Biochemical changes in sweat following prolonged ischemia

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Abstract—Much emphasis has been placed on the measurement of physical parameters at the body support interface in order to detect and moderate conditions which could result in pressure damage to soft tissues. Major difficulties are encountered both in the design of instrumentation and interpretation of the data collected. Metabolic processes in sweat glands that control sweat secretion have been shown to be sensitive to applied pressure, producing sweating rate suppression and changes in sweat NaCl concentration. In this study, we have demonstrated the feasibility of measuring lactate concentration in sweat collected locally using an electro-chemical stimulation technique (iontophoresis of pilocarpine nitrate). Elevated levels of sweat lactate concentration during local tissue indentation were detected in a group of able-bodied subjects. Upon removal of the indentor, however, levels of sweat lactate returned to normal.

Key words: sweat metabolism, electro-chemical stimulation, ischemia, pressure damage, soft tissue.

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INTRODUCTION

Pressure sores represent a severe problem for spinal cord injured individuals and often require prolonged hospitalization for treatment or surgical repair (7). If a reliable and practical clinical method for early detection of pressure sores could be developed, it is probable that in many cases, given suitable medical intervention, the process of tissue breakdown could be reversed or at least limited in its severity. Various techniques for early detection of pressure sores have been investigated to identify changes in mechanical, physical, or physiological properties of compromised tissues. None to date have yielded a reliable and clinically practical means to detect early tissue damage.

Current clinical practice for early detection of pressure sores relies upon frequent inspection of skin color. Persistent red areas are often classified “Stage I” pressure sores (1) and appropriate clinical measures taken. Several difficulties and limitations are, however, experienced with this highly subjective technique. First, it is important for the clinician or patient to differentiate between persistent redness and the normal, healthy, short-term redness of reactive hyperemia. Second, in the more advanced stages of pressure sore formation, the area becomes ischemic and cyanotic, with often only a margin of redness. Third, all skin color changes associated with early onset of pressure sores are difficult to detect in nonwhite patients.

In recent years, methods for evaluating skin status or the effectiveness of different body support
systems (cushions, mattresses, etc.) have revolved around the measurement of pressure and other physical parameters at the skin/support surface interface (2,3). Although these techniques have proved successful in reducing pressure sore incidence among spinal cord injured persons at a number of specific centers, they are not in widespread use nor have they been developed to address the needs of the broader population at risk, especially the elderly.

An alternative approach employs the tissues themselves as a direct source of information reflecting their viability. This approach is attractive, because it offers an opportunity to bypass the need to establish prescription criteria for physical parameters, if very sensitive techniques for detecting the early stages of tissue distress can be developed.

Techniques have been developed to monitor blood flow in tissues using noninvasive techniques (thermography, laser Doppler, $^{133}$Xe clearance), but all share a similar limitation in their clinical applicability. Their response to reactive hyperemia and inflammation associated with early onset of tissue trauma is similar and requires the clinician to wait for reactive hyperemia to resolve before an abnormal tissue response can be detected. In this respect, they offer only a marginal advantage (namely their objectivity) over skin color observation. Techniques capable of measuring tissue oxygenation ($\text{TCPO}_2$) on the other hand are promising as they provide direct information about the metabolic status of the tissues.

During the early stages of pressure sore formation, significant changes in tissue biochemistry are thought to occur. Even during an ischemic period that results in no adverse tissue response, metabolites are thought to accumulate, pH decreases, and $\text{PO}_2$ decreases with a corresponding increase in $\text{PCO}_2$ (6). Despite the potential that tissue biochemistry offers for monitoring tissue viability, this approach has been neglected primarily because it
implies the need for invasive sampling of local areas at risk. In addition to the difficulties inherent in sampling significant quantities of extra-vascular fluids, the risk that injection sites would produce foci for infection has deterred clinicians from developing biochemical tests.

Sweat glands are richly endowed with a capillary blood supply that carries biochemicals whose concentrations may serve as indicators for pressure sore formation. In principle, it would therefore seem feasible to use sweat as a vehicle for monitoring biochemical changes in the tissues using simple, established, noninvasive techniques.

Although a number of biochemicals come to mind as candidates for investigation, in this preliminary study we have demonstrated the concept for changes in lactic acid and Na⁺ concentration based on previous research studies involving whole limb response to ischemia (4) during thermally-induced sweating.

**METHODS**

Profuse localized sweating can be induced in humans and a few animals (including the horse, and the footpads of cats, rats, etc.), by introducing pilocarpine or acetylcholine intradermally. Analysis of sweat for sodium or chloride ions is a well-established technique for screening children for cystic fibrosis (CF), as the NaCl concentration in the sweat of CF children is significantly higher than normal. Routine screening by introduction of pilocarpine nitrate using iontophoresis is readily accomplished with inexpensive commercial equipment. In this study, a sweat stimulator (Westcor Inc., UT) employing pilocarpine-impregnated agar gel electrodes was used (Figure 1), and the sweat samples were collected (Figure 2) using a Macroduct disposable capillary tube system (Westcor Inc., UT). Sweat samples were obtained from the forearm of male and female able-bodied volunteers in the age range

*Figure 2.*
Macroduct sweat collector.
of 20 to 40 years. A typical sweat yield for these subjects following 5 minutes of stimulation with a current density of 25nA/mm$^2$ over an area of 500m$^2$ was 30µl, when collected for 30 minutes.

