Major operations performed or assisted at by registrars over three months

	Without help		Under supervision		Assisted at	
	Elective	Emergency	Elective	Emergency	Elective	Emergency
Median	13	11	3	0	3	0
Range	1-40	2-26	0-20	0-2	0-13	0-6

(25%), and inadequate by three (18%). Two stated that free discussion about management of patients was not encouraged, and one individual replied that this was tolerated but not encouraged.

Twelve registrars (75%) were actively encouraged to perform research, but fewer than half of these were supervised. One registrar considered the research opportunities of his post to be good.

Seven (44%) said that they would have recommended their post to a colleague and eight (50%) had some reservations. One individual did not consider his post suitable for registrar training. The most frequent criticism was that too little time was allocated for pursuing a research interest.

Comment

Effective audit depends on a three part cycle of reviewing and setting standards, comparing these standards with observed practice, and implementing appropriate change.[1] In the Mersey region there is no organised training programme or consensus on standards of training with which to compare the results of this audit. It is therefore impossible to comment on their acceptability.

On average, in this region, a registrar performs one major elective operation every week, but supervised training occurs only once each month. With the current surplus of highly experienced registrars it is not surprising that some consultants leave their juniors to perform major elective procedures without close supervision. One supervised operation each month is, however, probably inadequate training for most registrars. Supervision by consultants of emergency surgery is uncommon in the region.

At present the published record of a candidate's research experience and a higher degree are the two most important factors in obtaining promotion. While these yardsticks of ability continue to be applied the trainer must provide encouragement, ideas, advice, and free time for research so that his registrar may impress the next interview panel with his academic achievements. Only then will he be allowed to display his clinical skills at a higher level. Only one general surgical post in the Mersey region was considered to provide good opportunities and training in research.

Many registrars seemed satisfied with the quality of the training they had received. Most of the deficiencies cited could easily be corrected by more contact with a nominated supervising consultant and the allocation of free time for research.

1 Shaw CD. 4: Acceptability of audit. *Br Med J* 1980;**280**:1443-6.

(Accepted 7 April 1988)

Effect of amiodarone on circulating antithyroid antibodies

M Safran, E Martino, F Aghini-Lombardi, L Bartalena, S Balzano, A Pinchera, L E Braverman

Division of Endocrinology and Metabolism, University of Massachusetts Medical Center, Worcester, MA 01655, United States
M Safran, MD, *assistant professor of medicine*
L E Braverman, MD, *professor of medicine*

Cattedra di Endocrinologia, Università di Cagliari, Italy
E Martino, MD, *professor of endocrinology*
S Balzano, MD, *fellow in endocrinology*

Cattedra di Endocrinologia, Università di Pisa, Italy
F Aghini-Lombardi, MD, *fellow in endocrinology*
L Bartalena, MD, *assistant professor of endocrinology*
A Pinchera, MD, *professor of endocrinology*

Correspondence to: Dr Safran.

Long term treatment with amiodarone, a benzofuran antiarrhythmic drug that contains iodine, may cause hyperthyroidism and hypothyroidism induced by iodine.[1,2] It has been suggested that amiodarone itself induces thyroid antibodies and that this may account for the high incidence of thyroid dysfunction in patients receiving this drug.[3,4] We prospectively evaluated the development of thyroid autoantibodies in patients who were receiving long term amiodarone treatment.

Patients, methods, and results

Euthyroid patients were evaluated before, during, and after amiodarone treatment. Thirty one patients (21 men, 10 women; mean (SD) age 53 (15) years) lived in Pisa and Cagliari, Italy, regions fairly deficient in iodine, and 16 patients (11 men, five women; age 57 (14) years) lived in Worcester, Massachusetts, a region of iodine sufficiency. All patients were evaluated clinically and had tests of thyroid function, including serum concentrations of triiodothyronine and thyroxine by radioimmunoassay, thyroid stimulating hormone by sensitive immunoradiometric assay, and antimicrosomal and antithyroglobulin antibodies by passive haemagglutination with commercial kits (Fujizoki Pharmaceutical Ltd, Japan (Italy) and Ames Company, Miles Laboratory, Indiana (Worcester)). Before receiving amiodarone 10 patients from Pisa and Cagliari and four patients from Worcester had non-toxic goitre.

