Transcutaneous monitoring of pO_2 in hyperbaric medicine

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Summary

Transcutaneous oxygen measurements play an important role in the evaluation and management of problem wounds. No precise threshold or target values exist for the prediction of outcome, and it is quite possible that each wound will have highly individualized oxygen dose requirements.

Correction of ambient dermal oxygen tension should be the goal of adjunctive hyperbaric oxygen therapy, rather than the reliance on a particular ambient or hyperoxic value. We have found the four-step procedure, detailed above, to be effective in guiding the appropriate application of HBO therapy in problem wound cases.

Transcutaneous oxygen measurements have become an important diagnostic tool in assessing a patient's need for and response to hyperbaric treatment. Serial transcutaneous oxygen measurements can also provide an objective assessment of hyperbaric oxygen's effectiveness.

1. The clinical basis of hyperbaric medicine

The concept of using high pressure environments for therapeutic purposes was first proposed several hundred years ago. It was not until the early 20th century, however, that the first of several beneficial effects associated with such environments was clinically validated.

Utilizing the inverse relationship between pressure and volume, as described by Boyle's Law, hyperbaric medicine became the standard of care in the treatment of decompression sickness. Divers, aviators, and other compressed air workers who suffered this occupational disease were prescribed "recompression" in hyperbaric chambers, breathing air.

During the 1950s and 1960s, the effects of hyperbaric oxygen were investigated, and several additional beneficial effects were identified.

At three times atmospheric pressure (sea level), sufficient oxygen is dissolved in the plasma to meet basal metabolic requirements, in the absence of hemoglobin. This research demonstrated a mechanism of oxygen transport independent of chemical binding, and provided the physiological basis for the treatment of carbon monoxide poisoning, acute blood loss anemia and inadequately perfused skin flaps.

Cardiovascular surgeons recognized the value of hyperbaric oxygenation in increasing the brief periods of ischemia that were otherwise available during cardio-vascular surgery. Large hyperbaric "operating rooms" were constructed at major medical centers throughout the world. Such application was short-lived, however, following the introduction of extra-corporeal circulation (heart-lung machines).

During this period, the application of hyperbaric doses of oxygen was found to be helpful in the management of clostridial perfringens (gas gangrene).

Initially thought to be the result of a bacteriocidal mechanism, hyperbaric oxygen was determined to be bacteriostatic under clinical conditions, and interrupted the elaboration of a highly potent toxin. By the 1970s, hyperbaric oxygen was found to normalize and enhance leukocyte-mediated phagocytosis of aerobic bacteria, under ischemic oxygen-induced states. Arteriolar vasoconstriction had been recognized as early as 1948.

Exposure to hyperbaric doses of oxygen was found to compound this effect. Importantly, this phenomenon occurred without component hypoxia, as decreased flow was offset by the enhanced oxygen-carrying capacity of blood under conditions of hyperbaric hyperoxia. Resulting clinical applications included acute thermal burns (with reduced fluid loss/fluid resuscitation requirements) and compartment syndrome.

A mechanism of improved wound healing was first suggested in the management of thermal injury. Acutely burned patients undergoing hyperbaric oxygen therapy for concurrent carbon monoxide poisoning, appeared to heal their lesions more quickly, and with fewer complications, than burn patients who did not require hyperbaric oxygenation. Standardized burn models supported by hyperbaric hyperoxia improved would healing.

Several other wound models, including those complicated by infection, ischemia and radiation tissue injury, shared enhanced healing when subjected to hyperbaric oxygen.

Reperfusion injury is the most recent therapeutic mechanism to be identified. Much of the damage associated with this form of injury, which follows brief periods of complete ischemia, is mediated by the leukocytes.

Hyperbaric oxygen, provided shortly before, during or soon after flow is re-established, has been shown to blunt inappropriate leukocyte activity. Clinically, this mechanism is used in carbon monoxide poisoning and compromised skin flaps.

Several independent effects are anecdoted with the intermittent, short-term, high dose delivery of 100 % oxygen. Accordingly, wide-ranging disease states are considered to benefit when hyperbaric oxygen is added to standard medical and surgical management.

2. Hyperbaric medicine delivery systems

To achieve the benefits described above, 100% oxygen must be administered at pressures in excess of normal atmospheric conditions. This is accomplished by placing the patient into a hyperbaric (high pressure) chamber and compressing its internal environment.

Air or oxygen is used as the compression gas, depending upon chamber type. The patient, however, must breathe oxygen. All of hyperbaric medicine's therapeutic effects are "centrally" mediated. There is essentially no topical effect.

Two general configurations of hyperbaric delivery systems are available. One that accommodates several patients; the other is designed for single occupancy.

The multiple occupancy "multiplace" chamber has long been associated with the effect of diving and other compressed gas operations. It is constructed of steel, has two or more compartments, and is compressed with air.

Capacity is specified at the time of ordering, and typically ranges from four to eighteen people. Patients breathe oxygen via an individualized delivery system, involving either an oval nasal mask, hood/head tent or endotracheal tube. Patients are accompanied by one or more attendants, who breathe the chamber's air atmosphere.

An alternative approach involves the "monoplace" chamber. As the name implies, it accommodates a single unattended patient. Compression gas is oxygen. Patients breathe directly from the internal atmosphere, avoiding the need for an individualized oxygen delivery system.

Recent technical and biomedical advances allow the treatment of unstable and critically-ill patients in relative state of isolation.

Some variations of the multiple chamber are available. One system is configured to accommodate one patient and one attendant, a record is designed for the one patient/one attendant approach.

