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TREATMENT OF SCLERODERMA BY RHEOMACRODEX

Milhim D. Alani

From the Department of Dermatology, The Finsen Institute, Copenhagen, Denmark

Abstract. Nine patients with systemic scleroderma were treated with 3×500 ml Rheomacrodex weekly, a total of 7–12 infusions. The patients were followed clinically and by laboratory tests. The only change observed during the treatment was elevation of the erythrocyte sedimentation rate. This is explained by a reduction in the viscosity of the blood. The majority of the patients have reported improved mobility of the fingers, less pain, and fewer Raynaud attacks. However, an actual effect upon the scleroderma was not demonstrated, neither viscerally nor cutaneously. No complications or side effects occurred. A number of investigations are suggested before starting on the treatment.

Low molecular dextran (Rheomacrodex®) has been used as a plasma substitute in clinical practice, especially within surgery, since 1961 (9). It is a hypertonic solution, such that upon infusion of Rheomacrodex the plasma volume is increased by more than the infused quantity of dextran (10). Due to this effect and the dis-aggregating action upon the red cells (2, 17), the viscosity of the blood is reduced and the blood flow improved. The antithrombotic action of Rheomacrodex is explicable partly by a similar dis-aggregating effect upon platelets (19) and partly by its reducing the tendency of platelets to adhere to blood vessels (1). Most recently, it has been observed that Rheomacrodex reduces plasma lipids and cholesterol (7).

Rheomacrodex has proved effective in the treatment of a total of 23 patients with scleroderma (11). Measurement of the digital skin temperature before, during, and after administration of Rheomacrodex has demonstrated an appreciable rise, indicating improved peripheral flow. This has also been confirmed by capillary microscopy (3). These investigations have shown clinical improvement, subjective as well as objective, and this has been confirmed by subsequent studies (4, 6, 8, 12, 18) comprising a total of about 20 patients treated on the same principle.

The present study is an attempt to explain this effect of Rheomacrodex upon patients with scleroderma by systemic and cutaneous investigations and to record the clinical effect of the treatment as well as possible side effects.

MATERIAL

The material comprises 8 women and 1 man with systemic scleroderma. The clinical diagnosis was confirmed by histological examination of the skin. Prior to treatment all the patients had normal ECGs, chest radiography, serum creatinine, and creatinine clearance. The average age at onset of the disease had been 38 years, though at the institution of treatment it was 50 years.

All the patients had Raynaud phenomena and acrosclerosis; 4 had a history of digital ulcerations, still present in 3 when the treatment was started. Eight patients had severe sclerodermic limitation of finger movements, and X-ray showed in 6 of them halisteresis of a few distal phalanges. Five had cutaneous calcinosis, especially over the bones on the limbs; 3 had patchy hyperpigmentation and telangiectasia in the face or on the trunk. Radiography showed in all the patients reduced mobility of the oesophagus; 2 had gastric atony; 2 intestinal atony; 1 hiatal hernia, and 1 duodenal ulcer. Three patients had dysphagia and 2 dyspepsia; 1 chronic constipation; 1 chronic diarrhoea, and 1 polyuria.

Three patients, viz. one woman with localized scleroderma and two with ulcer of the leg, served as controls.

METHODS

The following investigations were performed before and after treatment: Histological examination of skin biopsy from the ulnar aspect of the hands, stained with haematoxylin-eosin and with PAS; qualitative mucopolysaccharide determination on the urine (5), ECG, Hb, R.B.C., W.B.C., differential count, ESR, serum creatinine, creatinine clearance, alkaline phosphatases, prothrombin, urine for albumin and sugar, and microscopic examination of the urine. The last 6 tests were done regulary

Table I. *Erythrocyte sedimentation rate mm/1 h*

	Before treatment	After treatment
(1) Systemic scleroderma (9 patients)	12	32
(2) Localized scleroderma	6	21
(3) Ulcer of the leg (2 patients)	36	37

once weekly throughout the period of the treatment. For technical reasons, not all investigations could be performed for 3 of the patients.

Dosage of Rheomacrodex

Infusion of 10% Rheomacrodex in physiological saline solution or in 5% dextrose was administered—3 infusions of 500 ml weekly, a total of about 10 infusions (7–12). The inflow time was 4–6 hours. In addition, 5 patients later received a further, single, infusion, or two at intervals of 1–2 months.

RESULTS

All laboratory analyses remained unchanged during and after the treatment or showed fluctuations within the normal range. The only exception was the sedimentation rate which showed a definite increase during and after the treatment (Table I).

Out of 3 patients with peripheral ulcerations, one exhibited healing of all ulcerations while the other 2 showed only incipient epithelialization of a few large ulcers and partial healing of small ones. Seven out of 8 patients obtained better mobility of the fingers and had less pain. Calcinosis diminished in 2 out of 5 patients.

Five patients reported a reduced intensity of the Raynaud phenomenon and longer intervals between the attacks. One patient stated that the Raynaud attacks had increased in frequency and 3 had not noticed any change. One patient had noted decreasing dysphagia.

In 3 patients and in 3 controls no effect was recorded.

Incidentally, there have been no side effects or complications during or after the treatment.