The table shows the results of the antibody studies. Only two of the patients from Pisa and Cagliari, both euthyroid with non-toxic goitres, had detectable antithyroid antibodies before beginning treatment with amiodarone and continued to have detectable antibodies (antimicrosomal only) while receiving amiodarone. One additional patient had detectable antimicrosomal antibodies (1:400) on day 86 of treatment but was subsequently found to have a negative titre on day 144. Another patient, who had negative titres of antibodies and had received treatment with radioactive iodine for diffuse toxic goitre three years previously, developed hypothyroidism after 119 days of treatment. One other patient developed hyperthyroidism after 2·5 years of treatment with amiodarone. In this patient antibodies, obtained 15 times during and after treatment, wer detectable (antimicrosomal 1:100) only twice after amiodarone was stopped. In 29 of the 31 patients thyroid dysfunction did not occur.

Four of the 16 patients from Worcester had detectable antimicrosomal antibodies before treatment with amiodarone. Two of the four patients who had detectable antimicrosomal antibodies (1:100) before amiodarone treatment had negative antibody titres on days 191 and 225 of treatment, respectively. Though two patients developed small non-toxic goitres while taking amiodarone, none developed thyroid dysfunction or antibodies.

Twenty patients from Pisa and Cagliari were evaluated one to 35 months after withdrawing amiodarone. Two patients had detectable antibodies during this time, one of whom is described above. The second patient had detectable antimicrosomal antibodies (1:100) 660 days after stopping amiodarone treatment but had no detectable antibodies on two subsequent occasions.

Thyroid antibodies in patients before and during long term amiodarone treatment

	n	Positive thyroid antibodies*		No of days of treatment with amiodarone	
		Before amiodarone	During amiodarone	Mean (SD)	Range
Pisa and Cagliari:					
Short term (≤three months)	19	1	1	41 (26)	13-98
Long term (≥four months)	12	1	2†	284 (266)	119-1078
Worcester:					
Short term (≤three months)	1	0	0	90	
Long term (≥four months)	15	4	2	299 (91)	174-413

*Antibody titres greater than or equal to 1:100 were considered to be positive.
†One patient developed intermittently positive antimicrosomal antibodies.

Comment

Evidence of thyroid autoimmunity has often been noted in patients who develop hypothyroidism while receiving amiodarone.[2] Between 30% and 50% of patients who have hypothyroidism induced by amiodarone iodine have antithyroid antibodies.[1,2] Antithyroid antibodies are less common in patients who have hyperthyroidism induced by amiodarone iodine.[1,5] Monteiro *et al* reported the development of antimicrosomal antibodies in six of 13 patients treated with amiodarone for one month.[3] Two of these patients had slightly increased serum concentrations of thyroid stimulating hormone, and all were euthyroid with negative antibody titres six months after the amiodarone had been withdrawn. Rabinowe *et al* noted a high prevalence (60%) of antimicrosomal antibodies in 10 patients who received amiodarone, but no data are available for these patients before treatment.[4] One of their patients developed hyperthyroidism while receiving amiodarone and showed a considerable increase in immune region associated antigen positive T cells, often found in patients who have Graves' disease, which resolved within three weeks of withdrawing the amiodarone.

The results of our prospective study, however, which included patients treated with amiodarone for both short and long periods and from regions of differing ambient iodine intake show that amiodarone treatment does not seem to be associated with an increased incidence of antithyroid antibodies.

This study was partly supported by a CNR grant, Rome, and grant No DK 18918, NIDDK, Bethesda, MD.

1 Martino E, Safran M, Aghini-Lombardi F, *et al*. Environmental iodine intake and thyroid dysfunction during chronic amiodarone therapy. *Ann Intern Med* 1984;**101**:28-34.
2 Martino E, Aghini-Lombardi F, Mariotti S, *et al*. Amiodarone iodine-induced hypothyroidism: risk factors and follow-up in 28 cases. *Clin Endocrinol* 1987;**26**:27-37.
3 Monteiro E, Galvao-Teles A, Santos ML, *et al*. Antithyroid antibodies as an early marker for thyroid disease induced by amiodarone. *Br Med J* 1986;**292**:227-8.
4 Rabinowe SL, Larsen PR, Antman EM, *et al*. Amiodarone therapy and autoimmune thyroid disease. *Am J Med* 1986;**81**:53-7.
5 Martino E, Aghini-Lombardi F, Mariotti S, *et al*. Amiodarone: a common source of iodine-induced thyrotoxicosis. *Hormone Res* 1987;**26**:158-71.

