

Project Title: Quantitative Studies of Sublingual PCO₂ as a Resuscitation End-Point in the Diagnosis and Treatment of Hemorrhagic Shock

ONR Award No: N000140310253

Award Period: December 11, 2002- September 30, 2005

Final Report

Distribution Unlimited

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DISTRIBUTION STATEMENT A

Approved for Public Release

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Scientific and Technical Objectives

This clinical study is examining the relationship between sublingual PCO₂ (PslCO₂) to real-time changes in microcirculatory blood flow of the sublingual mucosa in victims of traumatic and hemorrhagic shock. This relationship will assist in understanding the direct effects of blood loss on sublingual perfusion and thus PslCO₂ as a reflection of this. The study is also comparing the sensitivity and specificity of PslCO₂ to detect compensated shock states and the severity of uncompensated shock to other commonly utilized methods such as global oxygen delivery and consumption, systemic lactate and base, and other regional measures of perfusion.

Approach

Patients at risk for acute hemorrhage underwent PslCO₂ monitoring for 6 hours. Concomitant examination of the sublingual mucosa using orthogonal polarization spectral imaging, tissue oxygen spectroscopy are utilized to determine the extent to which PslCO₂ reflects changes in sublingual mucosa blood flow and oxygenation during evaluation and treatment. Simultaneous global and regional resuscitation end-points are monitored and compared to PslCO₂ during this time. These include oxygen delivery and consumption, systemic lactate and base deficit. Information from this study was used to construct receiver operator characteristic curves to determine performance of noninvasive monitoring variables to detect elevated lactate levels. Due to a manufacturing recall by Nellcor of the PslCO₂ probes, a commercially available transcutaneous CO₂ monitor was used to monitor to complete PslCO₂ monitoring.

Concise Accomplishments

Overcame problem of Nellcor equipment recall.

Completed collection of data on 67 subjects.

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Determined that PslCO₂ is not currently a candidate monitoring technique for evaluation of shock due to hemorrhage.

Have developed and maintained a human evaluation platform for evaluating and developing new techniques for tissue oxygenation monitoring.

Expanded Accomplishments

Introduction:

Detection of shock in the setting of hemorrhage can be difficult based on the physical examination especially in states of compensated shock. New technologies have been advocated as a means to enhance detection by examining tissue specific changes. These technologies include sublingual CO₂ (PslCO₂) and tissue hemoglobin oxygen saturation (StO₂).

Hypothesis:

The specific aim of this study was to compare the performance of PslCO₂ and StO₂ to detect shock due to hemorrhage.

Methods:

Patients at risk for hemorrhage had lactate, base excess (BE), PslCO₂, StO₂, hemoglobin (Hgb), and systolic blood pressure (SBP) measured. PslCO₂ was measured using either a fiberoptic or a modified Stow-Serveringhaus electrode. StO₂ was measured using differential absorption spectroscopy of the subcutaneous tissue of the thenar eminence. Shock was defined as a systemic lactate level > 3 mmol/L. Sensitivities and specificities were determined for each variable's ability at certain values to detect lactate levels > 3 mmol/L. This data was used to construct Receiver Operator Characteristic (ROC) plots for each measure to determine and compare performances between measures.

Results:

Sixty-seven patients were studied (32 trauma, 12 cardiac surgery, 20 hip arthroplasty, and 5 gastrointestinal bleed). ROC values (area under the curve) for each variable are noted in order of decreasing performance: BE: 0.85, StO₂: 0.67, SBP: 0.58, Hgb: 0.52, PslCO₂: 0.44. As expected, BE performed the best given its relationship to lactate. This was followed by StO₂. Surprisingly, SBP and Hgb performed better than PslCO₂. Analysis of PslCO₂-arterial CO₂ gap and PslCO₂-endtidal PCO₂ gap did not improve performance.

Conclusions:

The measure of PslCO₂ did not perform as well as anticipated. Reasons for this are unclear but may be related to such variables as the measurement location as well as technology specific issues in how the measures are made. More study is required before these technologies can be recommended for routine diagnostic and monitoring purposes.

Uploaded Files: These can be viewed on-line at ONR's web based reporting system.

[ONR ROC Curves.ppt](#)

Work Plan

This project has essentially been completed. The major remaining task is analysis of the orthogonal polarization spectral imaging data. This will be overlaid with previously reported data.

Until new technology is developed to measure PslCO₂, it is our opinion that the measurement provides no valuable data in regards to evaluating acutely injured patients over more readily available measurements such as blood pressure.

Additional manuscripts will be prepared and submitted for publication.

We have also used this monitoring tool set to examine tissue hypoxia in other health states including congestive heart failure and sickle cell disease vasoocclusive crisis.

Newer technologies are being developed and evaluated. A trial to used monitoring endpoints as a decision tool to determine/decide the need for transfusion is being developed.

Problems/Issues

The recall of the Nelcor PslCO₂ device caused a delay in enrollment and required development of an alternative technique to monitor PslCO₂.

Peer-Reviewed Journal Articles

Status	Text
Published	Hogan C, Hess M, Ward K, Kontos M, Pittman R, Gennings C: Tissue hemoglobin oxygen saturation in stable versus acutely decompensated heart failure: A quantitative measure to evaluate disease and impact outcome: Nanomedicine 2006 (In Press)
Published	Ward K, Ivautry R, Barbee R, Turner J, Pittman R, Torres I, Spiess B. Near Infrared spectroscopy for evaluation of the trauma patient: A technology review. Resuscitation 2006;68:27-44.
Published	Hogan C, Hess M, Ward K, Gennings C: The utility of microvascular perfusion assessment in heart failure: A pilot study. Journal of Cardiac Failure. 2005;11:713-719.