Regardless of chamber type, therapeutic benefits are identical. The decision to incorporate a particular type of chamber in a hospital-based therapeutic service is based largely on economic considerations rather than clinical case management issues.

3. Hyperbaric treatment protocols

Hyperbaric oxygen therapy schedules are based, in part, upon avoidance of oxygen toxicity rather than the provision of a precise dose of hyperoxygenation for a specific disease process.

It is only quite recently that investigations have begun to identify treatment schedules that maximize therapeutic benefit. However, this work is not yet complete. Several of the more commonly treated conditions, such as diabetic foot infections and compromised skin flaps, presently lack well defined management guidelines. Sequential transcutaneous oxygen assessments will play an important role in this regard.

It is reasonable to assume that some disease states for which hyperbaric oxygen is employed require highly individualized oxygen dosing. Again, transcutaneous oxygen measurements will help to determine such requirements. Hyperbaric treatment protocols employ three interrelated factors: pressure, duration and frequency.

As with any pharmalogic agent, provision of hyperbaric oxygen can range from therapeutic to overtly toxic doses. The commonly appreciated therapeutic range extends from 1.5 to 3.0 atmospheres absolute (ATA). Use of oxygen pressures greater than 3.0 ATA carries an unacceptable risk of central nervous system toxicity.

Where angiogenesis is the primary goal, as with healing complications in previously irradiated tissue, oxygen has been shown to be dose-dependent. The higher the oxygen pressure the greater the degree of neovascularization. This dose-dependent response has also been observed in the study of acute carbon monoxide poisoning and gas gangrene.

Duration of treatment is less well defined, and varies considerably. Typical treatments involve 60 to 120 minutes each. Additional variance exists in terms of what part of the hyperbaric procedure is considered the "treatment" period.

The 60-120 minute treatment may be recorded from initiating compression until the chamber has been returned to normal atmospheric conditions. Alternatively, it may be recorded as the time spent at the prescribed treatment pressure, and omits the compression/decompression phases.

Treatment duration for decompression diseases has been standardized for several decades, but studies are needed to determine optimal duration for conditions treated hyperbarically.

The final factor—frequency, is based upon individual response. In cases of acute carbon monoxide poisoning and decompression illness, one or two treatments may be all that is necessary.

Treatment of compressed skin flaps and wound infections is highly individualized, and may vary from five to fifteen treatments. Where angiogenesis is the primary treatment goal, the number may vary from fourteen to forty. A typical average course of therapy for all conditions can be accepted to be in the 18-20 range.

4. Clinically accepted indication for HBO

Air or gas embolism

HBO, the primary treatment of air embolism, decreases bubble size and increases the diffusion gradient of embolized gas. It reduces mortality and the risk of developing permanent neurological damage.

Carbon monoxide poisoning and smoke inhalation

Considered mandatory for severe CO poisoning, HBO hastens carboxyhemoglobin dissociation beyond a rate achievable by breathing pure oxygen at sea level. It mitigates tissue poisoning and markedly reduces permanent neurologic damage. When CO is complicated by cyanide poisoning, HBO may have a direct effect in reducing the toxicity of cyanide.

Clostridial Myonecrosis (Gas Gangrene)

Recommended treatment is a combination of HBO, surgery and antibiotics. When used early and before surgery, HBO saves lives as it requires less invasive surgery, radically diminishes the need for amputations, and brings the rapid cessation of alpha-toxic production, which is the lethal combination of gas gangrene.

Crush injury and other acute traumatic ischemias

HBO increases tissue oxygen tensions to levels which allow host responses to infections and ischemia to become functional. Effects include enhanced oxygenation at the tissue level, increased oxygen delivery per unit of blood flow and edema reduction.

Decompression illness

HBO is the primary treatment, as it establishes a favorable diffusion gradient, to rapidly resolve the inert gas bubbles and provide oxygenation to ischemic and hypoxic tissues. There is no alternative therapy.

Problem wounds

In a hypoxic environment, wound healing is halted by decreases in fibroblast proliferation, collagen production and capillary angiogenesis. HBO can restore a favorable cellular environment in which healing and antibacterial mechanisms are enhanced.

Exceptional blood loss anemia

In exceptional cases (Jehovah's Witnesses and certain hemolytic anemias) when cross-matched transfusion is not possible, the intermittent use of HBO dissolves enough oxygen in the severely anemic patient to support basic metabolic needs until sufficient RBC's are restored.

Necrotizing soft tissue infections

As an adjunct to debridement and systemic antibiotics, HBO adversely affects anaerobic bacterial growth by direct toxic mechanisms and decisively increases white cell bacterial killing. Published studies indicate its routine use can decrease mortality by two-thirds.

Refractory osteomyelitis

HBO is used as an adjunct to antibiotics, debridement, nutritional support and reconstructive surgery in cases of superficial, localized and diffuse osteomyelitis, particularly in the presence of localized or systemic host compromise. Host compromise is usually associated with refractory bone infections. HBO is demonstrably effective in sternal wound infections.

Radiation tissue damage

In proper coordination with surgical treatment, HBO has totally reoriented the approach to the repair of radiation necrosis. It has been shown to stimulate growth of functioning capillaries, fibroblastic proliferation and collagen synthesis in the radiated bone and soft issue itself. Healing can take place normally, and grafting of soft tissue or even bone is possible in previously irradiated tissue.

Compromised skin grafts, flaps and replants

Following ischemia or vascular repair in cases where there has been decreased microcirculation or hypoxia, HBO has been demonstrated to maximize the viability and final function level of the compromised nerve and muscle tissue.