Lactate levels in 5µl sweat samples were determined using a routine lactate dehydrogenase assay available in kit form (Sigma Chemicals Procedure #826-UV). Na$^+$ concentration was also measured routinely using an atomic absorption spectrophotometer (Perkin-Elmer Model 306). Sweat volume was estimated by weighing the Macroduct before and after collection.

A preliminary pilot study was conducted to determine whether Na$^+$ and lactate levels were influenced by the pilocarpine method of sweat induction. One subject was subjected to the following regimen on 3 separate occasions during the summer months. Pilocarpine-induced sweat was collected from one arm using the Macroduct system following careful cleaning with alcohol wipes and distilled water. The area was carefully dried. Following routine sweat induction and sampling, the subject was fitted with a Macroduct sweat collector on the other (non-stimulated) arm, and was asked to jog in an environmental chamber at 35-40°C and 70-90 percent relative humidity (RH) for 30 minutes. During this time, an adequate (20-30µl) sweat sample was collected for Na$^+$ and lactate analysis.

Two primary studies were undertaken to determine the effects of ischemia on Na$^+$ and lactate levels. In the first study, one forearm of each subject was subjected to continuous pressure of 150mmHg for 30 minutes using a 25mm diameter pneumatically-controlled indentor. The applied force was monitored, using a force transducer and recorded on a chart recorder. Room temperature was maintained at 30°C and 70 percent RH. Upon release, sweating was stimulated for 5 minutes and then collected for a subsequent 30 minutes. In the second study, the indentor was adapted to accommodate the sweat collection system (Figure 3).

![Figure 3. Sweat collection during indentation.](image-url)
Sweating was induced before and collected during indentation. In both studies, the subject's other arm was used as a control.

RESULTS

Table 1 compares the sweat volume, lactate and Na⁺ concentrations for thermally-induced and pilocarpine sweating. Although the number of tests performed was too small for rigorous statistical analysis, the results indicate that for this subject, no large differences in Na⁺ or lactate concentration were introduced by stimulating sweating using the iontophoresis technique.

Tables 2(a), 2(b), and 2(c) compare the sweat volume, sodium concentration, and lactate concentration for samples obtained during and after ischemia against their respective controls. These results were obtained for a total of 9 able-bodied subjects (4 male, 5 female). Sweat volume (Table 2a) was significantly depressed (p<0.05) for sweat collected during ischemia, but did not significantly differ from the control when collected during the reactive hyperemia phase after ischemia. This effect is well-documented for whole limb ischemia, and is known as the hemihidrotic effect (5).

Sodium concentration did not change significantly for the 2 test protocols. Statistically significant differences could not be detected between the ischemic and control sites or between the 2 protocols, although there is some evidence for elevated Na⁺ levels in sweat from the ischemic site, when collected during ischemia. Previous whole limb studies (4) have identified significant differences in Na⁺ concentrations comparing ischemic versus control sites. Large differences in Na⁺ concentrations between subjects contribute to the large standard deviations obtained in this part of the study and thereby tend to mask differences seen for each individual.

Lactate concentration (Table 2c) was observed to increase significantly (p<0.001) for the ischemic versus control site during ischemia, but did not differ significantly for the sweat samples collected during reactive hyperemia. This result compares favorably with those obtained in previous studies, and confirms that sweat biochemistry is very sensitive to tissue status. It should be noted, however, that the elevated levels of lactate in sweat are not thought to result from lactic acid transfer from plasma or extracellular fluid to the sweat. The sweat gland itself appears to function as a metabolic unit that reflects its oxygenation status through reduced output rate and increased lactate production. Previous studies (4) suggest sweat lactate concentration is relatively independent of blood lactate levels (elevated, for example, by muscle fatigue during exercise).

DISCUSSION

The results obtained in this study confirm that pilocarpine stimulation of sweating can be used effectively to monitor local tissue biochemistry. Tests with a single subject suggest that the iontophoresis technique does not modify the levels of lactate and Na⁺ when compared to normal profuse sweating induced by high environmental temperature coupled with exercise.

A previous study (4) for whole limb ischemia has
suggested that lactate levels during ischemia are attributable to changes in sweat gland metabolism, and that they are generally independent of capillary blood lactate levels. In this study, we have confirmed that similar results can be obtained by local sweat monitoring for locally applied ischemia. Our results demonstrate the sweat gland's capacity to return to normal lactate production as soon as capillary blood oxygenation permits normal (aerobic) metabolism. In this respect, these results suggest that, in principle, the sweat gland could be adopted as a physiological ischemia monitor if sweat can be collected during the ischemic event.

Further research is needed to determine the clinical applicability of sweat chemistry for early detection of pressure sores. Additional parallel tests are required to demonstrate that the stimulation technique does not produce artifactual changes in sweat composition. A collection system needs to be developed that permits monitoring of sweat composition at the loaded body support interface. Ideally, such a system could include an indicator for the concentration or presence of biochemicals indicative of tissue stress. However, basic research is required to identify pertinent biochemical factors that are released specifically in association with the early onset of pressure sores.

This study illustrates an approach to the evaluation of tissue responses during and following induced localized ischemia. If this approach proves to be viable following more detailed investigation, monitoring sweat biochemistry may help to eliminate the technical and interpretation problems associated with interface pressure monitoring.

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REFERENCES