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Amiodarone Photoreactions

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Roupe G, Larkö O, Olsson SB. Amiodarone photoreactions. Acta Derm Venereol (Stockh) 1987; 67: 76–79.

Four patients with photoreactions after Amiodarone therapy are described. The action spectrum for photosensitivity was found in the UVA region. Pigmentation seems to be due to wavelengths below 360 nm. (Received May 30, 1986.)

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Amiodarone is a potent cardiac antiarrythmic agent. Photosensitivity is a common skin complication to Amiodarone therapy but so is also a facial slate-grey pigmentation. These side effects were documented in 57% and 1.4% respectively in a recent review (1). The drug has been shown to possess phototoxic properties in the mouse (2). This is a report of four patients phototested during treatment with Amiodarone.

MATERIAL AND METHODS

Patients

Patient 1 (J.-B. T.)

This patient is a man who was born in 1938. Due to attacks of atrial fibrillation which remained unaffected by conventional antiarrythmic drugs he was in 1983 given Amiodarone in a dose of 200 mg three times daily for one week, thereafter 200 mg daily. After three months, the dose was increased to 300 mg daily with good antiarrythmic effect.

The patient belongs to skin type II. Four months after starting Amiodarone therapy he experienced side effects in the form of burning and itching sensations in his skin already one hour after sun exposure. In addition, sunexposed skin regions became swollen and red. After the summer of 1984, after having taken Amiodarone for one year, he noticed a slight grey bluish discoloration in the skin of

his face, expecially in that of his nose. There was no pigmentation under his goggles. He tried sunscreens without any obvious effect.

In spite of this side effect of Amiodarone, the patient wanted to continue with his medication as it was associated with a marked antiarrythmic efficiency. A slight worsening of the skin discoloration was noticed after the summer of 1984.

In January 1986, the patient reported the reappearance of frequent and long attacks of atrial fibrillation. It was then documented that the patient had developed a hyperthyroidism and Amiodarone treatment was discontinued. Since then, he has noticed an improvement of his skin sensitivity and is now able to stay outdoors for a whole day.

Patient 2 (K.-R. N.)

This man was born in 1921 and had combined mitral valvular disease of rheumatic origin.

In the early seventies transient atrial fibrillation followed a mitral valve prosthetic operation. In 1981, when conventional antiarrythmic drugs repeatedly failed to maintain sinus rhythm, he was given Amiodarone in a dose of 200 mg three times daily for one week, followed by a maintenance daily dose of 200 mg. This treatment did not restore sinus rhythm but the ventricular rate was adequate with regard to his physical activities and earlier symptoms associated with high heart rate disappeared.

In the late summer of 1983 acute sun exposure resulted in minor sensational itching and the patient got a successively increasing skin discoloration of his face. The skin discoloration noticed late in 1983 was deep bluish-purple. Due to this side effect of Amiodarone, the daily maintenance dose was decreased to 100 mg. During the late spring of 1984, he reported dyspnoea on exertion, which was interpreted as the result of increasing ventricular rate and progress of his combined aortic valvular disease. Further investigation of his aortic valve was planned, but during the summer of 1984 he developed a rapidly increasing heart failure and died before surgery could be performed.

Patient 3 (H. L.)

This man was born in 1910 and has suffered paroxysmal atrial fibrillation since 1970. In 1980, after an acute myocardial infarction he experienced frequent attacks of atrial fibrillation with symptoms and signs of cardiac ischaemia.

Traditional antiarrhythmic drugs were ineffective and the patient was therefore given Amiodarone in a dose of 200 mg three times daily for a week, then a maintenance dose of 200 mg daily. Since then, the arrhythmia has not caused any problems.

During the autumn of 1982 the patient noticed a successively increasing discoloration of his facial skin. The bluish discoloration prompted reduction of the Amiodarone dose to 200 mg every second day. His skin discoloration has remained unchanged since more than 3 years in spite of the decreased Amiodarone dose.

Patient 4 (L. S.)

A man, born in 1925, who had an atrial septal defect and attacks of atrial flutter, unaffected by surgical closure of the defect. Prophylactic antiarrythmic treatment with conventional antiarrhythmic drugs was unsuccessful and early in 1980 he was therefore given Amiodarone in a dose of 200 mg three times daily for one week, thereafter 200 mg daily. The attacks of atrial flutter were essentially uninfluenced by the treatment and therefore the dose was increased to 400 mg daily. In spite of this, attacks of the flutter occurred almost daily. Early in 1981, the Amiodarone treatment was postponed.

In 1982, elective antiarrythmic surgical treatment of his flutter was performed. Postoperatively, the attacks of atrial flutter reappeared and the patient was again given Amiodarone according to the same regimen as one year earlier. After four weeks of treatment with Amiodarone in a daily maintenance dose of 400 mg, his flutter attacks were abolished and have since then occurred altogether only four times.

