Hyperreactivity of the Central Sympathetic Nervous System in Vibration-Induced White Finger

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Summary: Vibration exposed workers with and without vibration-induced white finger (VWF), subjects with primary Raynaud's phenomenon and non-exposed controls were investigated in the present studies. The applied stimuli comprised cold stimuli, vibration exposure, and postural stimuli. The digital vasomotor responses to these stimuli were objectively quantified by measurements of finger systolic blood pressure and relative capillary blood flow rate in the skin of the finger. The results indicate that hyperreactivity of the central sympathetic nervous system may function as an abnormal element of the reflex mechanisms triggering the predominant portion of the vasoconstriction in episodic arterial closure of VWF. The hyperreactivity of the central sympathetic nervous system may be induced by prolonged exposure to hand-arm vibration, possibly by activation of the vibration elicited central sympathetic vasoconstrictor reflex mechanisms.

Key words: finger—Raynaud's phenomenon—sympathetic vasoconstrictor reflexes—vibration

Introduction

Since Raynaud (1862) described the visible signs of Raynaud's phenomenon (RP), conflicting theories have been advanced concerning the underlying vascular closure that causes these signs, the hemodynamic disturbance that is responsible for this closure, the mechanism that induces this disturbance and the abnormal element(s) of this mechanism. Today it is generally accepted that different forms of RP may have different pathophysiology, and therefore each form of RP should be evaluated separately. In the present paper the pathophysiological aspects of vibration-induced white finger (VWF) and less extensive those of primary Raynaud's phenomenon (PRP) are elucidated by an overview of studies performed by the author and his coworkers during the past several years.

Subjects and Methods

The present studies comprised in total 150 men (age: 21-73 years) and 17 women (age: 21-39 years). Except for RP all subjects were otherwise healthy. The vibration exposed group of 107 outdoor working men comprised the following groups: Eighteen quarriers; thirty-nine lumberjacks; forty-two road workers; and eight workers who used varying types of vibrating hand tools. Among the vibration exposed men 42 had VWF, five had possible PRP and not VWF, and the remaining sixty men did not have RP. Seven of 17 women had PRP.
All subjects were interviewed by the author. VWF was defined as RP with first appearance after professional use of vibrating hand tools and without other probable causes (Taylor and Pelmear, 1975). PRP fulfilled the clinical criteria demanded by Allen and Brown (1932). The severity of RP was graded according to the Taylor-Pelmear stage assessments (Taylor and Pelmear, 1975).

Indirect measurements of systolic blood pressures on the upper arm (ASP) and ipsilateral fingers (FSP) were performed to detect organic obstructions of circulatory significance in the digital or more proximal arteries. ASP was measured by auscultation using a 12 cm broad cuff that encircled the upper arm. FSP was measured with an inflatable cuff encircling the proximal phalanx of the thumb or the intermediate phalanx of the second to fourth finger, using a strain gauge on the outer phalanx to detect the initial systolic inflow of blood.

Standardized body cooling at average room temperatures of 15-19°C was performed with a cooling blanket (8-12°C) to facilitate the provocation of Raynaud-attacks. Local cooling of a finger or a hand was performed at standardized temperatures during 5 min ischemia to thermostate the digital arterial walls to the cooling temperatures (Nielsen and Lassen, 1977). The intermediate phalanx of the anamnestically most affected finger was thermostated at 30, 15, and 6°C whereas the ipsilateral hand subsequently was cooled only at 10°C. FSP was measured at 15 and 6°C with the same cuff and strain gauge technique as used at 30°C. Thus a decrease in FSP reflects the increase in the digital arterial tone. An indirectly measured zero pressure at 15 or 6°C was defined as an attack of RP (Nielsen and Lassen, 1977). The finger colours after hand cooling were evaluated by a direct visual inspection and by blind assessments of slides of the photographed hand.

In the present studies indirect measurements of relative blood flow rate in cutaneous tissue during postural or vibratory stimuli were performed by the local 133Xe washout technique (Sejrsen, 1969) at a room temperature of 24°C to investigate, if subjects with RP have an exaggerated vasoconstrictor response to other stimuli than cold as proposed by Raynaud (1862). The site of radioactive skin labelling was the dorsum of the distal interphalangeal joint, where there are no arteriovenous anastomoses (Grant and Bland, 1931).

