Transcutaneous monitoring of pO_2 in the assessment of peripheral vascular disease

December 1997

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There are several diagnostic approaches to identify and quantify different types of vascular disease. However, these methods usually do not reflect the condition of the cutaneous circulation.

Because transcutaneous oxygen reveals the status of cutaneous circulation, it has been shown to be a powerful diagnostic tool in the evaluation of various aspects of arterial and venous diseases.

Introduction

There are several diagnostic approaches to identify and quantify different types of vascular disease, e.g. segmental pressure, doppler velocity, various types of plethysmography.

In most cases they fulfill this goal as long as the prime objective of examination is the circulatory state of the skeletal muscle system. These methods, however, usually do not reflect the condition of the cutaneous circulation because it represents only about 1/10 of the total limb circulation.

Transcutaneous pO_2 (tcpO_2), on the other hand, reveals the status of cutaneous circulation. tcpO_2 has been shown to be very useful in the evaluation of various aspects of arterial as well as venous disease.

Arterial Disease

Peripheral arterial occlusive disease (PAOD) is one of the most widely encountered impairments of the arterial system. It has been shown that the perfusion of the lower extremity has to be significantly compromised to affect a reduction of the skin circulation [1].

This explains why tcpO_2 values reflect the degree of skin viability. Reduction in skin perfusion lead to a spectrum of different degrees of skin viability ranging from mild trophic changes (e.g. absence of hair, nail changes) to more severe complications such as non-healing ulcers.

However, non-healing ulcers can also develop in the presence of an adequate arterial inflow (neuropathic ulcer) or due to a severe insufficiency of the venous system (venous ulcer).

Venous Disease

The efficiency of the venous circulation can be compromised by an insufficiency of the venous valvular system, an obstruction of the deep venous system (deep venous thrombosis), or both.

It has been documented that venous ulcers develop mainly if the site of venous pathology is below the knee [2, 3]. From a hemodynamic point of view, distal valvular insufficiency, including the perforating venous system, is the most frequent cause of trophic changes of the skin culminating with the extreme form: venous ulcers.

Microvascular Disease

The definition of microvascular disease is equivocal. There is no question about there being a primary impairment of microcirculation, but there is a dilemma: Is the microvasculature dysfunctional and the large arterial system (> 1 mm diameter) intact?

Or is the microcirculatory disturbance caused by a decreased arterial blood supply or increased venous pressure induced by venous disease? The ambiguity can be overcome by preceding any description of microvascular disease with an assurance that the large arterial or venous system functions within normal physiological limits.

Physiology of the skin

The skin consists of three different layers: epidermis, dermis, and subcutaneous tissue. Each one has specific functions:

Epidermis - is the outer layer which protects the body from the external environment. The cornified epidermis is a barrier to infection and a protection against water loss. It contains no vessels. Oxygen which diffuses from the capillaries has to traverse the epidermis to reach its surface.

Dermis - is the middle layer with a dense vascularization, mainly of arterioles, capillary loops and venules. In addition, it is the site of different types of glands, hair follicles and nerve fibers. The arterioles are very sensitive to temperature changes - an increase in temperature reduces the resistance, leading to an increased blood flow.

Subcutaneous tissue - sometimes defined as the hypodermis, contains different types of connective tissue cells especially fat cells - adipose tissue.

Transcutaneous measurements

Evans and Naylor [4] demonstrated, for the first time, that it is possible to monitor pO_2 of diffused oxygen from the surface of the skin by using a modified Clark-type electrode. The pO_2 varied under these conditions between 0 - 3.5 mmHg.

They proved, in addition, that with the removal of some superficial layers of epidermis (e.g. by stripping with tape) or with increasing skin blood flow (e.g. by using ultraviolet light), the recorded pO_2 reached up to 30 mmHg. Heat-induced vasodilation was utilized by Huch *et al* [5] and Eberhard *et al* [6], demonstrating good arterializing by adding a heating element to the polarographic probe.

Measurement Technique

1. **Calibration** - following the calibration instructions recommended by manufacturer.

2. **Site selection** - an ideal site would be located over a homogenous capillary bed without large veins, skin defects, or hair. Placing it directly over bone may also give erroneous results, especially if a change in body position causes skin to be pulled against a protruding bone.

3. **Site preparation** - To improve oxygen diffusion and to standardize the measurement technique it is

recommended that excessive skin cells be removed by stripping the skin 10-15 times with an adhesive tape (e.g. 3MTM filament tape), using a fresh tape section each time.

4. **Probe placement** - Place the probe on the selected site immediately after calibration is completed. To prevent strain or tension on the probe, secure the cord against the skin by using standard medical tape.

5. **Measurement** - It takes about 15 minutes after the probe has been placed on the skin for the tcpO_2 to become stabilized.

Factors Influencing tcpO_2 Values

- Probe temperature (due to the affect on microvasculature and on the oxyhemoglobin dissociation curve).
- Arterial pO_2.
- Metabolic consumption of O_2 by the dermal tissue.
- Oxygen consumption by the electrodes.
- Skin thickness and skin resistance to O_2 diffusion (more pronounced to dynamics).
- Capillary density and rate of cutaneous blood flow.

