Lymphology 38 (2005) 81-86

TRANSCUTANEOUS OXYGEN TENSION IN ARMS OF WOMEN WITH UNILATERAL POSTMASTECTOMY LYMPHEDEMA

H.N. Mayrovitz, N. Sims, D. Brown-Cross, S. Humen, P. Cohen, C. Kleinman-Barnett

Department of Physiology, College of Medical Sciences, Nova Southeastern University, Ft. Lauderdale, Florida USA

ABSTRACT

Previous reports suggest that skin blood flow is reduced in arms of women with lymphedema due to breast cancer treatment. Since tissue oxygenation depends on blood flow, we sought to determine if transcutaneous oxygen tension ($TcPO_2$) is also reduced and if so, if therapy that reduces edema has a beneficial effect. $TcPO_2$ was measured in fibrotic areas of affected arms and in corresponding sites on non-affected arms of 15 women with unilateral arm lymphedema before and after CDP therapy sequences. Fibrosis was assessed by indentation recovery times (IRT) after applying an indenter-like device to tissue. Volumes and edema percentages were determined from circumferences using automated software calculations. Treatment significantly ($p< 0.01$) reduced arm edema from 28.6 ± 22.9% to 18.1 ± 17.7% (mean ± SD) and fibrotic segment edema from 42.6 ± 30.1% to 25.0 ± 20.4%, and softened fibrotic tissue judged by reductions in IRT (88.7 ± 60.7 sec vs. 23.1 ± 38.8 sec, $p<0.001$). $TcPO_2$ did not differ between arms initially and did not change with treatment, being 60.1 ± 8.8 mmHg at the start and 61.8 ± 9.2 mmHg at the end of treatment. Thus, despite significant amounts of initial edema, $TcPO_2$ was not initially less in affected arms nor was it changed by therapy that improved both edema and fibrosis.

Diffusion of oxygen from dermal capillaries and likely from small arteries and arterioles normally supplies the nutritional needs of the skin and underlying tissue (1). Measurements of transcutaneous oxygen tension ($TcPO_2$) have been used to assess the degree to which either or both microvascular perfusion and oxygen flux are altered in conditions such as diabetes (2,3), lower extremity vascular pathology (4,5), radiation therapy (6), and for wound healing prognosis (7-9). In many conditions, edema presence is associated with a decreased $TcPO_2$ (10,11) but therapy-related reductions in edema may (10) or may not (11) be associated with a significant improvement in $TcPO_2$. In patients with arm lymphedema secondary to breast cancer treatment, arm skin blood perfusion is reported to be reduced prior to therapy (12-14) and to be improved after therapy that significantly reduces the lymphedema (12,13). Contrastingly, total blood flow in arms with lymphedema has been reported as either greater (15-17) or not different (18) than in paired normal arms although blood flow per unit arm volume was reported as less in edematous arms (18). Venous outflow abnormalities in arms with lymphedema have also been described (19). Since tissue oxygenation depends partly on blood flow, we sought to determine if tissue oxygen, as assessed by $TcPO_2$, is also reduced and if so, if therapy that reduces edema and tissue hardness has a beneficial effect.

Fig. 1. Measurement of transcutaneous oxygen tension ($TcPO_2$) Patient is seated with her arm supported and resting comfortably at about heart level. Probe is shown placed on the affected arm in a region of fibrosis.

METHODS

Subjects

The study population consisted of 15 women with unilateral arm lymphedema who were about to undergo complete decongestive physiotherapy (CDP) with manual lymph drainage according to the Vodder method (20). All patients were referred for therapy by their attending physicians and treatment was given by experienced therapists certified in the technique. Prior to participating in the research part of the study, all patients signed an informed consent that was approved by the University's Institutional Review Board. Data are presented as mean ± SD (range). Patients were 75.6 ± 8.0 years of age (58-86 years), had had their mastectomy 13.4 ± 12.4 years earlier (0.5-44 years) and had had their arm lymphedema for 5.2 ± 5.5 years (0.2-18 years).