(*Accepted 12 April 1988*)

Respiratory muscle weakness in Addison's disease

Anne Mier, Clare Laroche, John Wass, Malcolm Green

Department of Respiratory Muscle Physiology, Brompton Hospital, London SW3 6HP
Anne Mier, MD, *research fellow*
Clare Laroche, MRCP, *research fellow*
Malcolm Green, DM, *consultant physician*

Department of Endocrinology, St Bartholomew's Hospital, London EC1 7BE
John Wass, MD, *reader in medicine*

Correspondence to: Dr A Mier, Charing Cross Hospital, London W6 8RF.

Patients with Addison's disease may rarely present with wheezing due to asthma.[1] More commonly they have non-specific symptoms such as weakness, dizziness, and weight loss. We describe a patient who presented with dyspnoea on exertion that was related to severe respiratory muscle weakness.

Case report

A 63 year old retired caterer presented with a two month history of dry cough and wheezing. Her tolerance of exercise was 400 metres on the flat, she had no orthopnoea but became breathless on stairs. She smoked 20 cigarettes a day, had lost 6 kg over the past year, but denied any abdominal pain, anorexia, or blackouts. Her menstruation had been normal until the age of 50, and she had one son aged 36.

On examination she was deeply tanned with pigmented palmar creases and intraoral pigmentation. She had no axillary hair and scanty pubic hair. Her blood pressure was 95/70 mm Hg when supine and 85/75 mm Hg when standing. She had a widespread expiratory wheeze; peak flow was 150 l/min, forced expiratory volume in one second 1·3 l, and forced vital capacity 1·5 l. The plasma concentration of sodium was 129 mmol/l, potassium 4·5 mmol/l, and urea 8·6 mmol/l; haemoglobin was 136 g/l, white cell count $5·05 \times 10^{12}$/l (8% eosinophils), and erythrocyte sedimentation rate 9 mm in first hour. The results of tests of liver and thyroid function were normal. Plasma cortisol concentrations during three short tests with tetracosactrin were 120 nmol/l, 140 nmol/l, and 120 nmol/l, the lack of a cortisol response being confirmed by a long test with tetracosactrin. Luteinising and follicle stimulating hormone concentrations were both in the menopausal range (>50 U/l), and adrenocorticotrophic hormone was 266·7 pmol/l (normal 2·2-17·8 pmol/l). Respiratory muscle studies[2] showed low maximal static expiratory mouth pressure (34 cm H_2O; normal >32 cm H_2O), low maximal static inspiratory mouth pressure (14 cm H_2O; normal >24 cm H_2O), and reduced transdiaphragmatic pressure during maximal sniffs[3] (48 cm H_2O; normal >70 cm H_2O). Phrenic nerve conduction times were 9 ms (normal 5-9·5 ms). Maximal voluntary contraction of the quadriceps muscles was 9 kg (normal >29 kg).

Full replacement treatment with hydrocortisone acetate was started. Ten months later her breathlessness had improved such that she was able to climb two flights of stairs. Peak flow had increased to 315 l/min, forced expiratory volume in one second to 1·6 l, and forced vital capacity to 2·5 l. Maximal static expiratory mouth pressure had increased to 45 cm H_2O, maximal static inspiratory mouth pressure to 20 cm H_2O, and transdiaphragmatic pressure during maximal sniffs to 75 cm H_2O. Phrenic nerve conduction times were unchanged. Maximal voluntary contraction of the quadriceps muscles increased to 22 kg.

Comment

In Addison's disease generalised fatigue is common and is usually attributed to non-specific malaise rather than muscle weakness. Our patient, however, showed evidence of weakness in both respiratory and quadriceps muscles, suggesting that all skeletal muscles were affected. Phrenic neuropathy was excluded by the finding of normal conduction times in the phrenic nerve. Although electrolyte disturbances may have partially contributed, weakness in the respiratory muscles probably resulted mainly from myopathy. Thus just as steroid myopathy may be induced by Cushing's syndrome or by excessive corticosteroid administration, so a lack of corticosteroid also seems to result in muscle weakness and myopathy.