The disappearance curve, corrected for background activity, was plotted against time in semilogarithmic scale. The washout rate constant, k, was computed from the regression line calculated from the least squares method. The sequence of the measurements was: 1) reference, k1; 2) test, k2; and 3) reference, k3 (Henriksen and Sejrsen, 1976). The change factor, F, was defined as:

$$F = \frac{k_2}{0.5(k_1 + k_3)}.$$  

F gives a measure of the relative blood flow rate through cutaneous capillaries of the finger. The change factor, F, was calculated for the anamnestically most affected fingers during each of the following three stimuli: 1) venous statis of 40 mmHg; 2) sitting position; and 3) local exposure to a standardized vibration. The fingers were kept at the level of the mid-axillary line when lying supine and at the level of the jugular notch when sitting upright.

Venular distention caused by an increase in vascular transmural pressure of about 25 mmHg or more elicits an arteriolar constriction, which is mediated by a local sympathetic venoarteriolar axon reflex mechanism (Henriksen and Sejrsen, 1976). Change in body posture from lying to sitting causes a venous pooling of blood in the lower part of the body during rest and thus a reduced baroreceptor activity,
which elicits arteriolar constriction mediated by central sympathetic reflex mechanisms comprising the spinal cord and/or higher centres in the brain (Blomqvist and Stone, 1983). In the vibration test the volar side of the distal interphalangeal joints of the index, middle, and ring finger, which included the finger labelled by $^{133}$Xe, were exposed to a vertical sinusoidal acceleration of 100 m•s$^{-2}$ (root-mean-square value, unweighted) at a frequency of 125 Hz.

The underlying mechanisms of the vasomotor responses to cold, sitting, and acute vibration exposure were investigated by repeated measurements performed during proximal nervous blockade in a varying number of subjects. The proximal nervous blockade was performed as a conventional digital block at the base of the finger. The investigated regions of the fingers were located 5-7 cm distal to the finger base, these distances exceeding the radius of action of the local sympathetic vasoconstrictor reflex (Henriksen and Sejrsen, 1976). Consequently a vasoconstrictor response to a given stimulus, which could be abolished by the nervous blockade, was assumed to be mediated by central sympathetic reflex mechanisms.

Site of Primary Vascular Closure

All blood vessels are closed in the white finger. However, closure of one single type of vessels may theoretically cause the cessation of cutaneous blood flow, i.e. is the primary vascular closure (Lewis, 1929).

Primary vascular closure has been suggested to be situated either on the venous (Brisco, 1918) or on the arterial side (Raynaud, 1862; Lewis, 1929) of the cutaneous capillary network. The finding of Landis (1930), that the directly measured cutaneous capillary blood pressure decreased to 5-8 mmHg during episodes of RP, casts considerable doubt on the venous closure theory and seems to be entirely compatible with the arterial closure theory. In 1977 Nielsen and Lassen described a method for indirect measurement of finger systolic blood pressure (FSP) after local cooling of the midphalanx. Their findings suggest that a measured zero FSP is due to a complete closure of both main arteries in the cooled segment of the finger.

In subjects with anamnestic VWF, a zero pressure after combined body and finger cooling was first measured by Olsen and Nielsen (1979). The findings of a zero pressure were to a great extent in agreement with the workers’ history of VWF, but a zero pressure was further recorded in some vibration exposed subjects without anamnestic VWF (Olsen and Nielsen, 1979; Olsen et al. 1982; Olsen and Nielsen, 1988). However, it was demonstrated that all vibration exposed workers without an actual history of RP but with a zero pressure after finger cooling either showed visual signs of RP in a subsequent hand cooling test or had a history of previously active VWF (Olsen, 1988). All these findings of the present studies indicate that the visible signs of RP in VWF reflect an underlying circulatory arrest, which is caused by a primary, pathognomic closure of all main arteries in the cooled segment of the affected finger.

The present findings of a zero pressure in subjects with VWF have later been confirmed in other studies (Thulesius et al. 1981; Ekenvall and Lindblad, 1982). Reversible closure of the proper digital arteries has further been confirmed by arteriographic findings before and after hand cooling in subjects with RP (Rösch et al. 1977).