Thermal burns

As an adjunctive to standard treatment in a burn center, HBO helps maintain microvascular integrity, minimizes edema and provides the substrate necessary to maintain viability. In severe burns, mortality, hospital stay and need for grafting have been markedly reduced.

5. Transcutaneous pO_2 Measurements - General

Transcutaneous pO_2 ($tcpO_2$) measurement was developed in the beginning of the 1970s by Huch *et al*. Good correlations were obtained with arterial pO_2 in the neonates, and the method has been widely used in the neonatal intensive care units.

The special design of the transcutaneous sensor makes it possible to obtain very accurate pO_2 (and pCO_2) measurements on the surface of the skin. The sensor application system ensures an airtight seal from the ambient atmosphere.

Thus, it measures the pO_2 in the contact liquid, which will be in equilibrium with the underlying dermal tissue pO_2, 10-15 minutes after skin application.

Physiology of the Measurement

The heating element of the transcutaneous sensor increases the temperature beneath the sensor. This results in increased blood flow of the dermal capillaries, which tend to become "arterial" in terms of O_2 content, due to relatively less extracted O_2.

Heating the blood causes a shift to the right of the oxyhemoglobin dissociation curve, resulting in a pO_2 above arterial pO_2 at the capillary level. The heat from the sensor also changes the lipid structure in the stratum corneum. Above 41 °C, the stratum corneum lipids are liquefied; thus, enabling transport of O_2 and CO_2 at a much higher rate than in unheated skin.

Although O_2 transport from capillary level to skin surface is facilitated, a diffusion barrier still exists, resulting in a pO_2 gradient across the skin surface. The O_2 consumption from living epidermal cells also accounts for a decrease in pO_2 capillary level to skin surface.

As a result, if blood perfusion is adequate and provides a sufficient supply of oxygen, the $tcpO_2$ is 0.8 times the arterial pO_2 in adults.

In conclusion, the following factors affect the measured $tcpO_2$ value:

1. Arterial pO_2
2. Skin blood flow
3. Skin composition: thickness, metabolism, capillarity
4. Capillary temperature under sensor

The most important factors influencing the $tcpO_2$ readings are arterial pO_2 and peripheral blood flow. The influence of factors three and four may vary between different application sites and from patient to patient, but are relatively constant over time.

Thus for practical purposes, a low $tcpO_2$ value can be interpreted as either:

- Reduced arterial pO_2, as in the case of patients suffering from cardiopulmonary diseases, or
- Reduced regional blood flow, due to impaired central supply or, e.g. arterioschlerosis of the legs.

Physiological considerations

$tcpO_2$ reflects tissue pO_2 which relies on a balance between oxygen supply and oxygen consumption. It has been shown that $tcpO_2$ is directly related to total systemic oxygen delivery to tissue, defined as the product of cardiac index and arterial oxygen content.

When cardiac index (flow/m^2 skin surface) or when tissue and skin blood flow are reduced, as in peripheral arterial disease, $tcpO_2$ will reflect the reduced O_2

delivery, even though maximal blood vessel dilation is induced by heating the skin.

Low tcpO_2 readings with high correlation to symptoms of peripheral vascular disease have been shown in a large number of investigations. tcpO_2 should be regarded as tissue pO_2 at a given time on a specific site on the body.

6. Site selection and site preparation

The ability to determine tissue oxygenation states, and the degree to which hyperbaric hyperoxia might influence these findings, is of great interest.

Of several methods available, transcutaneous oxygen measurements represent a safe, practical, reliable and reproducible assessment of dermal oxygen tension [1, 2]. It is a non-invasive technique that calls for the attachment of a heated polarographic electrode to the intact skin.

Transfer of heat to the skin surface:

1. Creates a local hyperemia [3]. Decreased flow resistance essentially arterializes subjacent arterioles and capillaries, producing greater oxyhemoglobin dissociation.
2. Dissolves and disorganizes the lipid structure of the keratinized cells within the epidermal layer, thereby increasing skin permeability and reducing sensor response time [4].

Where measured skin/subjacent tissue oxygen tensions are abnormally low, it is unlikely that sufficient blood will be available from deeper tissues to support healing by primary means or secondary intention [5].

The determination of hypoxia is fundamental to the provision of hyperbaric oxygen therapy. Whether or not the patient possesses the physiologic capacity to respond locally to centrally delivered hyperoxia is equally important, and can also be determined transcutaneously [6, 7, 8].

Several authors have suggested various transcutaneous oxygen values as necessary for the healing of amputations, in occlusive vascular disease [9, 10, 11, 12]. Other investigations have failed to demonstrate any such correlation [13, 14].

This inconsistency is apparent in several other clinical settings [15, 16]. Comparison of data is complicated by variability in technique, site selection, site preparation, electrode temperature and hyperoxic challenge. This will provide specific guidelines for the standardization of site selection and site preparation.

Site selection

Irradiated wounds/tissue beds

Irradiated wounds/tissue beds is a designation for e.g. soft tissue radionecrosis, soft tissue overlying osteoradionecrotic bone and ORN/STRN prophylaxis.

The angiogenic response of late radiation tissue injury to hyperbaric oxygen has been well described; in soft tissue [17, 18] and, more recently in bone [19]. Depressed transcutaneous oxygen diffusion from tissues that have been previously irradiated may suggest or support a diagnosis of late radiation tissue injury [20].

Serial transcutaneous studies during a course of hyperbaric oxygen therapy will serve to quantify the degree of revascularization [20]. Transcutaneous pO_2 is also helpful in determining the risk of healing complications when surgical procedures are planned within previously irradiated tissue beds [21].

