American Society for Reproductive Medicine 2018 Scientific Congress & Expo
October 6 to 10, 2018 ● Denver, Colorado, USA

Title:

INCREASED BODY MASS INDEX IS NOT CORRELATED WITH SEMINAL OXIDATIVE STRESS: A PROSPECTIVE ANALYSIS

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Objective:

Oxidation–reduction potential (ORP) is a measurement of oxidative stress that represents the redox imbalance between oxidants and antioxidants in biological samples. Reference values of ORP have been established in both infertile men and healthy men of proven and unproven fertility. High ORP measurements are associated with decreased quality and sperm parameters during a semen analysis (SA) or correlated with poor fertilization potential.

In humans, obesity is known to induce systemic oxidative stress through multiple biochemical mechanisms, such as the generation of superoxide radicals from NADPH oxidases (NOX), oxidative phosphorylation, glyceraldehyde auto-oxidation, protein kinase C (PKC) activation, and polyol and hexosamine pathways. The aim of this study is to evaluate the association between male body mass index (BMI) and oxidative stress levels in samples collected for semen analyses.

Design:

Prospective cohort analysis conducted in a single private IVF center.

Materials and Methods:

Semen samples were obtained from male patients that underwent diagnostic semen analysis between January 2018 and March 2018. Demographic data and semen analysis parameters (i.e. concentration, motility, and morphology) were collected. Patients were separated into cohorts according to the BMI-WHO Classification system (World Health Organization 1995). Patients with azoospermia or post vasectomy control samples, evidence of obstructive pathology or ejaculatory dysfunction, and incomplete semen collection were excluded from the analysis. Abnormal semen was categorized if had at least one of the following abnormal sperm parameters: semen volume <1.5 mL, sperm concentration <15 $X10^6$ sperm/mL, total motility <40%. or normal morphology <4%. Normal sperm parameters fell within the 2010 WHO normal reference ranges. ORP was measured in millivolts (mV) using galvanostat-based technology (MiOXSYS System; Aytu Bioscience, Englewood,CO, USA) using 30 µL of semen obtained after 30 minutes within the semen sample collection. Raw ORP values(mV) were normalized to sperm concentration. Data for normalized ORP are presented as $mV/10^6$ sperm/mL. A reported cut off value 1.36 $mV/10^6$ was used to categorize results as normal ORP values. A multivariate linear regression controlling for patients age and normal SA was used. Wilcoxon and Kruskall wallis ANOVA test was performed to compare differences between the cohorts.

Results:

A total of 36 patients were included in the study. Mean participant age was 35 (±5.4) years, mean BMI 27 (±5.3) and mean ORP was reported 3.44 (±8.7) $mV/10^6$ sperm/mL. Over half (52%) of

the SA samples were diagnosed as normal during sperm analysis (n=19/36). Patients were separated in 3 cohorts by WHO BMI classification. (Group 1= category 2 (n=16), Group 2= category 3 (n=9) and Group 3= category 4 (n=11). A significant difference was found on BMI among cohorts (p=<0.0001), no other significant differences where found when analyzing demographic characteristics and no difference were found when comparing normalized-ORP between cohorts (Table 1). A multivariate linear regression analysis adjusting for age and presence of normal SA parameters found no association between BMI and the odds of increased ORP value (p=0.17, R^2=0.28). On a sub-analysis, when correcting for age and BMI, a positive association was found on lower ORP and the detection of a normal SA. (p= 0.04).

Conclusions:

Obesity is characterized by chronic low grade inflammation with permanently increased oxidative stress. The hemato-testicular barrier could be a mechanism of protection for these oxygen reactants found in serum and other surrounding tissues. This study finding showed no association in male BMI with over-expression of oxidative stress and ORP levels of semen samples analyzed trough a novel technology.

Table 1:

Demographic characteristics of the populations analyzed, ANOVA Kruskal Wallis and Wilcoxon tests for differences. Alpha =0.05.

	Group 1		Group 2		Group 3			
	WHO BMI 2		WHO BMI 3		WHO BMI 4			
	n=16		n=9		n=11			
	Mean	SD	Mean	SD	Mean	Sd	p-value	significanc

								e
Age	34.49	5.90	37.00	5.96	37.09	4.21	0.33	NS
Abstinence days	7.00	10.66	2.89	0.78	3.36	1.12	0.46	NS
BMI	22.58	1.44	26.58	1.51	34.00	3.13	<0.0001	*
Normalized ORP ($mV/10^6$ sperm/mL)	6.83	12.59	0.67	0.39	1.03	0.88	0.96	NS
ORP (mV)	43.45	17.30	37.29	23.82	57.73	72.99	0.83	NS
Sperm volume (mL)	3.21	1.10	3.10	1.70	3.48	1.97	0.96	NS
Sperm concentration (million/mL)	49.00	46.49	57.33	42.78	67.14	51.42	0.67	NS
Sperm motility (%)	53.50	25.25	56.67	26.41	55.27	23.32	0.80	NS
Sperm strict morphology (%)	4.50	3.88	3.67	2.00	3.18	2.04	0.24	NS
Normal SA (Count / %)	8./15	53%	6./9	66.60 %	5./11	45.40 %	0.63	NS

Support:

None.