Transcutaneous pO_2 in arterial disease

Resting Values in Arterial Occlusive Disease

Numerous studies have documented that tcpO_2 values are usually reduced in severe PAOD, especially in critical ischemia [1, 8, 9, 10, 11, 12, 13], but the separation between normal and ischemic skin is not reliable, except in critical ischemia.

Hauser *et al* [14] introduced the "regional perfusion index (RPI)" which relates the limb tcpO_2 to that of the chest. It proved to be especially useful during exercise testing. In order to increase the sensitivity of the test, various sensitizing procedures, which are described below, have been proposed and tested.

In order to increase the sensitivity and specificity of tcpO_2 methodology, a number of "sensitizing" procedures have been applied. This applies not only to the improvement of diagnostic accuracy but also to better utilization of this methodology to prognosticate normal healing and optimal amputation level determination.

Sensitizing Maneuvers

Leg position - in normal lower extremities tcpO_2 values decrease with leg dependency if the skin temperature is maintained at 37 oC [15].

In patients with severe peripheral arterial occlusive disease (PAOD), an increase is usually observed. From a practical point of view the results with a 44 oC heated probe are more relevant. An average increase of 15.1 mmHg was observed in normal subjects when changing from a supine to sitting position, whereas in patients with PAOD the increase was significantly higher, 28.1 mmHg.

The effect of leg position was described by Becker *et al* [16] as a useful test to classify the severity of PAOD. Only 5 % of PAOD patients required amputation if forefoot tcpO_2 (44 oC) was > 40 mmHg in the sitting position, while patients with <10 mmHg could expect a 85 % chance of amputation.

These findings were recently confirmed by Scheffler *et al* [17], who could objectively identify critical ischemia if tcpO_2 in sitting position was found to be less than 40 mmHg.

Transitional Occlusion (Post Occlusive Reactive Hyperemia PORH)

The well described PORH response observed in flow studies, can be reproduced with tcpO_2 measurement with a probe temperature of only 37 oC [18] but, as described above, the results at this probe temperature, are not very reliable.

On the other hand, when the standard 43 oC or 44 oC probe temperature is used, the "overshoot" is not recorded (probably due to local vasodilatation) but the rate of circulatory recovery measured as tcpO_2, T/2 (the time it takes to reach 50 % of the initial tcpO_2 value) after a 4-minute occlusion can be easily measured: 87.1 seconds in control subjects and 136.1 seconds in patients with severe PAOD [19].

Similar results were reported by Kram *et al* [20] and Slagsvold *et al* [21].

Effect of Exercise

Exercise has been used to "sensitize" the investigative methods to separate claudicants from normal subjects. Standardized treadmill protocols were used by Hauser and Shoemaker [14] and Holdich *et al* [22], but the correlation of tcpO_2 with pain-free walking distance was not satisfactory.

A more severe exercise protocol was probably the reason for a better correlation obtained by Schmidt *et al* [23]. Byrne *et al* [8] found 20 % of claudicants with normal tcpO_2 values. However, they showed a significant decline after exercise (treadmill at a speed of 1.5 miles/hr and 20 degrees incline).

Oxygen Inhalation

Similar to leg dependency, oxygen inhalation helps to unmask hidden oxygen reserves by increasing O_2 saturation in the arterial blood. Under normal conditions, following inhalation of 100 % oxygen, tcpO_2 values from the foot increase by approximately 230 % [24].

This response is significantly reduced in patients with arterial disease [25, 26].

Determination of Optimal Amputation Level

There is a relatively wide range of critical tcpO_2 values that separate successful from unsuccessful amputation stump healing. The majority of researchers consider 30 mmHg as the critical dividing line [27, 28, 29, 30, 31]. Kram and coworkers [20], using the calf/brachial tcpO_2 ratio, concluded that a ratio >0.20 predicts successful stump healing.

Franzeck *et al* [19] originally considered 10 mmHg as a dividing line but in view of some primary stump healing occurring below 10 mmHg as well, they decided to apply oxygen inhalation as a "sensitizing" factor.

In subsequent studies from the same group, the 10 mmHg dividing line was reconfirmed, but the accuracy was increased if an increase of tcpO_2 beyond the 10 mmHg with oxygen inhalation was considered to predict successful amputation stump healing [25, 32]. McCollum *et al* [24] prefer the determination of rate of change of tcpO_2 during oxygen inhalation. A rate of increase of 9 mmHg/min is considered a dividing line.

Currently, it is difficult to explain the relatively wide range of tcpO_2 "dividing lines" separating potential successful from unsuccessful stump healing. A number of factors have to be considered: the average experience of the surgical group, electrical specifications of the probes and especially oxygen consumption of the probe. It seems useful that each institution, together with the instrumentation used, establish its own exact criteria.

Predicting Wound Healing

Patients with severe arterial occlusive disease may develop a poorly healing wound even after a small trauma. In the most severe stage (Fontaine IV), spontaneously developing ulcera usually resist standard conservative treatment.