Reference sites

The inclusion of reference sites to the transcutaneous oxygen assessment will permit a comparison of injured to normal tissue variance, and allow patients to serve as their own control by comparing central to local skin oxygen diffusion.

Contralateral/opposing anatomic site

Providing the control site is outside the irradiated field, a measure of the patient's "normal" state of dermal oxygenation is possible. During radiotherapy, it is increasingly common that several portals are used.

Therefore, the patient's Radiation Oncology records should be reviewed, and precise portal site(s) determined.

Chest - subclavicular

By convention, the 2nd left intracostal space is commonly used as the reference site. This is not a critical site, and that general anatomic (subclavicular) region is acceptable.

Deficiencies in central oxygenation and distribution, secondary to respiratory or cardiorespiratory disease, are reflected peripherally. This can prove problematic when somewhat arbitrary limb values are considered adequate or otherwise.

A limb oxygen value of 30 mmHg might be of concern when the "control" value is 85 mmHg. However, where the "control" value is 45 mmHg, there may well be no underlying local pathology with a dorsal foot reading of 30 mmHg.

Wound site selection

While the effects of late radiation tissue injury on skin are often readily apparent, one should make every effort to obtain the radiation portal photographs. These records, usually held on file in Radiation Oncology, represent a precise determination of the irradiated field(s).

Portal photographs are particularly helpful in selecting evaluation sites where skin changes are less apparent.

The late effects of radiation on the skin include:

- Increased or decreased pigmentation
- Thickening and fibrosis
- Atrophy
- Telangiectasis
- Sebaceous and sweat gland dysfunction
- Tumorigenesis
- Necrosis

The extent of the previously irradiated field and the size of any resulting wound, will determine the number of sites to be evaluated. Ideally, several sites should be selected, ranging from sites immediately outside of the irradiated field, across its portal, to a final opposing point immediately outside of the irradiated field.

Electrodes placed two to three cm apart will, in most instances, generate a characteristic curve, with the mid-point of the radiation portal being significantly more hypoxic than its periphery. External beam radiotherapy is given along isodose lines [22]. The tumor volume will receive 100 % of planned dosage, with peripheral and adjacent tissue receiving proportionally less exposure/dosage.

Over time (usually following a period of six to twelve months), the radiation's effect on the microvasculature will be one of an obliterative endarteritis, particularly where large doses (greater than 40 Gy) are involved [23]. The degree of this ischemia-producing insult has been demonstrated transcutaneously.

Exposure to hyperbaric doses of oxygen will produce an immediate elevation in oxygen tensions across the irradiated field, which are again demonstrated transcutaneously.

As hyperoxia-induced angiogenesis migrates inward from the lesion's periphery, tcpO_2 values will increase accordingly. Feedback inhibition shuts down angiogenesis as the oxygen gradient is eventually lost. At this point, tcpO_2 values are approximately 80 % of contralateral "control" tissue. Transcutaneous oxygen measurements play a key role in quantifying this process.

The above site placement recommendations apply to intact soft tissue overlying irradiated bone, and soft tissue defects that involve only a portion of the irradiated field. Where soft tissue wounds are significant and extend throughout the irradiated field, transcutaneous pO_2 will not be helpful.

Every effort should be made to ensure that follow-up transcutaneous studies are conducted at the previous sites of measurements. This can be best accomplished by photographing initial electrode placement and marking the skin contact points with indelible ink. Ink should be reapplied as necessary, between studies.

Non-irradiated wounds

Non-irradiated wounds can be defined as diabetic ulcers and wounds; venous stasis ulcers; sickle-cell ulcers; amputation stumps; PVD lesions; non-healing surgical incisions.

Basic and clinical studies have determined that hypoxia is the most common cause of unsuccessful wound healing [24, 25, 26, 27], and have demonstrated the ability of hyperbaric oxygen to increase wound oxygen tension [28, 29].

Initial investigations involved individual implantable oxygen microelectrodes [30]. This technique is now uncommon and the equipment difficult to obtain commercially. The most common method of assessment of dermal oxygenation in clinical practice today is by transcutaneous oxygen measurements [29, 31].

Reference sites - contralateral/opposing anatomic site

This reference site may be useful in situations of localized disease. One can get an appreciation of normal to abnormal tissue variance, and what the goal of hyperbaric oxygen therapy might represent. In cases of generalized or multifocal pathology, however, this "control" site may offer little useful information.

Wound site selection

In order to fully appreciate the degree of tissue (wound) oxygenation, several periwound measurements must be made. Electrode placement should be as close as possible to the periphery of the skin envelope injury.

Depending upon the number of electrodes available, this can be undertaken at one time with three or more electrodes, or via a single electrode making multiple measurements around the wound. Singular measurements at an arbitrary point adjacent to a wound may be inadequate.

Even in the presence of good regional large vessel patency, highly localized "islands of ischemia" may exist that are significant enough to compromise healing [32]. A comprehensive assessment of the wound's periphery is necessary for adequate determination of local dermal oxygen states.

When evaluating the foot, a measurement at the mid-dorsum will provide a global measurement of dorsal foot oxygenation [5]. When evaluating the distal foot, comparison should be made with mid-dorsum oxygenation. Where ischemic changes are evident within the toe(s), place the electrode immediately proximal to the toe(s) in question.

Site preparation

Electrode calibration

The sensor electrode should be calibrated in accordance with the manufacturer's instructions prior to each use. Standard practice has long involved a "two point" calibration, using both a zero (no oxygen) gas and a calibration gas of known oxygen concentration.

