/dl is shown in (table II), increased levels are only different from controls after therapy ($P < 0.05$).

IgA aqueous mean level before treatment 1,34 ± 1,56 mg/dl and after 1,70 ± 0,86 mg/dl is not different from controls ($P > 0.05$).

IgG aqueous mean level before 7,95 ± 10,81 mg/dl ($P < 0.05$) decreased to 7,40 ± 8,93 mg/dl ($P < 0.01$) and is shown in (table III).

C_{3c} aqueous mean level before 0,39 ± 0,52 mg/dl is not different from controls ($P > 0.05$).

AAT aqueous mean level before 4,76 ± 6,70 mg/dl ($P < 0.05$), and after has increased to 5,3 ± 5,06 mg/dl ($P < 0.01$), (table IV).

Serum Albumin mean level before therapy 3.924 ± 1.776 mg/dl is not increased ($P > 0.05$), (Controls 4395 ± 546 mg/dl), but after therapy it raised to 4967 ± 372 mg/dl ($P < 0.05$), all the other serum protein levels were not different from controls (table V)

DISCUSSION

There was an increased aqueous level of albumin and α_1 antyrypsine but only increased the level in serum albumin.

Increased aqueous albumin levels are perhaps reflecting not increased blood aqueous leakage but raised serum levels, as all patients have decreased clinical inflammatory signs and improved visual acuity.

IgA and C_{3c} were not increased, C_{3c} level is directly related with «in vivo» complement activation, (personnal observation).

IgG decreased level can be related with clinical improvement or/and immunosupressive effect of cyclosporine.

α_1 antitrypsine is sinthetized in liver and by macrophages, is not increased in serum ($P > 0.05$), but was increased in aqueous before 4,76 ± 6,70 mg/dl ($P < 0.05$ and after one month 5,3 ± 5,06 mg/dl ($P < 0.01$).

Enhancement of macrophage activity by cyclosporine was refered by Carlsen [16], and could explain thromboembolic complications in cyclosporine therapy, and could also explain local anti-inflammatory effect.

TABLE I — VISUAL ACUITY (SNELLEN) BEFORE AND AFTER ONE MONTH OF THERAPY WITH CYCLOSPORINE A

	BEFORE THERAPY		AFTER TERAPY (ONE MONTH)	
PATIENT	RIGHT EYE	LEFT EYE	RIGHT EYE	LEFT EYE
1	6/6	6/24	6/6	6/9
2	6/6	6/60	6/6	6/9
3	6/9	6/6	6/6	6/6
4	6/60	6/6	6/9	6/6
5	6/24	6/6	6/9	6/9
6	6/24	6/60	6/6	6/9