Measurements and Protocol

Research-related measurements were done within two days prior to the start of each patient's first CDP treatment (pre-treatment) and repeated within two days of their last treatment (post-treatment). Patients received 8-10 treatments spread over 16 ± 2 days. During the pre-treatment session the arm with lymphedema (affected arm) was examined and palpated in order to identify a region with the greatest amount of fibrosis. This region was outlined, photographed and its center marked and used as the target site for subsequent affected arm measurements. A corresponding site on the contralateral non-affected arm was also identified and marked. The following measurements and procedures were done on each arm in sequence with the patient comfortably seated.

Transcutaneous Oxygen Tension

$TcPO_2$ was measured at the center of the target site using a Novametrix TCO2M Monitor Model 860 (http://www.novametrix.com/products/860/860.html) *(Fig 1)*.

The sensing probe was calibrated prior to each use, and measurements were made at a temperature setting of 44°C. Baseline $TcPO_2$ values ($TcPO_{2B}$) were recorded 25 minutes after placement of the sensor on the target skin site. During this interval the patient's arm was horizontal and rested on a soft surface at the patient's heart level. At the end of the 25 minute interval the patient's arm was passively raised to a near vertical orientation with the aid of the therapist and was held in this position for two minutes. After two minutes, and with the arm still raised, the $TcPO_2$ value was again recorded ($TcPO_{2V}$). The same procedure was subsequently done on the other arm.

Arm and Segmental Volumes

During the 25 minute intervals in which $TcPO_{2B}$ was being measured, the total volume of the other arm was determined. Circumferential measurements were made using a Gulick tape measure (http://www.fwonline.com/gtape.htm) at previously marked 4 cm intervals starting at the wrist. Circumference values were entered into a software program that automatically calculated segmental and total arm volumes (LVP3.0, http://bioscience-research.net/lymphedema.html) based on the frustum model of the arm (21-25). The segmental volume of the target region corresponded to a 4 cm arm segment that included the site of the $TcPO_2$ measurements.

Tissue Indentation Recovery

Aspects of the physical properties of the tissue at the target sites were estimated by measuring the tissue indentation recovery time (IRT) following tissue indentation with a 1.5 cm diameter spherical surface using a standardized fixed force of 360 grams for 20 seconds. The device (TissuPress, http://bioscience-research.net/tissupress.html), works like a calibrated thumb, but provides a uniform indentation force. The IRT is determined by palpating the indented region immediately after removal of the force and registering the number of seconds for the indented tissue to return to its pre-indented condition. IRT is used as an index to assess changes in underlying edematous and/or fibrotic tissue.

Data Analysis

Possible effects of treatment on total and segmental volumes, $TcPO_2$ and IRT were separately tested for by using a general linear model for repeated measures with hand as the between factor (SPSS version 7.0). Statistical tests for differences in measured quantities between arms were tested using paired T-tests with a p-value < 0.01 taken as significant.

RESULTS

Results for whole arm and target segment before and after CDP treatment are shown in *Table 1*.

Whole Arm

For total arm volume, there was a significant treatment effect ($p<0.001$) resulting in a significant reduction in the affected arm total volume ($p=0.003$). The affected arm total volume was significantly greater than the control arm volume before treatment ($p=0.002$) and remained greater after treatment ($p=0.006$). Both edema volume and percentage edema were significantly reduced ($p<0.01$) after treatment.