More recently, improvements in design and manufacture have largely eliminated electrolyte pollution, stray currents within the electrode, and silver chloride build-up. "Zero current" is therefore essentially eliminated in modern high quality electrodes. Periodic "two-point" calibration is usually adequate. "Single point" calibration is appropriate when recommended by the manufacturer, unless the electrode appears erratic.

When the known "calibration gas" is atmospheric air, one must adjust for local barometric conditions and humidity. With decreasing barometric pressure (increasing altitude), there is a gradual decrease in oxygen tension. This relationship is not linear, however. Table I provides calibration values at selected barometric pressures, assuming the calibration is done with dry gas.

Normally, only the change in barometric pressure is of practical importance when calculating the calibration value in an indoor environment. Therefore, the value can as a rule, be determined from the formula below:

$$pO_2\ (cal) = B \times \frac{\%O_2}{100}$$

Where:

pO_2 (cal) = Calibration value

B = Barometric pressure (in mmHg or kPa)

% O_2 = Percentage of oxygen in atmospheric air (assumed to be 20.93 % in **Table 1**)

B• mmHg	pO_2 (CAL) mmHg	B• mmHg	pO_2 (CAL) mmHg
600	126	700	147
610	128	710	149
620	130	720	151
630	132	730	153
640	134	740	155
650	136	750	157
660	138	760	159
670	140	770	161
680	142	780	163
690	144	790	165

TABLE I. Calibration values (in mmHg).

• Barometric pressure

In atmospheric air the calibration value should be corrected according to the following formula:

$$\boldsymbol{pO_2(cal) = (B - pH_2O(T) \times RH) \times FO_2}$$

where

B = Barometric pressure (in mmHg)

$pH_2O(T)$ = Saturated water vapour pressure at the ambient temperature T (in mmHg or kPa)

RH = Relative humidity

FO_2 = Mol fraction in atmospheric air (normally 0.2093)

In the U.S., barometric pressure is commonly expressed in inches. To convert the value recorded on the transcutaneous monitor to mmHg:

i. multiply barometric pressure by 25.40 = mmHg
ii. multiply mmHg by 0.2093 = pO_2(cal), in mmHg oxygen

Example:

Barometric pressure is 30.26 inches
30.26 x 25.40 x 0.2093 = 160.9 mmHg oxygen

Electrode temperature

With the exception of neonatology, no firm criteria exists for setting sensor temperature. The temperature range of most commercially available transcutaneous oxygen monitors is 42-45 °C. Early clinical application, in neonates, involved a maximum recommended setting of 43 °C. As site evaluation times were often in the order of several hours, skin burns were largely avoided at 43 °C.

When transcutaneous monitoring of pO_2 was extended to orthopaedic, vascular and eventually, hyperbaric practice, it was common to maintain 43 °C as the sensor temperature, in the absence of any recommendations to the contrary.

Subsequent clinical experience has involved the entire temperature range. As site evaluation times are now in the order of 15-30 minutes, vs. many hours, studies involving temperatures as high as 45 °C have not been accompanied by complaints of skin burns.

There is theoretical concern that patients with localized areas of no-flow might suffer burns due to a failure to dissipate heat by convection. Further, patients who are insensate may not appreciate local burning at the electrode site. In the author's nine years of experience with transcutaneous monitoring, involving over 800 patients and 2,400 sites, these concerns have not been borne out.

During 30 minutes of complete occlusion of blood flow to the hand, no evidence of skin burns was apparent with a probe temperature of 44 °C [33].

It is recommended that a temperature of 45 °C be used for all transcutaneous oxygen measurements in the hyperbaric medicine setting.

A probe temperature of 45 °C provides three distinct advantages:

- It induces maximum hyperemia, within the constraints of the equipment.
- It eliminates the effects of ambient (room)

temperature fluctuations on blood flow/dermal oxygen tension [34].
- It largely overcomes sympathetic tone [34].

As serial transcutaneous oxygen measurements are common, an electrode setting of 45 °C effectively eliminates the influence of day-to-day room temperature fluctuations. Perhaps more importantly, 45 °C will largely overcome vasomotor tone, where it exists.

As electrode temperature is increased from 42 °C to 45 °C, there is a proportional increase in transcutaneous oxygen tension in the healthy lower extremity. This increase can be as great as 50 %.

In the paraplegic, for instance, where sympathetic response has been largely eliminated, increasing the electrode temperature fails to result in a corresponding increase in transcutaneous oxygen tension. As knowledge of the patient's underlying vascular status is often incomplete, particularly the degree of vasomotor tone, a temperature of 45 °C will essentially overcome any local or systemic influence.

This will, therefore, serve to standardize data collection, and make comparison of results more meaningful.

Skin preparation

Avoid positioning the adhesive patient electrode over a bony prominence. The weight of the electrode may compress underlying vasculature and interfere with dermal oxygen diffusion. Avoid large superficial vessels and pulse sites.

As one might expect, transcutaneous values will be increased over arteries, and this variance with surrounding dermal values is increased as a function of the oxygen challenge.