Under these conditions very low tcpO_2 values are recorded; usually between 10-20 mmHg. A 10 mmHg level is generally considered to be incompatible with spontaneous or conservatively treated healing process. With leg dependency, a value of 40 mmHg can be considered as a discriminant value [17].

Diabetic Neuropathy

Gaylarde *et al* [33] have shown that at 37 oC, tcpO_2 in the legs and feet of diabetic patients with peripheral neuropathy was significantly higher than in control subjects and diabetic patients without neuropathy.

After a probe temperature increase to 44 oC, tcpO_2 increased in all three groups, but the increase was smallest in diabetics with neuropathy. These results are consistent with a loss of vasoconstrictor tone. Similar results were reported earlier by Weindorf *et al* [34] using heat or rubefacients.

Therapeutic Control Using tcpO_2

Effect of Drugs

It is important to recognize that at probe temperature of 41 oC, local vasodilator administration does not increase tcpO_2 value [35]. It is therefore not surprising that studies using various vasodilator agents sometimes yielded confusing and even decreasing tcpO_2 values, especially in patients with arterial disease [36, 37, 38].

Positive results have been obtained, however, when probe temperature was kept at 37 oC [39, 40]. Under this condition it could be shown that there was a significant increase in tcpO_2 (at 37 oC) after an i.v. infusion of prostaglandin E in patients with critical ischemia.

Effect of Balneologic Treatment

Exposure to CO_2-containing water increased tcpO_2 (44 oC) from 63.8 mmHg to 71.3 mmHg (after 20 minutes) in patients with arterial occlusive disease. The effect of temperature was ruled out by a placebo study using standard water [41].

Transcutaneous pO_2 in venous disease

Most investigators have found tcpO_2 to be reduced in extreme cases of venous disease (e.g. in venous ulcers), while the results are normal in the unaffected skin. This is distinctly different in arterial disease, where reduced tcpO_2 can be detected in a significantly wider area.

An exception represents the liposclerotic skin where the overall tcpO_2 is reduced, but to a lesser degree than in the immediate proximity of the ulcer. It has to be pointed out that there is a pronounced overlap with normal values, except at the edge of ulcers where the tcpO_2 values are homogeneously lower.

An interesting explanation for the heterogeneity of tcpO_2 results was recently given by Roszinski and Smaller [42] who compared noninvasive tcpO_2 with invasive (needle electrodes) pO_2 determinations in the tissue.

While the results varied very little in normal patients when moving the needle in 1 mm intervals, the same movements of the needle in patients with venous trophic changes yielded alterations of 10-30 mmHg, depending on the severity of the condition.

The reduced tcpO_2 values in venous disease, reported by a number of investigators [43, 44, 45, 46, 47, 48, 49] can also be explained by the results obtained with a transparent tcpO_2 probe that permits simultaneous vital microscopy [11].

The correlation of tcpO_2 and morphologic characteristics also offers an explanation of the overlap reported by many authors. Franzeck *et al* [11] and, later, Hoffmann *et al* [50] demonstrated a direct correlation of tcpO_2 values with microvascular density.

At sites of white atrophy (atrophie blanche) there was also an unmeasurable tcpO_2 level which grew with the increasing numbers of capillaries. Moosa *et al* [51] confirmed the low tcpO_2 values close to venous ulcers, but could demonstrate a significant increase after oxygen inhalation.

Though the increase percentagewise was higher around the ulcers than in the healthy tissues, the final tcpO_2 values were still lower. This was interpreted by the authors as a confirmation of the "fibrin cuff" theory, which explains the trophic changes in venous disease by a layer of fibrin surrounding the capillaries thus compromising oxygen diffusion [52].

The lower post-oxygen inhalation tcpO_2 values can, however, also be explained by a decreased capillary density as discussed above. Partsch [53] argues that since oxygen inhalation leads to a higher tcpO_2 increase in the vicinity of venous ulcers than in the vicinity of arterial ulcers, the factor of diminished blood supply may be less of a contributing factor.

Effect of Drugs on tcpO_2 in Venous Disease

Neumann and van den Brock [54] observed a slight but statistically significant increase in tcpO_2 in patients with moderate degrees of venous insufficiency, after adminis-

tration of O-rutosides. Similar results were reported previously by Belcaro *et al* [55].

Factors Affecting tcpO_2 in Venous Disease

Edema

Edema reduction achieved for instance by external intermittent compression [56] did not influence the tcpO_2 reading which could be interpreted to mean that edema per se has no effect on tcpO_2. This question does not seem to be settled because Kolari *et al* [39] found an increase in tcpO_2 after edema reduction.

Similarly, Creutzig *et al* [38] recorded an increase in tcpO_2 (close to the ulcer) after compression (bandaging).

Elastic Compression

An interesting method to estimate a so-called venomotor index by comparing tcpO_2 values was obtained by Rooke *et al* [57] with two different temperatures (42 oC and 45 oC): the ratio of these two values represents the index.

They found in stasis dermatitis a decreased tcpO_2 and a decreased "venomotor" index which improved with elastic compression.

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