Target Segments

As for the total arm, there was a significant treatment effect ($p<0.001$) for target segments resulting in a significant reduction in the affected arm's target segment volume ($p=0.001$). The affected arm target segment volume was significantly greater than for the control arm before treatment ($p=0.003$) and remained greater after treatment ($p=0.01$). Both edema volume and percentage edema were significantly reduced ($p<0.01$) after treatment. For the control arm, IRT was less than one second which is recorded as 0.00 seconds in *Table 1*. For the affected arm, there was a significant treatment effect on IRT ($p<0.001$) resulting

TABLE 1
Parameters Before and After Therapy

	Pre-Treatment		Post-Treatment	
	Affected Arm	Control Arm	Affected Arm	Control Arm
Whole Arm				
Total Volume (ml)	3075 ± 1401*	2377 ± 952	2770 ±1184*¶	2346 ± 946
Edema Volume (ml)	698 ±721		432 ± 504¶	
Percent Edema (%)	28.6 ± 22.9		18.1 ± 17.7¶	
Target Segment				
Total Volume (ml)	283 ± 148*	191 ± 64	236 ± 116*¶	188 ± 66
Edema Volume (ml)	92.2 ± 98.1		52.4 ± 60.0¶	
Percent Edema (%)	42.6 ± 30.1		25.0 ± 20.4¶	
IRT (sec)	88.7 ± 60.7*	0.00 ± 0.00	23.1 ± 38.8*¶	0.00 ± 0.00
$TcPO_{2B}$ (mmHg)	60.1 ± 8.8	61.3 ± 10.1	61.8 ± 9.2	59.7 ± 10.4
$TcPO_{2V}$ (mmHg)	55.3 ± 8.0§	55.6 ± 8.5§	56.0 ± 9.7§	52.5 ± 10.2§

Values are mean ± SD. *significantly different than control arm ($p<0.01$), ¶ significantly different from pre-treatment ($p<0.01$), §significantly less than baseline $TcPO_2$ ($p<0.01$). $TcPO_{2B}$ is the baseline transcutaneous oxygen tension with the arm horizontal at heart level. $TcPO_{2V}$ is the value while the arm is vertically raised. IRT is the indentation recovery time.

in a significant reduction ($p<0.001$) from its pretreatment value of 88.7 seconds to a post-treatment value of 23.1 seconds.

Transcutaneous Oxygen Tension

Despite the large pre-treatment differences between arms in volume, edema and IRT, there was no significant difference in baseline $TcPO_2$ between arms either prior to the start of treatment ($p=0.662$) or after treatment ($p=0.547$), and there was no significant treatment effect ($p=0.924$). The arm-raising maneuver caused a significant reduction in $TcPO_2$ ($p<0.001$), but this reduction was not different between affected and control arms.

DISCUSSION

The main finding of this study indicates that despite significant lymphedema in affected arms of the present patient group, no significant difference in resting $TcPO_2$ between affected and non-affected arms was detectable. Treatments that significantly reduced edema volume and improved tissue properties had no detectable effect on $TcPO_2$. These results run counter to what we expected; that the presence of significant initial edema would reduce $TcPO_2$ and that effective lymphedema treatment would tend to improve $TcPO_2$ values.

In trying to explain these findings we have considered a number of possibilities that may have influenced the results. One possibility is that the amounts of arm edema and tissue changes present in this patient group were not large enough to significantly affect $TcPO_2$ but that greater amounts would possibly have had a measurable impact. However, the relationship between edema amount and its effect on $TcPO_2$ is complex since even in cases of significant postoperative edema of the lower extremity, no differences in $TcPO_2$ in edematous vs. non-edematous feet are detectable (26) and edema presence in ulcerated lower extremities appears to have little effect on $TcPO_2$ (11) . Corresponding data for the upper extremities is not available. A second possibility considered was that $TcPO_2$ features of upper extremities may be different from those reported for lower extremities. Most clinical assessments of $TcPO_2$ have targeted lower extremities in which reductions in $TcPO_2$ have been documented for conditions in which blood flow derangements or deficits were known or likely to be present (27,28). However, recent measurements of $TcPO_2$ on hands, without vascular impairment, indicate $TcPO_2$ levels to be between about 58 mmHg (29) and 74 mmHg (30), a range that encompasses the measured values on the arms of our patients. An additional possibility considered is that, although the resting levels of $TcPO_2$ did not differ between affected and non-affected arms, a difference might emerge under conditions in which muscular activity causes an increase in oxygen demand. Thus, it is possible that for the resting conditions used in the present study, microcirculatory blood flow was adequate to sustain resting $TcPO_2$ in the affected arm, but exercise might have demonstrated microvascular reserve to be inadequate. Indirect evidence for such a possibility comes from measurements of hand blood flow and $TcPO_2$ in patients in whom the radial artery of one arm was harvested for coronary artery bypass grafting (29,31). Although these authors found that artery removal was associated with a 15-20% decrease in total blood flow at rest, reductions in $TcPO_2$ of the operated hand compared to the normal hand were demonstrated only during isometric hand grip exercises (29). Whether similar features are present in patients with unilateral arm lymphedema is unknown and cannot be judged on the basis of the present evaluations that were done under resting conditions. However, in view of the potential clinical implications of this possibility, it seems that new studies are warranted to investigate the impact of isometric arm muscle contraction as is present when patients engage in a variety of normal activities.

