Insulin Resistance and Endogenous Insulin Production in Patients with Thermal Injuries on IIT

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The use of Army medical and/or other Army records in the preparation of this material is acknowledged, but it is not to be construed as implying official Department of the Army approval of the conclusions presented.

Introduction

Stress signals inherent to severely injured patients contribute to increased glucose production and impaired glucose utilization, as evidenced by hyperglycemia. Patients with thermal injuries are characterized by an exaggerated hyperdynamic physiologic stress response, hypermetabolic state, catabolism, and hyperglycemia due to alterations in endocrinologic and immunologic functions, glucose intolerance, and insulin resistance (IR). Hyperglycemia has been associated with increased infection rates, healing times, complications, mortality, and overall poor outcomes.

Recent studies report improved outcomes with glycemic control; thus, they advocate the need to attenuate hyperglycemia via insulin administration as a means to decrease associated risks. This clinical notion gained much acceptance; hence, intensive insulin therapy (IIT) protocols were adopted to decrease glucose levels and increase survival.

Langouche et al. found lower levels of C-peptide in patients on IIT; and by day 7, these levels were comparable to those of healthy volunteers. In part, as a function of insulin resistance severity, substantial insulin doses are administered. We hypothesize that IIT will disrupt and suppress endogenous insulin production.

Methods

Study Patients

- Patients admitted to the sole US military burn center (USAISR) with >20% TBSA burns undergoing IIT within the first 14 days of admission
- Recorded demographics, glucose values (laboratory and glucometer hourly checks), and units of insulin administered
- Collected plasma samples 3 X day for average of 7 days
- Quantified circulating insulin and C-peptide levels via ELISA
- Calculated IR from homeostasis model assessment - insulin resistance (HOMA-IR)

Healthy Volunteers

- Recorded age, sex, body mass index (BMI), and glucose values.
- Collected plasma samples
- Quantified circulating insulin and C-peptide levels via ELISA
- Calculated IR from homeostasis model assessment - insulin resistance (HOMA-IR)

Statistical analysis included: unpaired Student's t-test, chi-square tests for categorical data, and linear regressions. Values within the text are reported as mean±standard deviation and when necessary median (95% confidence interval [CI]). A *p*-value of less than 0.05 was considered to be a significant finding.

Results

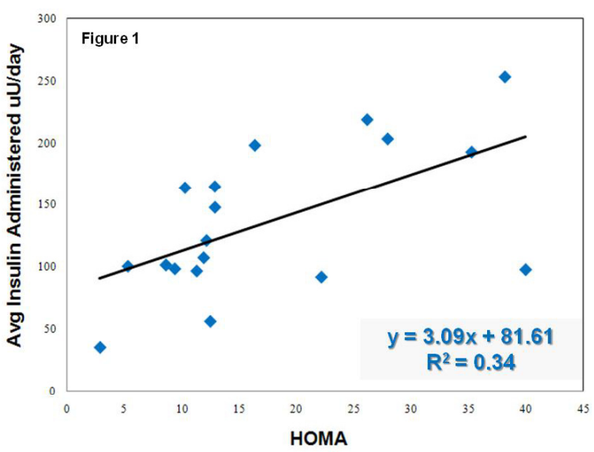
Study Patients on IIT (n=18)

	% or mean ± SD
Age (*yrs*)	32 ± 16.4
Sex (*% Male*)	83%
Military (*%*)	72%
ISS	32 ± 10.1
TBSA (*%*)	43 ± 21.1
TBSA (*% 3rd*)	30 ± 20.3
Inhalation Injury (*% Yes*)	72%
Mortality (*% Death*)	28%
Vent Days	19 ± 19.0
ICU Days	32 ± 20.2
LOS	60 ± 38.5
Pre-Existing Conditions	
Hemoglobin A1c	5.7 ± 0.58
Diabetes (*% Yes*)	6%
Heart Disease (*% Yes*)	6%
Study Period	
Enrolled Post Admission (*days*)	7 ± 2.5
Study Days	7 ± 2.7
Insulin Administration	
Daily Total Sum	136 ± 59.7
Hourly Rate	6 ± 2.8

