

DECREASED BLOOD FLOW IN A PAPAVERINE-INDUCED PASSIVE VASCULAR BED IN SCLERODERMAL SKIN

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Abstract. Blood flow was measured in the form of ^{133}Xe -non washout rate constants in a cutaneous vascular bed made passive by intracutaneous injection of a ^{133}Xe -papaverine mixture. Experiments were performed using injection volumes of 0.005, 0.02, 0.1 and 0.2 ml in 7 normals and 15 patients suffering from generalized scleroderma. Blood flow was closely related to the volume of fluid injected, probably reflecting dilution of tissues and increased diffusion distances when injection volumes were increased. When using injection volumes of 0.005 and 0.02 ml, blood flow was significantly reduced in the patients, as compared with normals, probably because of a decreased capillary density in cutaneous tissue in generalized scleroderma.

In patients suffering from generalized scleroderma, cutaneous blood flow on the dorsum of the hand is increased as compared with normals under resting conditions (6). However, in the patients, maximum blood flow in cutaneous tissue of fingers following 12 min of vascular occlusion was reduced in comparison with normals (7). Morphological studies on the vascular bed in cutaneous tissue in generalized scleroderma have revealed a reduced number of capillaries (9). Consequently cutaneous blood flow during maximum vasodilatation might be reduced in these patients.

In order to test this hypothesis, cutaneous blood flow was measured on the dorsum of the hand during maximum vasodilatation in patients with generalized scleroderma and in normal volunteers. Maximum vasodilatation was obtained by local injection of papaverine, which paralyzes vascular smooth muscle. In the passive cutaneous vascular bed thus created, injection volumes might influence the washout of ^{133}Xe . Consequently various injection volumes were employed and this influence studied.

MATERIALS AND METHODS

The experiments were performed on 7 healthy volunteers (3 men and 4 women, aged 28 to 62) and in 15 patients (4 men and 11 women, aged 20 to 75) suffering from generalized scleroderma (acrosclerosis type). The disease duration ranged from 3 to 17 years. Thirteen of the patients were suffering from Raynaud's phenomena, and all had definite sclerosis of the area investigated. Informed consent was obtained in all cases.

Blood flow in cutaneous tissue was measured by the local ^{133}Xe washout technique (9). ^{133}Xe was injected intracutaneously into the back of the hand and was administered with admixture of papaverine, the papaverine concentration in the mixture being 25 mg/ml. Injection volumes chosen were 0.005, 0.02, 0.1 and 0.2 ml and Hamilton microsyringes were used. The subjects were seated with the hand under study immobilized at heart level. Immediately following the injection, measurement of ^{133}Xe washout was started. The γ -emission of ^{133}Xe was detected using a NaI (Tl) scintillation detector placed 5 to 10 cm above the radioactive field. The pulses from the detector were fed into a γ -spectrometer with a window set around the 81 keV photopeak of ^{133}Xe . The activity was recorded at intervals of 10 sec, and the washout was observed for about 5 min. The washout rate constant (k) was computed from the logarithmically converted radioactive data, corrected for background activity, as a function of time, according to the least squares method. The steepest part of the ^{133}Xe washout curve was used for the calculation. Students t -test for paired samples and the randomization test for unpaired samples were employed for statistical comparison. 0.05 was chosen as the limit of significance.

RESULTS

The results are summarized in Fig. 1. In normals, the washout rate constant decreased significantly when the injection volume increased from 0.005 to 0.02 ml ($p < 0.05$) and also when the injection volume increased from 0.02 to 0.1 ml ($p < 0.01$). In the patients, the washout rate constant decreased sig-

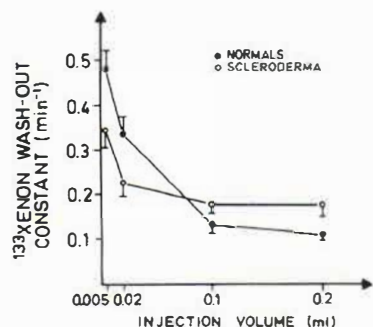


Fig. 1. Mean washout rate constants plotted against injection volumes. Range bars denote ± 1 Standard Error of the Mean.

nificantly when injection volume increased from 0.005 to 0.02 ml ($p < 0.05$). Increasing the injection volume from 0.02 to 0.1 ml in the patients did not result in further decrease ($p > 0.1$). When using injection volumes of 0.005 and (0.02 ml), the washout rate constant was significantly higher in normals ($p < 0.05$ and $p < 0.01$, respectively). The washout rate constant obtained after injection of 0.1 and 0.2 ml did not differ significantly between normals and patients ($p > 0.3$ and $p > 0.05$, respectively). When injection volumes exceeding 0.02 ml were used, a short "delay" was observed before the washout reached its maximum. This phenomenon was observed in normals as well as in patients. This part of the curve was excluded when the washout rate constants were computed. Mean "delay" when using 0.1 ml was 22.5 sec in normals and 26.4 sec in the patients. After injection of 0.2 ml the mean "delay" was 45 sec in normals and 39 sec in the patients. The differences were not significant ($p > 0.8$).

DISCUSSION

The main finding of the present study was the decreased initial washout rate constant in cutaneous tissue during maximum vasodilatation in patients with generalized scleroderma. This was apparent only when injection volumes did not exceed 0.02 ml.

The initial washout rate of $^{133}\text{Xenon}$ injected intracutaneously is influenced by four factors, viz. washout of tracer from cutaneous tissue, washout from subcutaneous adipose tissue, transport of tracer from cutaneous to subcutaneous tissue, and trauma of injection (10). In the case of atonia of the

vascular bed in cutaneous tissue, as induced in the present study, $^{133}\text{Xenon}$ accumulated in subcutaneous tissue will have a negligible influence on the initial washout rate constant which will be correlated to cutaneous blood flow (9).

The washout rate of $^{133}\text{Xenon}$ is dependent on capillary density. When excessive amounts of fluid are injected, the tissues are diluted and the diffusion distances for $^{133}\text{Xenon}$ increase. This phenomenon, together with the acute rise in tissue pressure following the injection, is probably responsible for the "delay" and for the progressively slower washout rate when injection volumes increase. The decreased washout rate of $^{133}\text{Xenon}$ observed in the patients could be due to an increased cutaneous tissue to blood partition coefficient for $^{133}\text{Xenon}$, though this possibility seems unlikely as morphological studies indicate a diminished fat content which more likely would imply a decreased tissue to blood partition coefficient (2,6). Another possibility might be a decreased arterial perfusion pressure head, but as arteriography indicates that, in generalized scleroderma, arterial narrowing is usually located more peripherally (1) this explanation is also unlikely.

The observed reduced maximum blood flow in the patients is most likely due to an increased vascular resistance in the papaverine-induced passive vascular bed, which would indicate that in cutaneous tissue in generalized scleroderma, a reduced capillary density and/or structural arteriolar changes may prevail.

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