Determination of Fingertip Lacticemy Before and After Cold Stimulus in Patients with Primary Raynaud's Phenomenon and Systemic Sclerosis

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ABSTRACT. ***Objective.*** Establishing a cold stimulus test based on the measurement of finger tip lacticemy (FTL) in Raynaud's phenomenon (RP).

Methods. Twenty-seven controls and 79 patients with RP [30 systemic sclerosis (SSc) and 49 isolated RP] were studied. The latter were further classified into probable primary RP (PPRP) and probable secondary RP (PSRP). FTL was determined before (pre-CS) and after (post-CS) a cold stimulus and the percentage difference was designated ΔCS-FTL.

Results. Pre-CS-FTL was marginally higher in SSc patients than in isolated RP and controls. Post-CS-FTL was significantly higher in SSc and PSRP than in PPRP and controls. SSc and PSRP patients had higher post-CS-FTL than pre-CS-FTL (positive ΔCS-FTL) while controls presented a negative ΔCS-FTL. Post-CS-FTL had a heterogeneous behavior in patients with PPRP.

Conclusion. CS-FTL test was shown to be an easy method for evaluation of fingertip effective perfusion before and after a cold stimulus. Further studies are warranted to test its possible clinical application in discriminating between patients with SSc and controls, as well as between patients with PPRP and PSRP. (J Rheumatol 2002;29:1401–3)

Key Indexing Terms:
RAYNAUD'S PHENOMENON
COLD STIMULUS
LACTIC ACID
SYSTEMIC SCLEROSIS

Raynaud's phenomenon (RP) affects 4–30% of the population[1-5], being prevalent in autoimmune rheumatic diseases, especially systemic sclerosis (SSc), in which it occurs in roughly 95% of the patients[6,7]. Ancillary methods to study RP, such as plethysmography, digital thermography, and laser Doppler fluxometry, focus mainly on biophysical variables[8-11]. Nailfold capillaroscopy (NFC) provides morphological assessment of the microvascular bed[12,13]. None of these approaches focuses on the biochemical consequences of the ischemia generated by RP episodes. Such a biochemical variable might be valuable in providing information on the ultimate consequences of the ischemic attack.

The determination of lactic acid concentration in blood obtained from fingertips (fingertip lacticemy, FTL) provides an accurate estimate of the degree of anaerobiosis and has been widely used in sports medicine to assess the physical fitness of athletes[14]. We adapted fingertip lacticemy to study the ischemic stage of RP (FTL before and after cold stimulus) and tested this method in controls, in patients with isolated RP, and in those with SSc-associated RP. Our preliminary data suggest that this approach may be useful for pathophysiologic investigation as well as for diagnosis and clinical staging of RP.

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Supported by the National Council for Research Development (CNPq) and São Paulo State Foundation for Research (FAPESP).

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Submitted April 20, 2001; revision accepted January 9, 2002.

MATERIALS AND METHODS

Patients and classification. The study involved 27 nonsmoking healthy adults and 79 patients with RP, diagnosed by history of transient episodes of finger pallor and/or cyanosis elicited by exposure to cold temperature. Patients were consecutively selected from the Scleroderma Spectrum Outpatient Clinic at UNIFESP Medical School Hospital. Exclusion criteria for patients and controls were the following: active fingertip ulceration, smoking, arterial hypertension, diabetes mellitus, and heart, renal or respiratory insufficiency. After giving informed consent, all individuals underwent a thorough rheumatologic examination and NFC[13]. Oral vasodilators were withdrawn 3 days before the procedure.

Thirty patients were classified as RP secondary to SSc (American College of Rheumatology criteria[15]) and 49 as isolated RP with no clinical evidence of systemic disease. Among the latter, 31 were further classified as probable primary RP (PPRP) and 18 as probable secondary RP (PSRP). PPRP was defined when patients presented negative antinuclear antibody (ANA) test and NFC with no avascular area and not more than 1 enlarged loop per finger. PSRP was defined when patients presented low titer ANA (up to 1/160, not including centromeric and nucleolar patterns) and/or NFC depicting several enlarged loops (1 or more per finger), but no capillary deletion.

Procedures. Before cold stimulus-fingertip lacticemy test (CS-FTL), individuals were stabilized for 1 h at 24°C ± 1°. Then a brisk puncture was performed at the volar surface of the left 4th fingertip. The first blood drop was adsorbed onto a lactate strip (Boehringer-Mannheim, Germany) and processed immediately in a portable spectrophotometer (Accusport, BM, Germany). Next, patients submerged both hands in 10°C water for 1 min. After 10 min, a new FTL was determined as before, selecting the right 4th finger or the finger with the most prominent discoloration.