The patient belongs to skin type II. After the summer of 1983, a grey bluish discoloration of this facial skin appeared, preceded by an increased light sensitivity. The patient clearly stated that he would rather have his facial discoloration than the paroxysmal arrythmias and he has since then continued with Amiodarone 400 mg daily. He has been carefully informed not to expose himself to sun radiation and the skin discoloration has remained stable. He has tried sunscreens without any help.

Equipment for phototesting

The patients were tested with a monochromator (Clinical Photoirradiator, Applied Photophysics) containing a 900 W xenon arc lamp. A liquid-filled light guide was attached to the monochromator and transmitted the radiation to the patient's skin. The irradiated area was 0.5 cm in diameter. Irradiations were made at 300 nm ±5 nm, 320±10 nm, 340 nm ±10 nm, 350 nm ±30 nm, 380 nm ±10 nm. For each

Table I. *The table demonstrates the monochromator test results*

Minimal erythema dose. ND=not done

	Wavelength				
	300±5 nm (mJ/cm²)	320±10 nm (J/cm²)	340±10 nm (J/cm²)	350±30 nm (J/cm²)	380±10 nm (J/cm²)
Patient					
1. J.-B. T.	56	5	ND	20	>14
2. K.-R. N.	112	ND	10	10	10
3. H. L.	28	ND	7	10	20
4. L. S.	80	>10	ND	40	>14
Normal	30	2[a]	20[a]	40 J/cm²	140 J/cm²[a]

[a] Personal communication Dr Brian Diffey, Dryburn Hospital, Durham, England.

spectral region the radiant exposure was increased by $\sqrt{2}$, thus doubling alternate exposures. Irradiations were measured using a thermopile.

All further testing was carried out on the back and the irradiated sites were examined 24 h after exposure. The minimal erythema dose (MED) was registered as the radiant exposure dose which produced a slightly perceptable erythema.

RESULTS

The results are seen in Table I. It is evident that the maximum photosensitivity is in the UVA region. In no case there was an increased sensitivity at 300 nm.

DISCUSSION

During Amiodarone therapy a high incidence of sun intolerance has been observed. These data are suggestive of a phototoxic mechanism. Some authors have found the action spectrum to be in the UVA region (3, 4), whereas Zachary et al. claim that the action spectrum includes the UVB (5). In this study the UVB test was normal in all four tested patients. One patient (LS) showed no increased light sensitivity. This remains unexplained but may be due to increased pigmentation. The test was performed during the summer months.

Many previous studies have been reported from Southern Europe (6). As the action spectrum is in the UVA region one can expect problems to occur even at more northern latitudes. The doses necessary to elicit erythema in the UVA region in this study are easily encountered even in Sweden during a substantial part of the year. Also, most sun screens give a bad protection for these patients as the major protection spectrum is UVB. With the data available today we think that we should advice out patients to photoprotect themselves with clothes rather than sunscreens. For areas where it is impossible to use protective clothing, opaque sunscreens should be used if possible.

Three of our patients with a slate-grey pigmentation of the face had experienced photosensitivity before the development of pigmentation.

Histologically it is known that lipofucin deposits can be found in the dermal tissue (7) but also an elastic degeneration. Photosensitivity might predispose to elastic degeneration with subsequent increased deposition of lipofucin and skin discoloration. Whether the

phototoxicity is due to the substance itself, a photoproduct, or a metabolite is not yet established (3, 8).

One of our patients, who wore goggles, did not show any pigmentation in this area. Goggles normally filter out the UVB component of sunlight. In this case the patient's goggles were made of plastic. Measuring for transmission at 300, 320, 340, 360 and 380 nm revealed that very little UV-radiation penetrated below 360 nm. Thus, pigmentation is probably due to wavelengths below 360 nm.

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The Heterogeneity of Tumours Associated with Epidermodysplasia verruciformis

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A patient with epidermodysplasia verruciformis also had lesions of seborrheic keratosis, irritated seborrheic keratosis, and intraepidermal and invasive squamous cell carcinoma as well as infiltrating squamous cell carcinoma associated with eccrine poroma. Electron microscope studies revealed intranuclear virus particles. Immunoperoxidase studies using rabbit anti-bovine papilloma virus serum showed a positive reaction. (Received May 5, 1986.)

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Epidermodysplasia verruciformis (EV), often associated with in situ and invasive squamous cell carcinoma, is now generally recognized to have a viral etiology (1). The pathogenic agent is considered to be human papilloma virus (HPV) (2): HPV 3 has been found in the benign flat lesions of EV and HPV 5 in lesions showong malignant transformation (3, 4, 5). Patients with both types of viruses have also been reported (3, 5).

We hereby present a case of malignant transformation of EV in which one of the lesions showed infiltrating squamous cell carcinoma associated with eccrine poroma.