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Evaluation by Integrated Thermography of the Beneficial Effect of Cyclofenil in Severe Subcutaneous Arterial Insufficiency

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ABSTRACT

Integrated thermographic measurements were made in a patient suffering from a complex syndrome which included scleroderma, Osler-Weber-Rendu disease and a marked atherosclerotic circulatory insufficiency. A new anti-estrogenic drug, cyclofenil, elicited a rapid and prolonged curative effect against the entire syndrome. The circulatory amelioration was registered periodically by integrated thermography of the face and both hands. This method enables temperature distribution functions to be calculated and seems to hold considerable promise for the evaluation of circulatory changes and in particular those changes evoked by therapeutic agents.

INTRODUCTION

The infrared (IR) emission from the skin can be monitored by colour thermography. This technique is thus a valuable tool for evaluating the influence of new drugs on the blood circulation and also for assessing clinical changes in the skin and subcutaneous connective tissue.

Earlier clinical studies have indicated beneficial effects of cyclofenil on scleroderma and arteriolar insufficiency (1, 4, 5, 6). Colour thermography has also been used to record the potent vasodilatory effect of cyclofenil in scleroderma (7). The aim of the present study was to test a more accurate method which was recorded at the same time and on the same patient as the colour thermographic study reported in Herbai & Boczan (7). Topographic analysis of the IR emission from areas of the body, such as the face and hands have been described previously (2, 3).

METHOD

The apparatus used in this investigation was an AGA Thermovision IR camera (AGA, Infrared Systems AB, Sweden). The detector in the camera unit transduces the IR emission into electrical signals. The indium antimonide photovoltaic detector is cooled by liquid nitrogen (-196°C) to attain high sensitivity in

the spectral band 2.0 to 5.6 μm. After amplification the signals then modulate the electron beams of a TV monitor tube. The sweep of these beams is synchronous with the camera scanning. The thermal image is build up of 100 x 100 pixels, where the intensity of each pixel represents the temperature of a corresponding area of the skin. The scanning frequency was 16 per second.

With the integrating system used the thermal data from the pixels are stored in the memory bank of the computer and it is thus possible to calculate average temparature values for the different areas. These temperatures are recorded in 1°C intervals and the values are given in Figs. 1, 2 and 3.

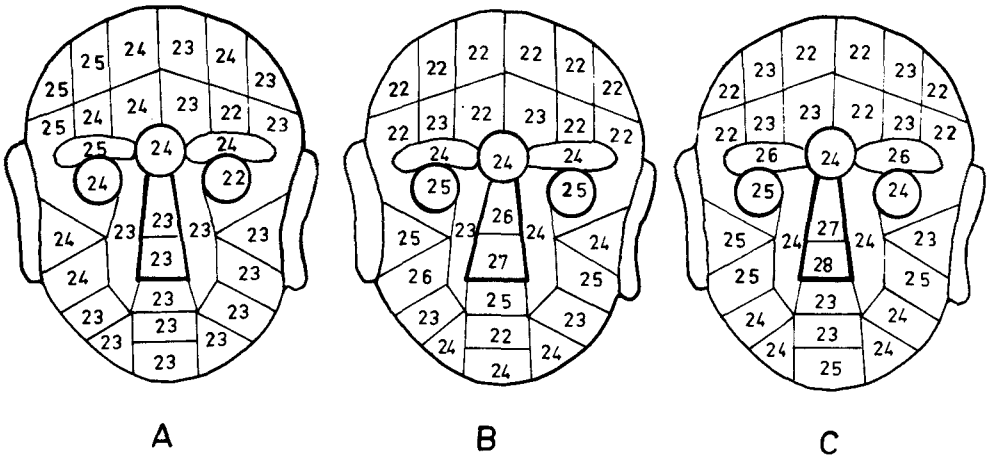

Fig. 1. Effect of cyclofenil on mean path temperatures of face. A before treatment, B after treatment for one month and C after treatment for four months.

For the evaluation of the measured fields in the face, and in the hands, which covered a large part of their area a topographically predetermined patch system was used. The distribution schemes for the fields measured in the face and the volar surfaces of the right and left hands are shown in Figs. 1, 2 and 3, respectively.

The physiological principle underlying this application of thermography is the warming effect of circulatory blood on the skin and subcutaneous tissues. The heating effect will depend on the constitution of the skin and subcutaneous tissues and may be expected not only to vary from individual to individual but also from time to time in the same individual. In addition, even assuming insignificant differences in the thermal emissivity of different skin regions the geometrical relations between skin areas, particularly on the