The following steps will maximize optimal patient electrode contact and serve to eliminate erroneous or conflicting data:

1. Select a slightly convex area, if possible.
2. Carefully remove all body hair from the intended site. A dry razor is usually sufficient.
3. Cleanse the area with an alcohol prep.
4. Remove the stratum corneum. This will optimize both electrode contact and oxygen skin diffusion [4]. Repeated applications of clean adhesive tape, until the tape remains clear, will effectively denude the skin of relative barrier. Typically, 15-20 applications are required.
5. Carefully affix the adhesive ring.
6. Apply sufficient contact solution, or gel, to completely cover the exposed skin surface within the electrode ring. Too little solution will delay equilibration. This may occur when operators switch from contact gel models (requiring one drop) to monitors requiring a solution.
7. Avoid excess solution. When the sensor electrode is attached to the patient electrode, compression of excess solution may alter the structure of the electrolyte within the sensor electrode. This may produce a drop in the calibration value of some 10-15 mmHg. If one suspects this has occurred, the electrode should be recalibrated. If the recalibration value has fallen to the degree noted above, replace the electrode membrane. Excess solution may also be expressed between the adhesive ring and the skin surface, creating a channel that will allow leakage of ambient oxygen back towards the sensor electrode.
8. Remove any air bubbles from the adhesive ring
9. Once the site has been prepared and the adhesive ring with contact solution has been attached, connect the sensor electrode to the patient and support the electrode cable to avoid applying tension at the patient electrode.

Site evaluation procedure

The patient should be supine or semi-recumbent, remain quiet, and refrain from unnecessary conversation.

Allow sufficient time for the electrode to equilibrate. Typically, this will take between 10-15 minutes, depending upon the patient's underlying physiologic status, skin thickness and any other relative barriers to diffusion.

The monitor's trend indicator or a strip chart recorder will determine stabilization. Remember, however, that the dermis is living tissue with varying metabolic needs. Therefore, one can expect a constant variation in transcutaneous oxygen tension, within relatively narrow margins.

Record the stabilized reading as the ambient skin/subjacent tissue oxygen value.

Repeat this study, as necessary, in order to obtain ambient values at each of the desired sites. Where only a single electrode is available, proceed with the oxygen challenge (below) before moving to the next site. If recommended by the manufacturer, recalibrate the sensor prior to each relocation.

Oxygen challenge

An oxygen challenge has been reported to improve the diagnostic accuracy of transcutaneous pO_2, when selecting amputation levels [6, 35, 36], thereby providing maximum conservation of tissue in limb salvage situations [15]; predicting skin flap survival [34], and assessing limb ischemia [38].

More specifically, it has important implications regarding suitability of a patient to undergo a course of HBO therapy.

Oxygen challenge can be administered at normobaric or hyperbaric pressure. At normobaric pressure, a standard wall outlet can be used to provide oxygen to an oral/nasal mask with a reservoir bag. The mask should be carefully placed and secured into position, with oxygen delivery set to high flow (12-14 L/min). Vent holes in the face mask should be sealed with tape to maximize oxygen delivery.

It is not critical that the patient receive 100 % vs. 95 % oxygen during this test. What is important is the standardization of oxygen delivery during the course of the test.

Record the transcutaneous oxygen response during a ten minute oxygen breathing period

There is a growing body of evidence to suggest that a hyperbaric oxygen challenge is more predictive than normobaric air or normobaric oxygen in studies involving problem wounds [26, 39, 40, 41, 42, 43].

Until 1990, hyperbaric oxygen challenge was limited to the air compressed in multiplace and duoplace chambers. Assessment was accomplished by either taking the entire monitoring system into the chamber, or, preferably, maintaining the monitor at one atmosphere and connecting the electrode into the chamber via a through-hull penetrator.

The heated electrode was considered a fire hazard in the oxygen-filled monoplace chamber. Recently, a transcutaneous oxygen monitor has been approved for use under hyperoxic conditions. The monitor remains at one atmosphere, with the sensor electrode interfaced into the chamber via a through-hull penetrator.

It has recently been suggested that oxygen leakage occurs at the adhesive patient electrode when the study is undertaken in the oxygen-filled monoplace chamber [44]. This has not been our experience.

While we have not looked at this potential problem specifically, we have evaluated several patients with areas of ischemia who fail to respond to hyperbaric oxygen. Transcutaneous values of 1-10 mmHg that either did not improve at all, or did so very marginally, are highly suggestive of little or no contamination of the electrode by the surrounding oxygen atmosphere.

In reviewing the abstract referencing this apparent leakage, increased transcutaneous oxygen values might be attributed to:

- the "loosely" covered adhesive dressing placed over the electrode compressing the sensor electrode as the space occupied by the dressing is decreased in volume upon compression
- comparative studies being made at different times. There is a significant amount of variation in dermal oxygen values on a day-to-day basis in the same patient/subject at the same anatomic site.

When conducting transcutaneous oxygen studies hyperbarically, it will be necessary to compensate for the high oxygen tensions likely to be recorded. In most cases, the monitor display is limited to 999. At 2.0 atmospheres absolute oxygen and above, tissue oxygen values may exceed this value. It is advisable, therefore, to recalibrate the monitor to a value lower than normal oxygen value.

Where the standard calibration is 160 mmHg, recalibration to 80 mmHg will double the recording capacity. In this case, one must be careful to adjust the display value accordingly. Under the above circumstances, a readout of 250 mmHg is doubled to 500 mmHg as the actual transcutaneous oxygen tension.

Be certain to recalibrate the monitor back to normal atmospheric conditions after each hyperbaric assessment

Summary

Transcutaneous oxygen measurements have become an important diagnostic tool during the consultation and subsequent case management of hyperbarically referred patients. In order to optimize the value of this procedure, efforts should be made to standardize site selection and preparation.

Serial transcutaneous oxygen measurements can provide an objective assessment of hyperbaric oxygen's effectiveness. Follow-up studies have also been helpful in determining when the patient is approaching an end point to therapy, thereby providing a more clinically appropriate and cost effective management.