CONCLUSION

In this limited study of a small group of post-mastectomy patients, treatment of the affected arm significantly reduced total arm and fibrotic segment edema and softened fibrotic tissue. However, despite significant amounts of initial edema of the affected arm, its $TcPO_2$ value was not initially less in the non-affected contralateral arm nor was $TcPO_2$ changed by therapy.

REFERENCES

1. Lubbers, DW. The relationship between tissue oxygen pressure, skin surface PO2 and transcutaneous PO2. In: *Clinical Oxygen Pressure Measurement*. Ehrly AM, J Hauss , B Huch (Eds.), Springer-Verlag; 1987.
2. Uccioli, L, G Monticone, F Russo, et al: Autonomic neuropathy and transcutaneous oxymetry in diabetic lower extremities. Diabetologia 37 (1994), 1051-1055.
3. Mayrovitz, HN, PB Larsen: Functional microcirculatory impairment: A possible source of reduced skin oxygen tension in human diabetes mellitus. Microvasc. Res. 52 (1996), 115-126.
4. White, RA, L Nolan, D Harley, et al: Noninvasive evaluation of peripheral vascular disease using transcutaneous oxygen tension. Am. J. Surg. 144 (1982), 68-75.
5. Quigley, FG, IB Faris: Transcutaneous oxygen tension measurements in the assessment of limb ischaemia. Clin. Physiol. 11 (1991), 315-320.
6. Rudolph, R, P Tripuraneni, JA Koziol, et al: Normal transcutaneous oxygen pressure in skin after radiation therapy for cancer. Cancer 74 (1994), 3063-3070.
7. Dooley, J, J Schirmer, B Slade, et al: Use of transcutaneous pressure of oxygen in the evaluation of edematous wounds. Undersea Hyperb. Med. 23 (1996), 167-174.
8. Christensen, KS, M Klarke: Transcutaneous oxygen measurement in peripheral occlusive disease. An indicator of wound healing in leg amputation. J. Bone Joint Surg. Br. 68 (1986), 423-426.