Data analysis. Pre-CS-FTL and post-CS-FTL were compared

intra-individually using Wilcoxon's test. Quantitative variables between 2 and among 4 groups were compared by Mann-Whitney and Kruskal-Wallis test, respectively. The difference between post and pre-CS FTL (designated as ΔCS-FTL) was defined by the formula: ΔCS-FTL = (post-CS-FTL – pre-CS-FTL) × 100/pre-CS-FTL.

RESULTS

No objective side effects due to the test were observed. SSc patients reported no distress but 2 controls needed interruption of the cold exposure due to pain.

Pre-CS-FTL was higher in SSc than in isolated RP and controls but no statistically significant difference was observed among the 4 groups. Post-CS-FTL was significantly higher in SSc than in the other groups (Table 1). Intra-individual comparison between post- and pre-CS-FTL showed unique results in each group (Table 1, Figure 1). There was a significant decrease in FTL after CS (negative ΔCS-FTL) in controls. Conversely, there was a significant increase in FTL after CS (positive ΔCS-FTL) in SSc and PSRP patients. In the PPRP group post-CS-FTL depicted a heterogeneous behavior (Figure 1).

DISCUSSION

We sought to establish a sensitive method for evaluation of blood perfusion through open capillaries. Previous observations from our group have shown a good reproducibility using this method: FTL obtained from the same fingertip 4 times sequentially in 8 healthy volunteers depicted variability ranging from 8 to 12% (Kayser C., unpublished data). The FTL test was then used with controls and patients with different forms of RP in basal conditions and after cold exposure.

Patients with SSc had slightly higher basal FTL compared to controls and patients with RP. Further, 10 min after a cold stimulus, SSc patients and those with PSRP showed an additional and significant increment, while controls showed a decrease in FTL. The PPRP group presented a heterogeneous behavior in this respect. These observations suggest that patients with a convincing history of RP and either a positive ANA test or altered NFC findings (PSRP) behave similarly to SSc patients in the CS-FTL test. In contrast, patients with no clinical or laboratory evidence of secondary RP (PPRP) may have either a normal or abnormal CS-FTL test. Although some overlap has been observed between the study groups, the ability of the CS-FTL test to discriminate between most SSc and PSRP patients as well as between some of the PPRP patients and controls might add to the diagnosis and classification of RP in early stages of disease.

The different behavior observed between healthy and SSc individuals deserves comment. The abnormally high basal FTL in scleroderma is consistent with the concept that structured derangement in the arteriolar/capillary bed in this disease results in chronic hypoxia in fingertips, which may be relevant to the progressive resorption of soft tissue and bone. Conversely, the observation that patients with primary RP presented basal FTL comparable to controls is consistent with the absence of structured abnormalities in their arterioles and capillary bed. Accordingly, fingertip trophic phenomena are not usually observed in these patients.

An increase in blood flow (reactive hyperemia) characterizes a normal response to cold stimulus induced vasospasm. This phenomenon might be implicated in the observed decrease in FTL 10 min after cold exposure in controls by means of restoring aerobiosis and by a washout effect. Patients with SSc also present reactive hyperemia, but it is usually milder and delayed in comparison to controls[8,9], which may result in the persistence of anaerobiosis and accumulation of lactic acid 10 min after cold stimulus. The high post-CS-FTL levels observed in SSc patients suggest these patients undergo more severe consequences of cold exposure in comparison to controls and

Table 1. Pre- and post-cold stimulus (CS) fingertip lacticemy (FTL) (mean, standard deviation, and median) in controls, patients with probable primary RP (PPRP) or probable secondary RP (PSRP), and patients with systemic sclerosis associated RP.

Groups of Patients	Pre-CS-FTL*, mg/dl	Post-CS-FTL**, mg/dl	ΔCS-FTL***, %	Wilcoxon Test† Pre- × Post-CS-FTL
Controls (n = 27)	1.59 ± 0.62 (M = 1.60)	1.23 ± 0.44 (M = 1.20)	–19 ± 23 (M = –12)	3.32 (p < 0.05)
PPRP (n = 18)	1.61 ± 0.60 (M = 1.60)	1.58 ± 0.86 (M = 1.30)	–0.9 ± 36 (M = 0)	0.223
PSRP (n = 31)	1.50 ± 0.74 (M = 1.35)	2.16 ± 1.69 (M = 1.80)	+ 39 ± 55 (M = +33)	3.35 (p < 0.05)
Scleroderma-RP (n = 30)	2.13 ± 1.02 (M = 1.85)	3.23 ± 1.66 (M = 3.05)	+60 ± 62 (M = +50)	3.96 (p < 0.05)

* Pre-CS-FTL: SSc × PPRP × PSRP × controls [Kruskal-Wallis (H = 7.753; 3 df); p = 0.067]. ** Post-CS-FTL: SSc> PSRP, PPRP, controls [Kruskal-Wallis (H = 34.035; 3 df); p < 0.001]. *** ΔCS-FTL: SSc and PSRP > PPRP and controls [Kruskal-Wallis (H = 36.042; 3 df); p < 0.001]. † Wilcoxon test: critical value for p < 0.05 (critical z = 1.96). M: median.