The above procedural recommendations will serve to standardize the transcutaneous oxygen assessment, thereby improving comparison of published data.

7. Transcutaneous pO_2 measurements - interpretation

Introduction

Regional transcutaneous pO_2 measurements represent an excellent diagnostic technique for the determination of limb oxygenation [1]. The superiority of transcutaneous oxygen (tcpO_2) mapping in the non-invasive vascular diagnosis of patients with diabetes and PVD has been established in several comparative studies [1, 2, 35, 36, 45].

Selection of level of amputation can be optimized [12, 36, 46] and subsequent healing more accurately predicted [10, 14, 47]. Transcutaneous pO_2 is a sensitive indicator of vessel patency in limb part reimplantation [33], has improved survival prediction of skin flaps [37] and quantified peripheral vascular disease [48, 49].

In several of the above studies, various threshold tcpO_2 values were proposed; values below which wounds would fail to heal and surgical wounds become complicated. A critical analysis, however, fails to demonstrate any exacting correlation [10, 47, 50].

In a large group of patients, Wyss [50] noted that, even where below knee tcpO_2 tensions approached zero, "a few limbs did heal after amputation, although they usually healed slowly".

Clearly, tcpO_2 values of zero don't necessarily mean subdermal oxygen values of zero. Blood pressures as high as 50 mmHg have been measured in the feet of diabetics with impending gangrene, while tcpO_2 values remained at zero [13].

In summary, then, while there does appear to be a correlation between increasing hypoxia/ischemia and the probability of healing complications [50], it is quite clear that no threshold tcpO_2 value exists.

Hyperbaric medicine

What does transcutaneous pO_2 give the hyperbaricist? If no threshold tcpO_2 value exists for prediction of healing amputation sites, where diseased tissue has been ablated, how might transcutaneous pO_2 guide hyperbaric case management, where the principle goal is one of salvage rather than amputation?

Sheffield and Dunn [30] first recognized the importance of tissue oxygen measurements in the hyperbaric treatment of soft tissue wounds. Their investi-

gations sought to determine dose response curves via implantable polarographic electrodes.

Hypoxia was confirmed as a complication of refractory soft tissue wounds, as was the ability of hyperbaric vs. normobaric oxygen to elevate wound oxygen tension [30]. In a follow-up paper several years later, involving transcutaneous polarographic electrodes [51], Sheffield identified an important characteristic, which appears to have been lost in many of today's clinical investigations.

It was the change in baseline over a course of HBO therapy, rather than the ambient baseline value in itself that correlated with outcome. Emhoff and Myers [41] similarly reported that response to serial HBO therapy, not the initial value or even initial response to hyperbaric-hyperoxic, predicted outcome.

Several more recent studies have likewise been unsuccessful in correlating preliminary $tcpO_2$ observations of dermal oxygen content on outcome [43, 52, 31, 29, 40].

Rather than strive for an elusive predictive value, it is recommended that $tcpO_2$ studies be used to guide the hyperbaric consultation and case management of wound healing patients by addressing the following questions:

1. Is wound healing complicated by hypoxia?
2. In such cases, does the patient possess the physiologic capacity to respond locally (wound site) to centrally delivered doses of hyperbaric oxygen?
3. Is the patient responding to hyperbaric oxygen therapy?
4. Has the patient developed "host competency," i.e. has a critical mass of neovascularization been generated, sufficient in degree to support continued healing in the absence of continued HBO?

These four pieces of data, all readily obtainable during the transcutaneous assessment of problem wound patients, will do much to direct the appropriate application of hyperbaric oxygen therapy.

Selection criteria, secondary vascular work-up requirements and hyperbaric therapy can be optimized, and non-responders to HBO identified early in the course of treatment.

Wound hypoxia

The basis of hyperbaric referral of problem wound cases is correction of hypoxia. Transcutaneous oxygen mapping of the periwound area will consistently demonstrate hypoxia, where systemic and local factors contribute to ischemia, with one exception.

Where highly localized small vessel disease exists within a digit, a $tcpO_2$ study may not detect hypoxia at the most distal site attainable. A limitation of the transcutaneous method of tissue oxygenation assessment is the need for a relatively large, flat skin surface. The adhesive patient electrode will normally not seal on the toes.

Tissue oxygen tensions below 30-40 mmHg are considered suboptimal for wound healing [53, 54] and control of infection [55]. A finding of hypoxia, therefore, represents an important component of the evaluation and diagnosis of the hyperbaric referral.

Step one, then, is to determine the presence or absence of hypoxia. Oxygen tensions below 40 mmHg should be considered potentially problematic. Values below 30 mmHg represent an increasing adverse influence on oxygen-dependent wound healing factors.

Where no evidence of hypoxia is apparent, the patient needs to be worked for other factors that influence wound healing, if this has not already been done. Absence of hypoxia via $tcpO_2$ does not necessarily rule out the use of HBO.

Assessing local response

Once hypoxia has been demonstrated, step two is to determine whether or not hyperbaric oxygen therapy can influence dermal oxygen tensions. This is accomplished by the administration of a hyperoxic challenge, either at normobaric or hyperbaric pressure.

An advantage of the normobaric "oxygen challenge" is

that one does not need to undertake the full hyperbaric consultation necessary before exposing a patient to the risks associated with hyperbaric hyperoxia. The normobaric study can be completed and made available prior to a formal evaluation.

Where the normobaric oxygen challenge is equivocal, one can always proceed to hyperbaric oxygen challenge, where indicated.