Comparison of healthy volunteers versus study patients

	Healthy Volunteers		Study Patients		
	n	% or mean ± SD or median [CI]	n	% or mean + SD or median [CI]	*P*
Age (*yrs*)	15	38 ± 11	18	32 ± 16.4	NS
Sex (*% Male*)	15	60%	18	83%	0.03
BMI	15	27 ± 5	18	26 ± 3.4	NS
Underweight	-	-	-	-	
Normal	6	40%	6	33%	NS
Overweight	4	27%	10	56%	NS
Obese	5	33%	2	11%	NS
Glucose Level (mg/dl)	15	124 ± 14.3	18	123 ± 10.7	NS
C-Peptide (ng/ml)	15	4.0 ± 2.12	18	4.9 ± 2.97	NS
Circulating Insulin Level (uU/ml)	**15**	**26.2 ± 31.13**	**18**	**56.1 ± 32.50**	**0.012**
		43 (39.9 - 72.2)		**13 (11.9 - 23.2)**	
HOMA-IR	**15**	**8 ± 10.0**	**18**	**18 ± 11.3**	**0.019**

Severity of Insulin Resistance and Exogenous Insulin



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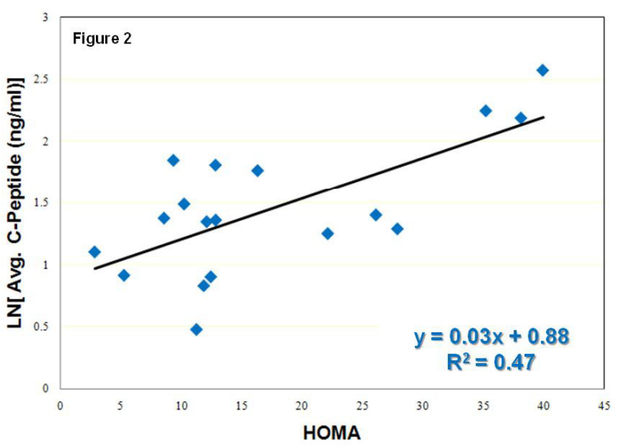
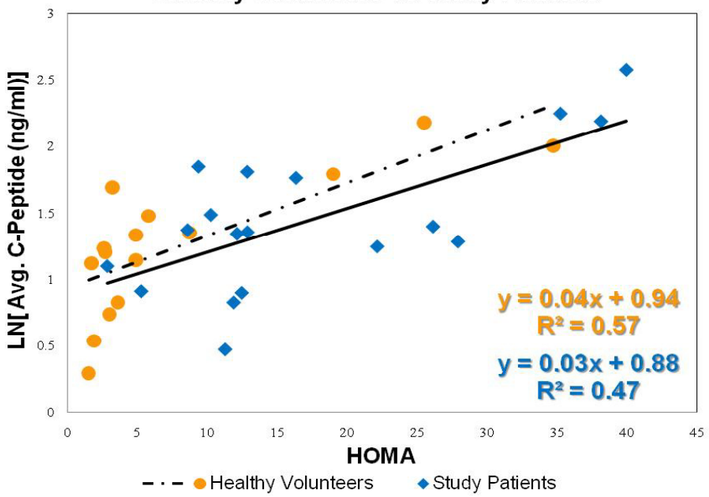


Severity of Insulin Resistance and Endogenous Insulin Healthy Volunteers vs Study Patients



Conclusions

- Patients with thermal injuries exhibited a significant decrease of insulin sensitivity when compared to the healthy volunteers.
- As the severity of insulin resistance increased, the amount of administered insulin to maintain glycemic control also increased.
- In spite of the high doses of exogenous insulin, endogenous insulin production also increased in association with insulin resistance severity, as indicated by circulating C-peptide levels.

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