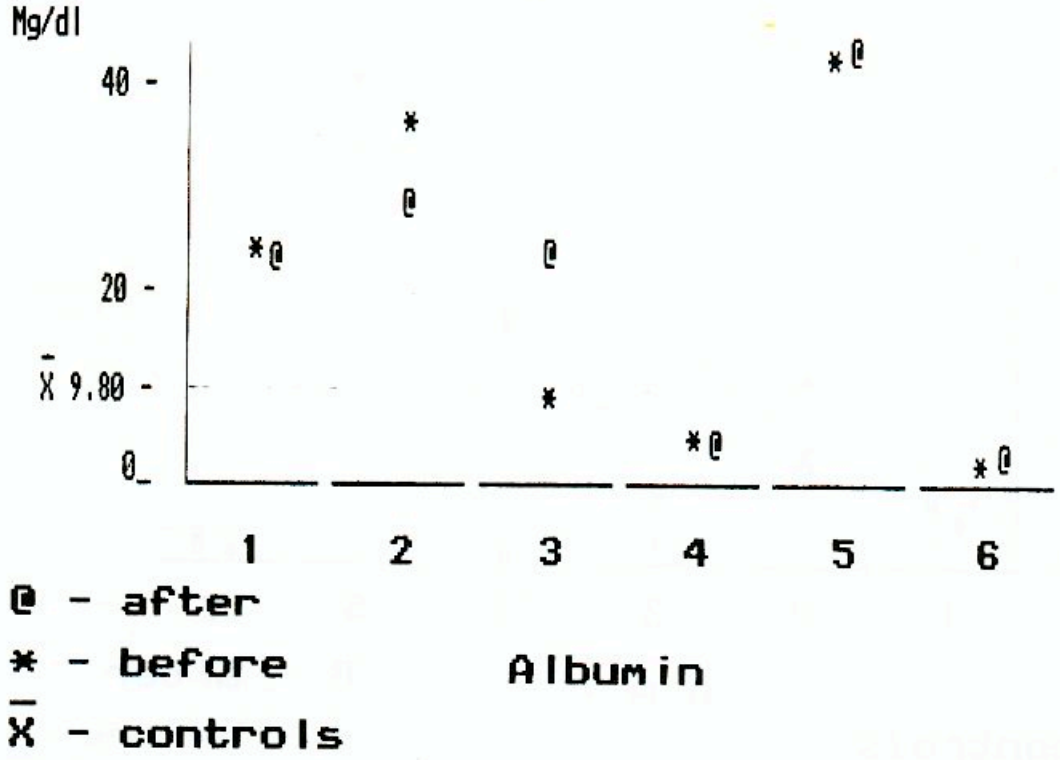

TABLE II — ALBUMIN AQUEOUS LEVELS BEFORE AND AFTER ONE MONTH OF CYCLOSPORINE A THERAPY

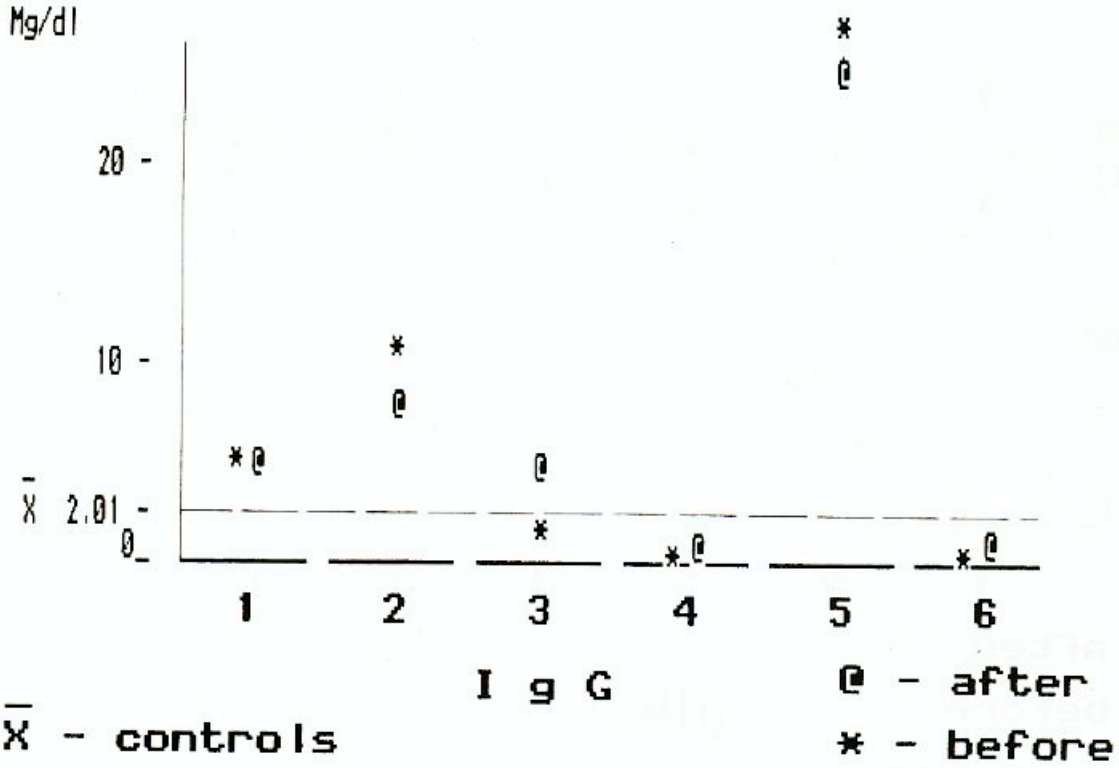

TABLE III — I_gG AQUEOUS LEVELS BEFORE AND AFTER ON MONTH OF CYCLOSPORINE A THERAPY (DECREASED LEVELS AFTER TREATMENT)

