CLINICAL RESEARCH

Antithyroid antibodies as an early marker for thyroid disease induced by amiodarone

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Abstract

Changes in thyroid function may occur during treatment with amiodarone. A double blind prospective trial of amiodarone and placebo was performed in 37 patients in the subacute phase of myocardial infarction. Though none of the patients assigned to receive placebo developed any antibody, six of 13 patients treated with amiodarone developed antithyroid microsomal antibodies. There was no difference in triiodothyronine and thyroxine concentrations between the two groups, but a significant difference in concentrations of thyroid stimulating hormone was noted on day 30 ($p < 0.05$). Six months after the withdrawal of amiodarone autoantibodies could not be detected and concentrations of thyroid stimulating hormone were normal.

These antibodies have not previously been reported to develop during short term treatment with amiodarone. They could have an important role in the detection of early thyroid changes in patients given amiodarone.

Introduction

Several cardiovascular drugs are associated with an increased prevalence of antinuclear antibodies.¹ Amiodarone, an antianginal and antiarrhythmic drug, has a chemical structure similar to that of triiodothyronine. Not surprisingly, therefore, alterations in thyroid function induced by treatment with amiodarone have been described. Hypothyroidism and hyperthyroidism have been reported both during treatment with amiodarone and after withdrawal of the drug.^{2,4} We performed a double blind prospective

trial, using amiodarone and placebo, to establish the endocrine changes that occur during treatment with amiodarone.

Patients, methods, and results

We studied 37 patients (33 men, four women) with a recent myocardial infarction. All were enrolled into this study seven to 10 days after their infarction. None had been taking digitalis or any antiarrhythmic drugs, and none had a history of thyroid disease. Their ages ranged from 30 to 77 years (mean 55.3).

Concentrations of triiodothyronine, thyroxine, and thyroid stimulating hormone were determined by radioimmunoassay. Organ specific antibodies (thyroid microsomal and gastric parietal cell) and non-organ specific antibodies (antinuclear, smooth muscle, and antimitochondrial) were assayed using an indirect immunofluorescence method.⁵ Thyroid tissue obtained from thyrotoxic patients, stomach tissue obtained from patients with peptic ulcer, and rat kidney and liver were used as the substrates, and rabbit antihuman γ globulin conjugated with fluorescein isothiocyanate was the second antibody. Statistical analysis was performed using Student's *t* test.

Design of study—On day 1 blood was collected for determination of basal concentrations of triiodothyronine, thyroxine, and thyroid stimulating hormone and the detection of any pre-existing autoantibodies. Patients were assigned randomly to receive either amiodarone or placebo and took 1000 mg amiodarone/day or placebo on days 2 and 3, 600 mg amiodarone/day or placebo on days 4-7, and 400 mg amiodarone/day or placebo on days 8-30. Blood samples were collected on days 7 and 30 and assayed for triiodothyronine, thyroxine, thyroid stimulating hormone, and autoantibodies.

*Median serum concentrations of triiodothyronine, thyroxine, and thyroid stimulating hormone in patients taking amiodarone or placebo**

	Day 1	Day 7	Day 30
Triiodothyronine (nmol/l):			
Amiodarone	1.8	1.6	1.7
Placebo	1.8	1.9	1.8
Thyroxine (nmol/l):			
Amiodarone	115	114	125
Placebo	105	104	104
Thyroid stimulating hormone (mU/l):			
Amiodarone	3.39	4.18	4.65
Placebo	3.32	3.14	2.91

* Normal ranges: triiodothyronine 1.1-3.2 nmol/l; thyroxine 67-144 nmol/l; thyroid stimulating hormone 1.0-7.5 mU/l.

Conversion: SI to traditional units—Triiodothyronine: 1 nmol/l $\approx$ 0.65 ng/ml. Thyroxine: 1 nmol/l $\approx$ 0.08 μ g/100 ml.

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Fourteen patients were assigned to receive amiodarone and 23 placebo. Two patients (one in each group) died before the end of the study.