Books or Book Chapters

Status	Text
Published	Ward KR, Bisera J: Cardiac arrest resuscitation monitoring. In, eds Paradis, Halperin, Kern, Wenzel, Chamberlin (eds) Cardiac Arrest: The Pathophysiology and Therapy of Sudden Death (2nd Edition), Cambridge; 2006 (accepted).
Published	Ward KR, Torres I: Oxygen transport monitoring: The basis for developing transfusion triggers. In: Spiess B, Spence R, Shander A (eds): Perioperative Transfusion Medicine, Lippincott William and Wilkins 2006, pp. 55-66.

Technical Reports (Non-refereed Publications)

No technical reports reported.

Abstracts/Presentations/Posters/Conference Proceedings

Abstract: Aisiku IP, Smith WR, Penberthy LT, Sikka V, Ward, KR: Cutaneous oxygen saturation in sickle cell vasoocclusive crisis. Acad Emerg Med 2005;12 (suppl 1): p 154.

Abstract: Hogan CJ, Hess, ML, Ward, KR: Microvascular tissue perfusion in stable versus decompensated heart failure: Acad Emerg Med 2005;12 (suppl 1): p 56.

Abstract: Hogan C, Hess M, Ward K, Kontos M: Microvascular hypoperfusion persists prior to discharge in patients admitted for decompensated heart failure. Crit Care Med 2005;33 (Suppl):p A54.

Poster: K.R. Ward, MD; M.H. Tiba, MD; G.T. Draucker; R.W. Barbee, PhD; P.S. Reynolds, PhD; I.P. Torres-Filo, MD. PhD; R.R. Ivatury, MD Utility of Sublingual CO₂ to Detect Tissue Dysoxia in Humans. Department of Defense Advanced Technologies in Combat Casualty Care. August 2005 St. Pete Beach Florida.

Abstract: Ward KR, Tiba H, Draucker J, Reynolds P, Torres R, Barbee RW, Ivatury RR: Performance of noninvasive tissue oxygenation indicators in detecting shock due to hemorrhage. Crit Care Med 2005;33(Suppl):p A23.

Presentation: 2005: Plenary Session Presentation: 2005 Department of Defense Advanced Technologies in Combat Casualty Care Conference: Oxygen is Good, Blood Goes Round and Round. August 16, 2005.

Awards/Honors/Invention Disclosure

2006: Society of Critical Care Medicine Educational Scholarship Award: Award given for one of 10 best abstracts submitted to 35th Critical Care Congress (out of 800 abstracts). Performance of Noninvasive Tissue Oxygenation Indicators in Detecting Shock Due to Hemorrhage.

Patents Submitted

Methods for Real-time Remote Monitoring of Oxygen Debt and Critical Illness/Injury Metabolic Stress

Patents Issued

No patents issued reported.

Technology Transfer

We have used ONR funding from this project to demonstrate the overall value of clinical metabolic monitoring to understand tissue hypoxia in states of critical illness and injury. This has led to recent partnerships to develop new noninvasive means to make these measures and well as to create new models for study.

One such partnership is with the company BodyMedia in Pittsburgh, PA. We are working with BodyMedia to modify their existing technology for wellness monitoring for adaptation in the critically ill and injured patient.

The data generated in the ONR project resulted in a grant award from USAMRMC to characterize tissue oxygenation changes in a human lower body negative pressure model of hemorrhagic shock.

We will leverage these findings and relationships to develop strong testing platforms for use in developing and testing new generations of noninvasive monitors in critical illness and injury.

ONR Database Statistics

Use of Human Subjects	Yes
DoD Personnel Used	
Use of Animals	No
Animals Used	
Use of Recombinant DNA	No
Degree(s) Granted	0

PI/CoPI Information

	Minority	Non-Minority	Total
0 PI/CoPI Minority Women **			
0 PI/CoPI Non-Minority Women			
0 PI/CoPI Minority Men **			
2 PI/CoPI Non-Minority Men			
	Women	0	0
	Men	0	2
	Total	0	2

Post Doctoral Information

	Minority	Non-Minority	Total
0 Post Doctoral Minority Women **			
0 Post Doctoral Non-Minority Women			
1 Post Doctoral Minority Men **			
0 Post Doctoral Non-Minority Men			
	Women	0	0
	Men	1	1
	Total	1	1

Grad Students Information

	Minority	Non-Minority	Total
0 Grad Students Minority Women **			
0 Grad Students Non-Minority Women			
0 Grad Students Minority Men **			
	Women	0	0

0 Grad Students Non-Minority Men	Men	0	0	0
	Total	0	0	0

Undergrad Students Information				
0 Undergrad Students Minority Women**		Minority	Non-Minority	Total
0 Undergrad Students Non-Minority Women	Women	0	0	0
0 Undergrad Students Minority Men**	Men	0	0	0
0 Undergrad Students Non-Minority Men	Total	0	0	0

Publication Totals	
Total Number of Peer-Reviewed Journal Articles:	3
Total Number of Books or Chapters:	2
Total Number of Technical Reports:	0
Total Number of Abstracts/Presentations/Posters/Conference Proceedings:	6
Total Number of Patents Issued:	0
Total Number of Patents Pending:	1

** Under-represented or minority groups include Blacks, Hispanics, and Native Americans. Asians are not considered an under-represented or minority group in science and engineering.

*** Supported at least 25% this year on contract/grant.

Other Sponsored Work

TITLE	SPONSOR	FUNDING	START DATE	END DATE
Characterization of Global and Microvascular Oxygen Transport in a Lower Body Negative Pressure Model of Hemorrhagic Shock	USAMRMC	\$665,000	October 1, 2005	September 30, 2008

Foreign Collaborations

No foreign collaborations reported.