In order to evaluate the normobaric oxygen challenge, record the periwound response during a 10 minute oxygen breathing period. Again, there is no target value. One is assessing the ability of the systemic circulation to deliver additional oxygen to the wound site.

Should the oxygen challenge result in a "normalization" of transcutaneous oxygen tension or better, one can be confident that the rationale for a trial of hyperbaric oxygen therapy has been met. Namely, that hypoxia is present and the patient does possess the capacity to respond locally to increased central oxygen delivery.

If there is no local response, the patient should be referred for a more detailed vascular work-up if local diffusion barriers (edema, etc.) have been ruled out.

Interpretation of pathology

Transcutaneous pO_2 is an excellent screening tool. It does not, however, provide specifics regarding local or systemic influences. While it is not always necessary to diagnose underlying pathology in order to recommend hyperbaric oxygen therapy, it does of course provide a more complete picture and ensures that all possible interventions are considered.

Interpretation of transcutaneous oxygen data can be simplified if local effects are distinguished from systemic effects. The Regional Perfusion Index (RPI) can accomplish this to some degree [48].

RPI is the ratio of oxygen tension at the wound site and oxygen tension at a control (disease free) site. RPI functions in much the same manner as the ankle-brachial (blood pressure) index. Comparison of local to central oxygen tension "corrects" for the effects of any pulmonary or cardiopulmonary disease.

Example:

Where the periwound oxygen tension is 35 mmHg and the chest control site is 85 mmHg, the RPI would equal 0.41 (35/85) - a value associated with complications in amputation healing [15]. Should the chest control site be recorded at 45 mmHg, however, this would produce an RPI of 0.78 - a value associated with uncomplicated healing [15].

Factors that influence local tissue oxygen diffusion can be assessed via history, physical and oxygen challenge. They include edema; late effects of therapeutic radiation; infection; small vessel disease; thickened skin; regional large vessel stenosis.

Assessing response to hyperbaric oxygen therapy

Once the decision is made to administer hyperbaric oxygen, one needs to ascertain whether or not the patient is responding. Marx has characterized the angiogenic response of radiation-injured tissue to a course of hyperbaric oxygen therapy as three distinct phases [56].

Each phase is based upon dermal oxygen tension, with improved vascularity proportionally increasing tcpO_2 values. In the wound healing patient, a repeat tcpO_2 value is recommended after 14 treatments and again at 20 treatments. Comparison is made with the baseline study.

If the patient is responding clinically, improvement in the ambient tcpO_2 value will be apparent. This improvement may also be reflected in the oxygen challenge value, either as an increased end point or a steepening of the ten minute curve.

If little or no tcpO_2 response is evident, one needs to work the patient up, as a potential non-responder. It is uncommon for us to extend a course of hyperbaric oxygen therapy beyond 20 treatments, where no tcpO_2 improvement is noted in uncomplicated (i.e. infection free) refractory wounds.

End point of therapy

Almost as important an issue as when/who to start on a course of HBO therapy for wound support is, the determination of end point of therapy. Many early reports of HBO for wound healing involved lengthy courses of therapy, sometimes exceeding 100 treatments [57, 58].

End point of therapy was poorly defined, and likely involved treatments until complete re-epithelialization had occurred. This has been entirely corrected today.

Perhaps a more appropriate approach would be to treat the patient to the point of host competency? Hyperbaric oxygen does not in itself heal wounds. Rather, it provides the necessary stimulus, where ischemia/hypoxia complicates oxygen-dependent wound healing factors.

Once correction of underlying ischemia/hypoxia has occurred, one should theoretically, at least, be able to discontinue HBO.

Where follow-up ambient tcpO_2 values are within, or close to, the normal physiologic range, consider interrupting HBO therapy. In the presence of improved wound characteristics, we may elect to interrupt HBO following 14-20 treatments.

The patient is then re-evaluated, usually after seven days [7]. If the wound is continuing to progress in a satisfactory manner, the patient is seen again in 7-10 days. No further HBO is ordered. In the presence of "normalized" tcpO_2 values, it is not uncommon for the wound to continue to heal with conservative care alone.

This approach can greatly reduce the total number of treatments, providing a more efficient use of resources and reduced risks to the patient.

Should follow-up be associated with inadequate wound progression, or deterioration is apparent, one can always resume HBO for an additional period (7-10 days) with subsequent decision making as above.

A second method of assessing end point has recently been suggested [8]. It is proposed that reappearance of vasomotor tone in ischemic tissue might be the goal of hyperbaric oxygen therapy.

Using transcutaneous oxygen monitors and laser doppler flowmetry to assess hyperoxygenation in focal ischemia, the authors failed to demonstrate vasoconstriction in ischemic tissue. It was determined that oxygen tensions in ischemic tissue did not extend beyond the "normal" range during periods of hyperoxia.

Therefore, local microcirculatory regulation was largely unchanged. Further, it was proposed that reappearance of vasomotor tone following correction of ischemia might represent the point of maximum benefit [8]. This hypothesis has not been tested.

In the absence of a laser doppler monitor, vasomotor tone can be assessed via transcutaneous pO_2 measurements, using the vasodilation index (VI) [59].

$$\mathbf{VI = \frac{tcpO_2 \text{ @ (42 °C)}}{tcpO_2 \text{ @ (45 °C)}}}$$

Undertake a tcpO_2 evaluation at the site in question with a sensor temperature of 42 °C. Record the value, then recalibrate the sensor at 45 °C and repeat the study.

When skin is vasoconstricted, the VI is low (less than 0.5). With vasodilation, the VI is increased and could theoretically reach 1.0 under conditions of maximum dilation.

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