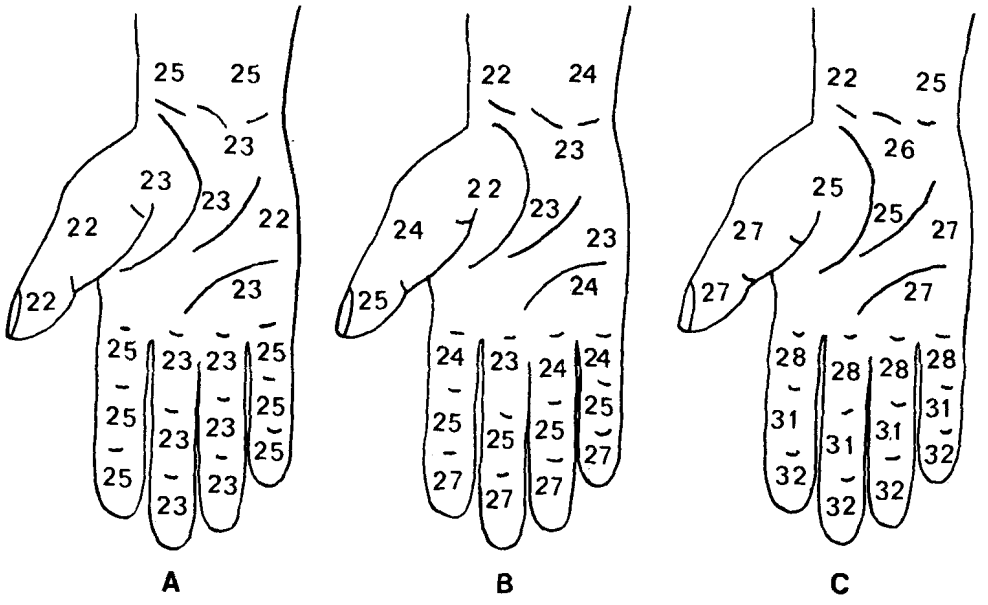

Fig. 2. Effect of cyclofenil on mean path temperature of right hand. A before treatment, B after treatment for one month and C after treatment for four months.

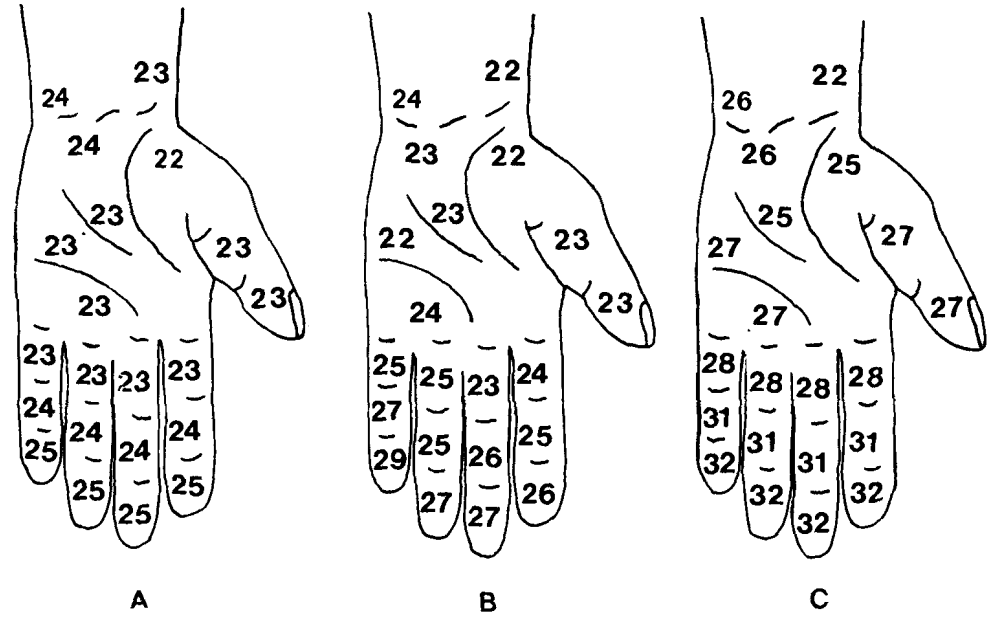

Fig. 3. Effect of cyclofenil on mean path temperature of left hand. A before treatment, B after treatment for one month and C after treatment for four months.

face, and the detector vary somewhat from individual to individual. For these reasons this type of thermography must be regarded as an approximate technique and great caution must be exercised in comparing different individuals. In this study the same individual has been compared on three occasions.

CASE REPORT

The patient was a 67 year old housewife with no family history of either connective tissue or vascular disease. She was a non-smoker and had two healthy sons.

Her present illness began when she was about 45 with morphea which started with cutaneous telangiectasia of the Osler type and continued with relapsing gastrointestinal telangiectases giving rise to severe abdominal pains, hematemesis and melena. Scleroderma appeared at 48 and developed progressively. When she was 53 Raynaud-like signs became manifest particularly in the arms and hands with severe impairment of the vascular condition. Temporary relief was obtained with large doses of nicotinic acid and vitamin E. However, the principal physical signs, including severe melena, continued and she received blood transfusions on 18 occasions. At the age of 57 she developed a rapidly progressing esophageal stenosis just above the cardia. She then had to be tube-fed with a liquid and semifluid diet. During this period there was a gradual loss of weight leading to cachexia.

The persistent signs were treated intermittently with large doses of nicotinic acid, vitamin D, prednisolone and penicillamine, which produced several side effects, without any obvious improvements. Pharmacological evaluation of the drugs and others tested later has been reported elsewhere (5).