9. Nemeth, AJ, WH Eaglstein, V Falanga: Clinical parameters and transcutaneous oxygen measurements for the prognosis of venous ulcers. J. Am. Acad. Dermatol. 20 (1989), 186-190.
10. Kolari, PJ, K Pekanmaki, RT Pohjola: Transcutaneous oxygen tension in patients with post-thrombotic leg ulcers: Treatment with intermittent pneumatic compression. Cardiovasc. Res. 22 (1988), 138-141.
11. Nemeth, AJ, V Falanga, SP Alstadt, et al: Ulcerated edematous limbs: Effect of edema removal on transcutaneous oxygen measurements. J. Am. Acad. Dermatol. 20 (1989), 191-197.
12. Brorson, H, H Svensson: Skin blood flow of the lymphedematous arm before and after liposuction. Lymphology 30 (1997), 165-172.
13. Brorson, H: Liposuction gives complete reduction of chronic large arm lymphedema after breast cancer. Acta Oncol. 39 (2000), 407-420.
14. Stanton, AW, JR Levick, PS Mortimer: Cutaneous vascular control in the arms of women with postmastectomy oedema. Exp. Physiol. 81 (1996), 447-464.
15. Jacobsson, S: Blood circulation in lymphoedema of the arm. Br. J. Plast. Surg. 20 (1967), 355-358.
16. Svensson, WE, PS Mortimer, E Tohno, et al: Increased arterial inflow demonstrated by Doppler ultrasound in arm swelling following breast cancer treatment. Eur. J. Cancer 30A (1994), 661-664.
17. Jacobsson, S: Studies of the blood circulation in lymphedematous limbs. Scand. J. Plast. Reconstr. Surg. Suppl. 3 (1967), 1-81.
18. Stanton, AW, B Holroyd, JW Northfield, et al: Forearm blood flow measured by venous occlusion plethysmography in healthy subjects and in women with postmastectomy oedema. Vasc. Med. 3 (1998), 3-8.
19. Svensson, WE, PS Mortimer, E Tohno, et al: Colour Doppler demonstrates venous flow abnormalities in breast cancer patients with chronic arm swelling. Eur. J. Cancer 30A (1994), 657-660.
20. Johansson, K, E Lie, C Ekdahl, et al: A randomized study comparing manual lymph drainage with sequential pneumatic compression for treatment of postoperative arm lymphedema. Lymphology 31 (1998), 56-64.
21. Sander, AP, NM Hajer, K Hemenway, et al: Upper-extremity volume measurements in women with lymphedema: A comparison of measurements obtained via water displacement with geometrically determined volume. Phys. Ther. 82 (2002), 1201-1212.
22. Karges, JR, BE Mark, SJ Stikeleather, et al: Concurrent validity of upper-extremity volume estimates: Comparison of calculated volume derived from girth measurements and water displacement volume. Phys. Ther. 83 (2003), 134-145.
23. Mayrovitz, HN, N Sims, J Macdonald: Assessment of limb volume by manual and automated methods in patients with limb edema or lymphedema. Adv. Skin Wound Care 13 (2000), 272-276.
24. Mayrovitz, HN: Limb volume estimates based on limb elliptical vs. circular cross section models. Lymphology 36 (2003), 140-143.
25. Casley-Smith, JR: Measuring and representing peripheral oedema and its alterations. Lymphology 27 (1994), 56-70.
26. Jacobs, MJ, RC Beckers, PJ Jorning, et al: Microcirculatory haemodynamics before and after vascular surgery in severe limb ischaemia—the relation to post-operative oedema formation. Eur. J. Vasc. Surg. 4 (1990), 525-529.
27. Zimny, S, F Dessel, M Ehren, et al: Early detection of microcirculatory impairment in diabetic patients with foot at risk. Diabetes Care 24 (2001), 1810-1814.
28. Kalus, U, J Koscielny, A Grigorov, et al: Improvement of cutaneous microcirculation and oxygen supply in patients with chronic venous insufficiency by orally administered extract of red vine leaves AS 195: A randomised, double-blind, placebo-controlled, crossover study. Drugs R D 5 (2004), 63-71.
29. Manabe, S, N Tabuchi, M Toyama, et al: Oxygen pressure measurement during grip exercise reveals exercise intolerance after radial harvest. Ann. Thorac. Surg. 77 (2004), 2066-2070.
30. Daviet, JC, P Dudognon, PM Preux, et al: Reliability of transcutaneous oxygen tension measurement on the back of the hand and complex regional pain syndrome after stroke. Arch. Phys. Med. Rehabil. 85 (2004), 1102-1105.
31. Rafael Sadaba, J, JL Conroy, M Burniston, et al: Effect of radial artery harvesting on tissue perfusion and function of the hand. Cardiovasc. Surg. 9 (2001), 378-382.

Harvey N. Mayrovitz, Ph.D.
Professor of Physiology
College of Medical Sciences
Nova Southeastern University
3200 S. University Drive
Ft. Lauderdale, Florida 33328
Phone: 954-262-1313
Fax: 954-262-1802
e-mail: mayrovit@nsu.nova.edu