Permanent Hemodynamic Disturbances

The basic hemodynamic disturbance of arterial closure in RP may be either tran-
sient, i.e. exclusively associated with the closure, or permanent, i.e. independent of the closure period (Lewis and Pickering, 1934).

In the present studies possible permanent hemodynamic disturbances in VWF were evaluated by measurements of blood pressures before finger cooling. The systolic blood pressure gradient (SPG) from the upper arm to the most affected finger was normal in forestry workers of stage 2 and increased in lumberjacks in stage 3 (Olsen et al. 1982). In other studies, a normal SPG was found in vibration exposed workers with RP (Olsen et al. 1987; Olsen and Petring, 1988; Olsen, 1988). These results of SPG indicate that episodic arterial closure of VWF often occurs in subjects without significant obstructions or compressions of the arteries in or leading to the affected fingers (Hirai, 1978). Thus the hemodynamic disturbance of VWF seems to be a transient disturbance that may or may not be combined with permanent disturbances.

The present results have been confirmed and supported by strain gauge measurements in other studies (Ekenvall and Lindblad, 1986). Arteriographic findings have demonstrated an equal frequency of arterial obliterations of hands and fingers in subjects with VWF and age-matched, non-exposed, hard manual workers without RP (Wegelius, 1972). In microscopic, biopsy studies of proper digital arteries no obstructive changes could be observed in mild and moderate cases of VWF whereas subintimal and periarterial fibrosis was seen in more severe cases (Ashe and Williams, 1964; Takeuchi et al. 1986). Thus the results of the present and most other studies indicate that the basic hemodynamic disturbance of episodic RP is transient and not permanent in non-complicated VWF.

Transient Hemodynamic Disturbances and Their Mediating Mechanisms

The basic transient hemodynamic disturbance of episodic arterial closure in VWF may be either active, i.e. an exaggerated contraction of vascular smooth muscle cells, or passive. Active disturbances may be mediated by local mechanisms, humoral mechanisms, or central sympathetic reflex mechanisms. Passive disturbances may be transient thromboembolic events possibly caused by vibration-induced endothelial damages, and vibration-induced changes to cold stimuli in viscoelastic properties of the arterial wall.

In the present study of VWF the exaggerated arterial vasoconstrictor response to cold decreased during proximal nervous blockade to a value not different from that of controls without nerve block (Olsen et al. 1985). These results indicate that the predominant disturbance of VWF is a transient, active disturbance of the proper digital arteries, which is mediated by central sympathetic reflex mechanisms. The results do not exclude the possibility that transient, passive disturbances and transient, active disturbances mediated by humoral and local mechanisms may contribute to a minor extent in the establishment of episodic arterial closure in VWF.

The present comparison between the quantified, centrally mediated cold response of digital arteries and that of other transient mechanisms in episodes of RP has never been performed in other studies. Our finding of a predominant central sympathetic cold response in episodic arterial closure is in agreement with the original proposal of Raynaud (1862) for vasospastic RP and in disagreement with the "local digital vascular fault" theory of Lewis (1929). This result may be explained theoretically by one or more abnormal elements of the central sympathetic reflex mechanisms: An exaggerated sensory in-
CENTRAL SYMPATHETIC HYPERREACTIVITY

Abnormal Elements of Postural Vasoconstrictor Reflex Mechanisms

The present results of a normal vasoconstrictor response to venous stasis of 40 mmHg and an exaggerated vasoconstriction to sitting in subjects with non-complicated VWF indicate a normal function of the local sympathetic veno-arteriolar axon reflex and an augmented function of the orthostatically elicited central sympathetic reflexes (Olsen et al. 1987). This may freely be explained by a normal net resultant function of postganglionic elements, i.e. postganglionic sympathetic nerve fibres, neurovascular synapses, pre- and postsynaptic adrenergic receptors and digital arteriolar smooth muscle cells, and a hyperreactivity of the preganglionic elements, i.e. the central sympathetic nervous system, in subjects with vasospastic VWF. Similar results were obtained in subjects with non-complicated PRP (Olsen et al. 1987). Our findings seems to accord with Raynaud's (1862) original suggestion of hyperreactivity of the central sympathetic nervous system to stimuli other than cold in subjects with vasospastic types of RP. This hyperreactivity may be of constitutional origin in subjects with PRP and may be induced by prolonged activation of the vibration elicited central sympathetic vasoconstrictor reflex mechanisms (Olsen and Petring, 1988) in subjects with VWF. In contrast with our results in vasospastic RP, the local axon reflex mechanism is absent in patients with severe generalized scleroderma (Kristensen, 1980), who often suffer from an obstructive type of RP.