Detection of autoantibodies—None of the patients treated with placebo had or developed autoantibodies. On day 1 none of the patients treated with amiodarone had detectable autoantibodies. On day 7 three of the 13 surviving patients treated with amiodarone had detectable antithyroid microsomal antibodies, and on day 30 six had them (55%). Tests for all other autoantibodies yielded negative results in both groups.

Thyroid function—The table shows the serum concentrations of triiodothyronine, thyroxine, and thyroid stimulating hormone. No differences were seen in triiodothyronine and thyroxine concentrations between the two groups. A significant difference in concentrations of thyroid stimulating hormone between the two groups was noted on day 30 ($p < 0.05$). In three patients treated with amiodarone the concentration of thyroid stimulating hormone rose to the hypothyroid range (8.3, 8.6, and 8.8 mU/l). Two of these three patients had antithyroid antibodies.

Discussion

The finding of thyroid antibodies in 55% of patients after they had been taking amiodarone for 30 days suggests that this drug has a

toxic effect on the thyroid even when taken for fairly short periods. Previously such antibodies have been reported only in patients given long term treatment.³ Follow up evaluation six months after the withdrawal of amiodarone in the seven patients who had detectable antimicrosomal thyroid antibodies showed complete clearance of the autoantibodies. Similarly, concentrations of thyroid stimulating hormone in these patients reverted to normal. Thus the toxic effect seems to be reversible when the drug is used for short periods.

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(Accepted 18 November 1985)

Distinct IgG recognition patterns during progression of subclinical and clinical infection with lymphadenopathy associated virus/human T lymphotropic virus

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Abstract

Longitudinal IgG recognition patterns of viral proteins were studied in 15 men who had seroconverted for lymphadenopathy associated virus/human T lymphotropic virus (LAV/HTLV-III). Antibodies to the major viral core protein p24, which is a cleavage product of the gag gene encoded precursor protein pr55, appeared first. These were soon followed by antibodies to pr55 and more gradually by antibodies to the other gag gene encoded cleavage product p18, the env gene encoded transmembrane glycoprotein gp41, the env gene encoded glycoproteins gp65 and gp110, and the putative pol gene product p33.

In 13 subjects who remained healthy the reactivity to the different proteins increased or stabilised with time, while in two men who developed acquired immune deficiency syndrome (AIDS) the reactivity, most noticeably to gag encoded proteins, diminished before or at the onset of symptoms.

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Introduction

Lymphadenopathy associated virus (LAV),^{1,2} also designated human T lymphotropic virus type III (HTLV-III),³ is the causative agent of acquired immunodeficiency syndrome (AIDS). IgG antibodies to LAV/HTLV-III are found in nearly all patients with AIDS or signs preceding AIDS, whereas they are virtually absent in populations not at risk.^{4,7} Furthermore, LAV/HTLV-III can be isolated from many subjects with AIDS or signs preceding AIDS,⁸ and transmission of the virus by blood transfusion has led to the subsequent development of AIDS.^{9,10}

In a Swiss seroepidemiological study Schüpbach *et al* found evidence for the following pattern of IgG antibody response in human LAV/HTLV-III infection: in early and asymptomatic infection antibodies to the gag gene encoded protein p24^{11,12} predominate, whereas in later and symptomatic infection antibodies to the env gene product gp41^{11,12} are found most consistently, and with progression to AIDS antibody titre to p24 declines or disappears.¹³

We present data on the protein recognition patterns of LAV/HTLV-III in sequential serum samples from 15 individuals, two of whom eventually developed AIDS, that were followed from seroconversion to a maximum of three and three quarters years later.

Subjects and methods

Sequential serum samples obtained from 13 homosexual men who participated in a study of the efficacy of hepatitis B vaccine between 1980 and 1982¹⁴ and had seroconverted for LAV/HTLV-III¹⁵ were studied. Blood was collected at monthly intervals during the initial five months of the trial and every three months thereafter. In these 13 subjects the average time from the last serum sample that was negative for anti-LAV/HTLV-III to the first that was positive for anti-LAV/HTLV-III was 10.9 weeks (range 1-16 weeks). One subject developed AIDS three years after seroconversion. Six men entered a new prospective study on AIDS, which started in October 1984.