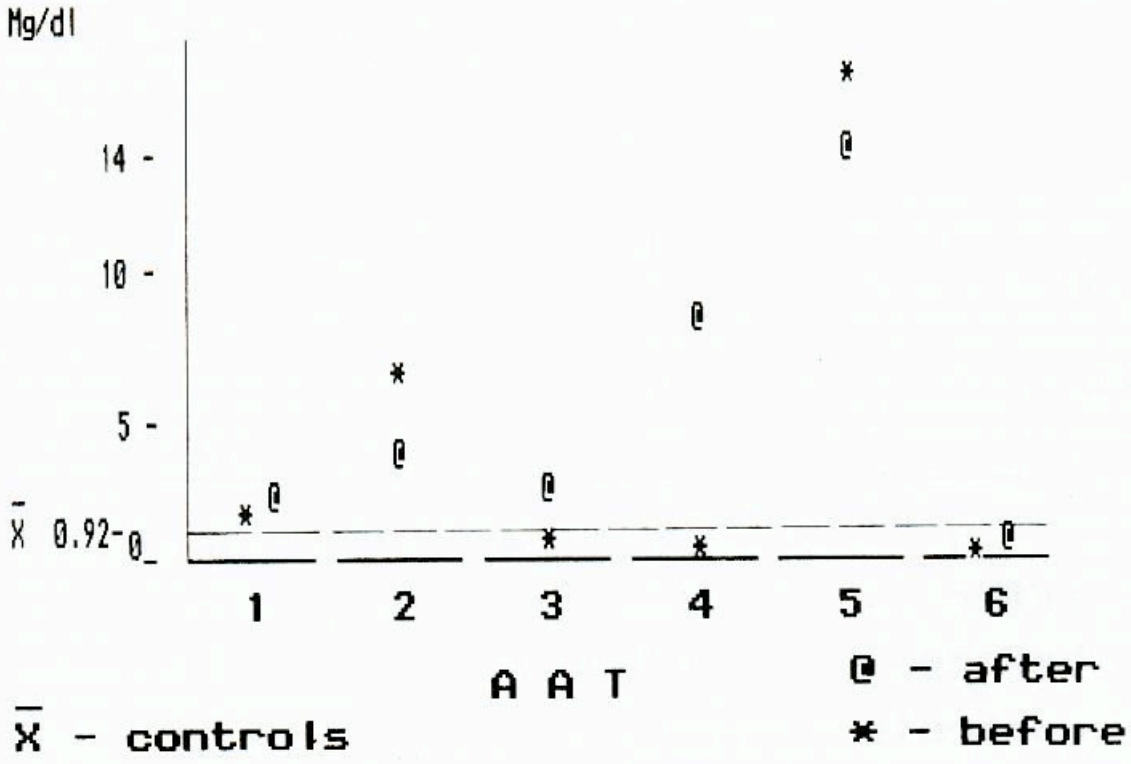

TABLE IV — AAT AQUEOUS LEVELS BEFORE AND AFTER ONDE MONTH OF THERAPY (INCREASED LEVEL AFTER AND BEFORE THERAPY)

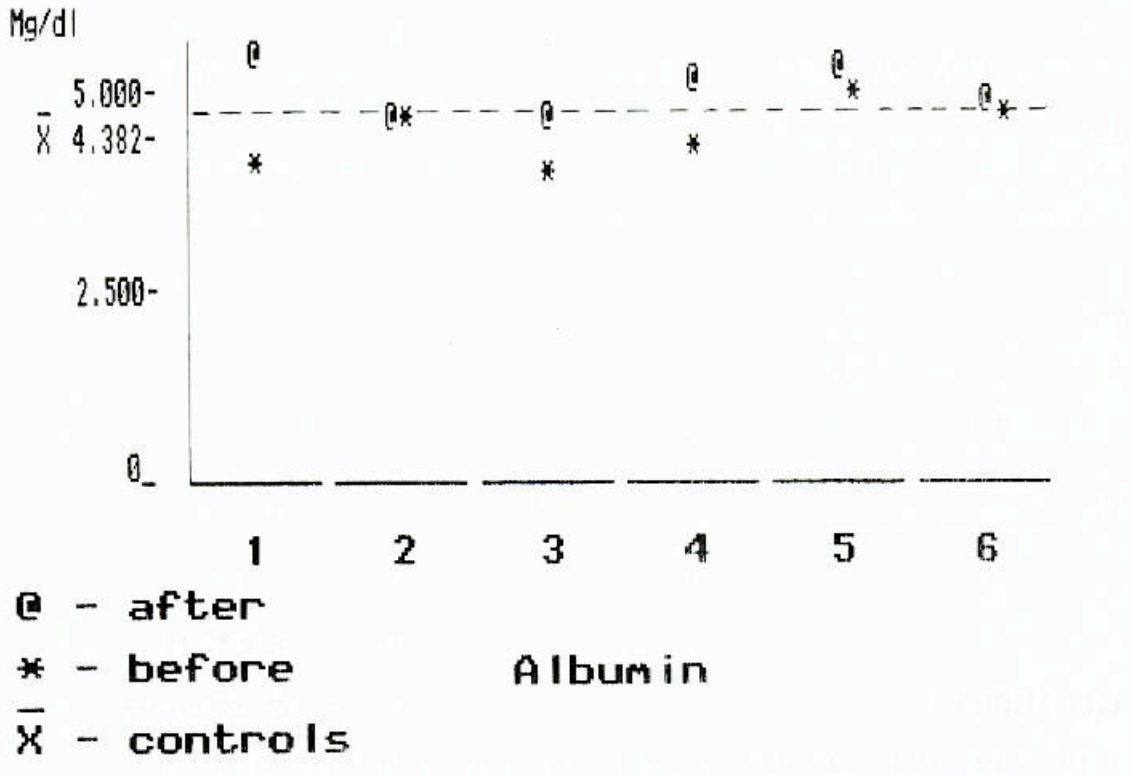

TABLE V — ALBUMIN SERUM LEVELS ARE INCREASED AFTER THERAPY

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