At 64 years of age a progressive obliterative atherosclerosis developed in her legs, first on the right side and later on the left. There was marked gangrene with severe pain in toes I and II of her right foot. The circulatory insufficiency together with the contractures of the knee joints made walking impossible and she could only sit or lie down. A year later bilateral sympathectomy was performed but this ameliorated neither the pain nor the gangrene. Repeated infusion of Rheomacrodex® (Pharmacia, Sweden) were also tried but to no avail.

After extensive X-ray investigations it was decided to amputate her right leg at the mid-femoral level. Skin samples from the amputated limb revealed the following histopathological results: There was atrophy of epidermal layers, flattening of the papillae and of the rete pegs. There was a complete absence of all epidermal appendages. Sub-epidermally there were tight, broken and slightly basophilic streaks and dense collagen fibres with thick streaks. The histopathological findings were thus consistent with a diagnosis of severe scleroderma with necrotizing arteriolitis.

Clinically, the patient's condition deteriorated week by week after the amputation. There was a 90° contracture in the left knee and she could only move about in a wheel chair. There was severe pain in the entire left leg and gangrene developed in the tip of the fourth toe. Strong analgesics were required daily. Amputation of the left leg was also considered but the patient refused this and became severely depressed.

Oral treatment with cyclofenil (a non-steroid compound with anti-estrogenic activity) was then started in a dose of 200 mg t.i.d. and continued for four months during which her progress was monitored with laboratory tests and thermography.

RESULTS

Clinical improvements

Almost immediately after beginning cyclofenil treatment there was a subjective improvement; within a week she was no longer depressed. She had a feeling of warmth in her face and all her limbs. The severe leg and toe pains were markedly relieved and strong analgetics were no longer required. Swallowing became much easier and she gained weight. Further she was soon able to walk with a prosthesis and a crutch. The gangrenous region of the tip of the fourth left toe which had been purulently infected dried up and became well demarcated; a year later the wound had healed completely.

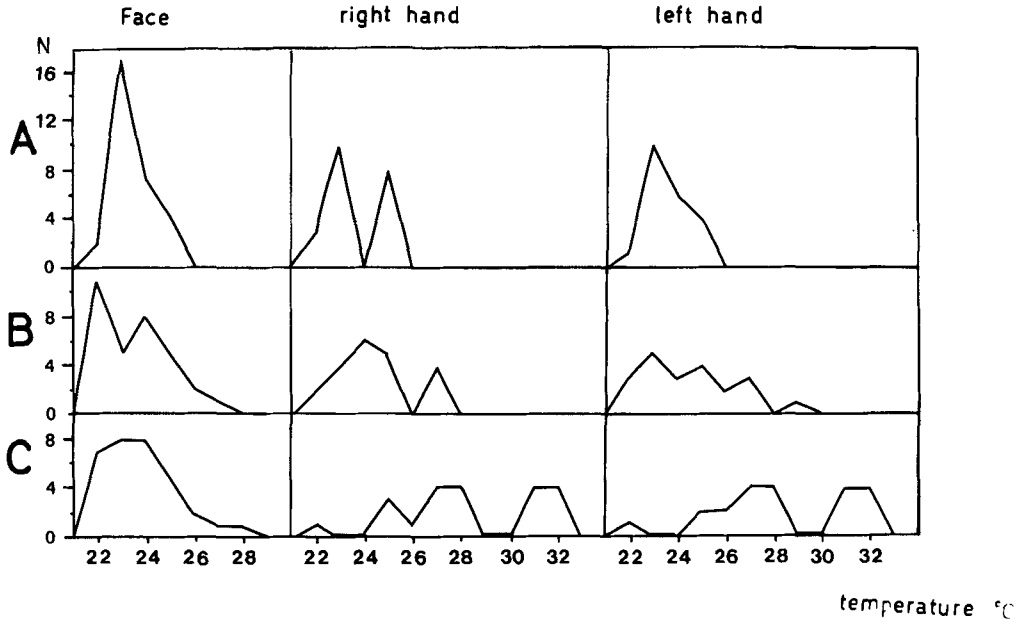

Fig. 4. Frequency distributions of isothermal patches shown in Figs. 1-3. A before treatment, B after treatment for one month and C after treatment for four months.

Integrated thermography

The thermographic measurements of the face and volar aspects of the right and left hands before and after cyclofenil treatment for 1 and 4 months are shown in Figs. 1, 2 and 3, respectively. The figures illustrate clearly distribution of temperatures. These results are summarized in Fig. 4 which shows the frequency distributions of the temperatures of the measured areas. In all the body regions measured it was apparent that the drug treatment resulted in a warmer skin in the sense that higher temperatures appeared in some of the areas. This was much more apparent in the hands and from Figs. 2 and 3 it is clear that the most marked increase in temperature was in the tips of the fingers which became 7-9°C warmer during cyclofenil treatment.

CONCLUSIONS

There seems to be no doubt about the clinical improvement in this case due to the marked vasodilatatory fact of cyclofenil which is reflected in the thermographic data. This type of integrated thermography, where an estimate of the temperature distribution is contained, thus seems to be promising as a means of monitoring spontaneous circulatory changes or therapeutic effects.

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