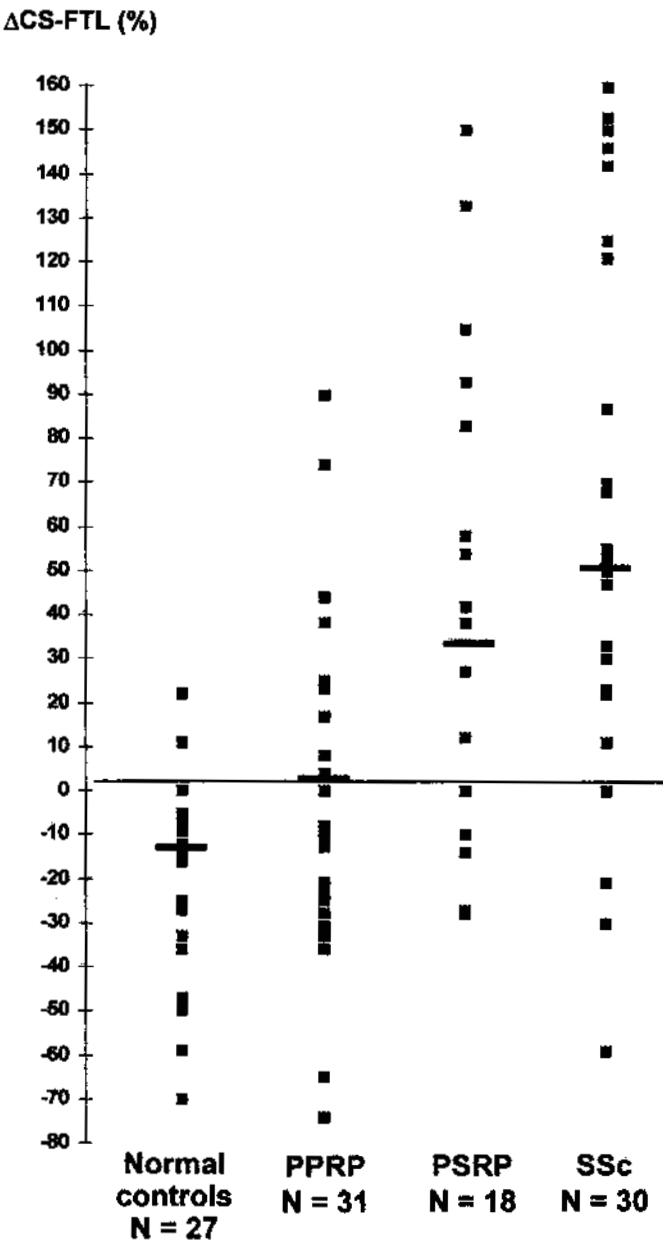

Figure 1. ΔCS-FTL in controls and patients with SSc, probable secondary and probable primary RP. Each point represents the ΔCS-FTL for one patient or control. Horizontal bars represent the median for each group.

emphasize the importance of advising maintenance of comfortable corporal temperature.

The need for cold stimulus in the design of the CS-FTL test was confirmed by the fact that post-CS-FTL and ΔCS-FTL were better discriminators between the 4 study groups than isolated pre-CS-FTL. The establishment of a 10 min interval between cold exposure and the 2nd fingertip blood sampling was based on previous plethysmographic and thermographic studies showing that recirculation after a cold stimulus starts around 8 min in healthy individuals[9].

Although this was not the aim of our study, our results suggest that the CS-FTL test may play a role in the clinical evaluation of patients with isolated RP. A positive ΔCS-FTL seems to bring more confidence to a diagnosis of secondary RP. Conversely, a negative ΔCS-FTL increases the odds against the existence of structurally based RP and suggests benign neurovegetative dysregulation. Prospective studies will be required to explore this possibility.

The CS-FTL test was shown to be a rapid, easy, inexpensive, and well tolerated method for evaluation of fingertip effective perfusion before and after a cold stimulus. The test was able to discriminate most patients with PSRP and SSc associated RP from controls and to identify heterogeneity among PPRP patients. The CS-FTL test is a novel tool that might contribute to further understanding of Raynaud's phenomenon.

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