DISCUSSION

In previous publications on the effect of Rheomacrodex no mention has been made of an effect upon the erythrocyte sedimentation rate in normal persons (2, 17). The elevation of the ESR noted in the present study must be considered a specific change in sclerodermics during Rheomacrodex therapy. The same result of this treatment has been noted by Zackheim (20). An elevation of the sedimentation rate indicates either an increased aggregation of the red cells or a change in the viscosity of the blood. For instance, it becomes elevated if red cell aggregation is intensified or if the viscosity of the blood is reduced (16). The elevation found in the present study can presumably not be explained as a consequence of the former mechanism, since previous studies have shown that Rheomacrodex therapy results in increased blood flow in patients with scleroderma (11). This result could not be obtained if aggregation of the red cells were increased. On the other hand, the other mechanism might explain the raised sedimentation rate, as all the patients have had Raynaud phenomena and as it is known (14) that in patients with Raynaud phenomena the viscosity of the blood is increased.

In the present study Rheomacrodex could not be shown to exert any effect upon the dermal changes in scleroderma. The excretion of mucopolysaccharides was unchanged, indicating that Rheomacrodex had no effect upon the connective tissue (13). The histological examination of the skin also showed no change after treatment. Apparently, Rheomacrodex improves only the peripheral blood flow and thereby the blood supply to the skin which presumably causes abatement of the secondary cutaneous changes.

The patients have been followed for about one year. In 5, who later received regular infusions, the effect with respect to improved mobility of the hands has been sustained. Moreover, these patients have not had recurrence of large ulcerations. The above-mentioned reduction of calcinosis in 2 patients has been observed in another investigation (6).

According to the present study, as well as previous studies, Rheomacrodex therapy very seldom causes side effects or complications. Nevertheless, it is advisable, before starting the treatment, to investigate the patients for haematological, cardiac, and renal diseases. The latter is of great importance, since a number of sclerodermics have shown renal changes (13, 15).

REFERENCES

1. Bennett, P. N., Dhall, D. P., McKenzie, F. N. & Matheson, N. A.: Effect of dextran infusion on the adhesiveness of human blood-platelets. Lancet *2*: 1001, 1966.
2. Björk, V. O., Intonti, F. & Nordlund, S.: Effect of haemodilution upon erythrocyte aggregation. Acta Chir Scand *128*: 466, 1964.
3. Brodie, S., Messina, E. & Redish, W.: Yearbook of Derm., p. 294, 1966–67.
4. — Personal communication, 1968.
5. Clausen, J. & Asboe-Hansen, G.: Urinary acid mocopolysaccharide in mastocytosis (A new technic for quantitative estimation). Clin Chem Acta *13*: 475, 1966.
6. Denis, H. L.: (The treatment of scleroderma with Rheomacrodex) Le traitement des sclerodermis par le Rheomacrodex (Thèse) Editione A.G.A.M.P., 40 Rue Pascal, Paris, 1967.
7. Flotte, C. T. & Buxton, R. W.: Reduction of serum-cholesterol and lipids by dextran. Circulation, suppl. *II*: 85, 1965.
8. Fountain, R. B. & Stevens, A.: Scleroderma treated with low molecular weight dextran. Brit J Derm *78*: 605, 1966.
9. Gelin, L. E. & Ingelman, B.: Rheomacrodex—a new dextran solution for rheological treatment of impaired capillary flow. Acta Chir Scand *122*: 294, 1961.
10. Gruber, U. F., Meili-Gerber, E., Grass, S. & Allgöwer, M.: Volume effects of new plasma expander in hypovolaemic subjects proc. 10th Congr. int. Soc. Blood transt., Stockholm 1964: 1116, 1965.
11. Holti, G.: The effect of intermittent low molecular dextran infusion upon the digital circulation in systemic sclerosis. Brit J Derm *77*: 560, 1965.
12. Kantor, I.: Scleroderma treated with dextran 40 (Rheomacrodex). Arch Derm (Chic) *94*: 675, 1966.
13. Korting, W. G. & Holzmann, H.: Die Sklerodermie, p. 61. Stuttgart, 1967.
14. Pringle, R., Walder, D. N. & Weaver, I. P. A.: Blood viscosity and Raynaud's disease. Lancet *1*: 1086, 1965.
15. Rowell, N.: *In* Textbook of Dermatology (ed. A. Rook & D. S. Wilkinson), vol. I, p. 560. Oxford and Edinburgh, 1968.
16. Samson Wright: Applied Physiology, p. 172. London, 1952.
17. Thorsén, G. & Hunt, H.: Aggregation, sedimentation and intra vascular sludging of erythrocytes. Acta Chir Scand *187*, 1950.
18. Waddington, E.: Scleroderma. Practitioner *199*: 121, 1967.
19. Weiss, H. J.: The effect of clinical dextran on platelet aggregation, adhesion and ADP release in man: in vivo and in vitro studies. J Lab Clin Med *69*: 37, 1967.
20. Zackheim, H. S.: Personal communication, 1968.

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Milhim Alani, M.D.
Department of Dermatology
The Finsen Institute
Strandboulevarden 49
Copenhagen Ø
Denmark