Raynaud (1862) suggested that emotion could provoke episodes of RP whereas Lewis (1929) never observed an attack due to a stimulus other than cold. In the present studies all subjects with RP had a clear washout of radioactivity from the labelled depot during the applied postural and vibration stimuli, which indicates that these stimuli did not provoke episodes of RP (Olsen et al. 1987, Olsen and Petring 1988). However, it seems reasonable to assume that the indicated hyperreactivity of the central sympathetic nervous system...
to orthostatic stress in subjects with VWF and PRP functions as an abnormal element also in their central sympathetic vasoconstrictor response to cold. It has been hypothesized that hypertrophy of digital arteriolar musculature is the predominant abnormal element in the central sympathetic cold response of subjects with VWF (Hyvärinen et al. 1973). However, biopsy studies have shown no changes in digital arterioles of subjects with VWF (Gurdjian and Walker, 1945) or in digital arteries of subjects with mild and moderate VWF (Ashe and Williams, 1964). Thus a hypertrophy of vascular smooth muscle cells cannot be an original abnormal element in VWF, which is in accordance with the present finding of a normally functioning local axon reflex mechanism.

The association between VWF and hearing loss has been documented in several recent studies and has been proposed to be caused by identical abnormalities in digital and cochlear vasoconstriction (Iki et al. 1985; Pyykö et al. 1986). It may be explained by the hyperreactivity of the central sympathetic nervous system.

Abnormal Elements of Vibration Elicited Vasoconstrictor Reflex Mechanisms

The augmented function of the vibration elicited central sympathetic vasoconstrictor reflex in subjects with PRP (Olsen and Petring, 1988) was freely explained by their hyperreactive central sympathetic nervous system (Olsen et al. 1987). For similar reasons, an exaggerated vasoconstriction to acute vibration exposure was to be expected in subjects with VWF but a normal response was shown (Olsen and Petring, 1988). This may be explained by a vibration-induced peripheral sensory neuropathy (Lidström et al. 1982), whereas an adaption of the central nervous system to vibration seems less probable (Pyykkö et al. 1982).

An augmented decrease in finger pulse volume to acute vibration exposure has been observed in about 40% of subjects with VWF (Hyvärinen et al. 1973), which does not statistically contrast to the present findings (Olsen and Petring, 1988).

It is uncertain whether this indicated peripheral sensory neuropathy may further involve the peripheral sensory elements of the central sympathetic reflex mechanisms of the cold response in subjects with VWF. However, it may inhibit aggravation of the vibration-induced hyperreactivity of the central sympathetic nervous system and in this way improve the prognosis of VWF.

Conclusions

The main results of the present studies indicate some aspects of physiological significance concerning vibration-induced white finger (VWF). These aspects are given below.

The visible signs of episodes of Raynaud's phenomenon (RP) reflect an underlying circulatory arrest, which basically is caused by a primary closure of all proper digital arteries in the cooled segment of the affected finger. The basic hemodynamic disturbance of this epistic arterial closure is a transient vasoconstriction of the digital arteries, which is predominantly mediated by central sympathetic reflex mechanisms.

At thermoneutral conditions in subjects with VWF, central sympathetic reflex mechanisms constricting digital resistance vessels have a possible decreased net resultant function of their peripheral afferent, mechanoreceptive elements, a hyperreactivity of their central, preganglionic elements, and a normal net resultant function of their postganglionic elements. During exposure to cold, this hyperreactivity of the central sympathetic nervous system may function as an/the abnormal element of the central sympa-
thetic vasoconstrictor reflex mechanisms triggering the predominant portion of the basic, transient vasoconstriction in episodic arterial closure of VWF. The hyperreactivity of the central sympathetic nervous system may be induced by prolonged exposure to hand-arm vibration, possibly by activation of the vibration elicited central sympathetic reflex mechanisms.

References


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