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Male oxidative stress infertility (MOSI): proposed terminology and clinical practice guidelines for management of idiopathic male infertility

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Review Article

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Male Oxidative Stress Infertility (MOSI): Proposed Terminology and Clinical Practice Guidelines for Management of Idiopathic Male Infertility

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Male Oxidative Stress Infertility (MOSI): Proposed Terminology and Clinical Practise Guidelines for Management of Idiopathic Male Infertility

Caerus Biotechnologies, 2023

MiOXSYS[®] is the cornerstone of Male Oxidative Stress Infertility (MOSI) diagnostics and management



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MOSI Clinical guidance

MOSI should be suspected in infertile men with abnormal semen characteristics and OS Many of these men were previously classified as idiopathic male infertility – with no underlying endocrine, genetic or anatomical causes of infertility 3

These men should be offered testing for OS (or ORP by MiOXSYS) to potentially diagnose MOSI

The mean ORP of the infertile men with a varicocele might be ~3.5x higher than that of the normozoospermic controls



138 infertile men with varicocele (Grade 1, 24 cases; Grade 2, 47 cases; Grade 3, 67 cases) and 102 men with normozoospermia without varicocele were evaluated.

The mean ORP of the infertile men with a varicocele was three times higher than that of the normozoospermia controls (p<0.01).

Human Fertility, Seminal oxidation-reduction potential and sperm DNA fragmentation index increase among infertile men with varicocele. ISSN: 1465-7273 (Print) 1742-8149 (Online) Journal homepage: https://www.tandfonline.com/loi/ihuf20

Varicocele repair improves ORP

SEMEN	MEA	NS	P VALUE	95% CI
PARAMETERS	PRE- VARICOCELE	POST- VARICOCELE		
sORP (mV/10 ⁶ sperm/mL)	4.73	2.03	0.001	-1.382.68
Progressive Motility (%)	19.98	27.98	0.001	24.69-30.20
Total Motility (%)	45.88	54.85	0.01	49.60-59.09
Morphology (%)	3.82	4.27	NS	3.44-5.21
Sperm Concentration (10 ⁶)	28.11	37.85	.05	2.77-15.78
Total Sperm (10 ⁶)	85.21	111.96	NS	2.66-48.08

Post varicocele repair compared to pre varicocele repair revealed significant improvement in ORP (P<0.001), SDF (P<0.001) total motility (P<0.01), and progressive motility (P<.0.001).

Although there was an improvement in morphology, it was not statistically significant.

This study validates previous data that varicocele repair improves bulk semen parameter values and SDF, but is the first to demonstrate it improves ORP.

Inflammation matters: IL-6 correlates with ROS and ORP levels

The IL-6 levels correlated significantly with the ROS levels in the infertile patients with varicocele (r = 0.39; p = 0.01).

Inflammatory marker IL-6 concentration was significantly higher in patients with high ORP (p=0.002).





IL-6 concentrations (±SE)

Pomm K. et al. Data on file.

II -6 and ROS level differences in infertile

Nallella KP, Allamaneni SS, Pasqualotto FF, Sharma RK, Thomas AJ Jr, Agarwal A. Relationship of interleukin-6 with semen characteristics and oxidative stress in patients with varicocele. Urology. 2004;64(5):1010-1013. doi:10.1016/j.urology.2004.05.045

Caerus Biotechnologies, 2023

Chronic inflammation increases ORP levels and impairs male fertility



Males diagnosed with inflammatory bowel diseases have worse basic sperm parameters compared to those who are healthy.

Regarding the sperm of males ill with Inflammatory bowel diseases, the phenomenon of oxidative stress is intensified, which may be the cause of the deterioration of semen parameters, as well as an intensified DNA fragmentation.

An asymptomatic carrier state of bacteria may contribute to the intensification of oxidative stress.



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ORP increases with paternal age

Study Objective:

• To investigate the relationship between the ORP and paternal age with the goal of using the ORP as an indicator of semen oxidative stress.

Study Location:

• Yokohama University Medical Center, Japan

Results:

 The semen ORP level was positively correlated with age (p<0.05). The rate of ORP positivity was significantly increased in men ≥34 years of age compared with that in men <34 years of age (33% compared with 12%, respectively; p<0.01).



Comparisons of the rate of static oxidation reduction potential (sORP) positivity between men aged <34 and \geq 34 years. The vertical axis shows the rate of positive sORP, with the horizontal axis showing age. sORP \geq 1.38 was defined as a positive level. ** p<0.01.

Healthy diet decreases seminal ORP



Patients who follow vegan diet demonstrate decreased ORP levels.

A Preliminary Study: Ipact of the Vegan diet on sper m quality and sp er m oxidative stress values Kljajic M, Kasha M, Seyfried S, Solomayer EF Department of Gynecology, Obstetrics and Reproductive Medicine University Medical school or saarland, 1. Homur/ Saarland, Germans There is no evidence for the benefit of other medical therapies (e.g. hCG, androgens) for treatment of male infertility

hence, the medical therapy is empirical

What about antioxidants?

Impact of antioxidant therapy on semen parameters and natural pregnancy outcomes: a meta-analysis



Clinical pregnancy

Therapy with Antioxidants improves clinical pregnancy rate compared to placebo/no treatment (OR 1.97, I² =20%; p<0.01).

	AO)	(Placebo/No Treatment Odds F		Odds Ratio	Odds Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
Azizollahi 2013 (1)	1	40	0	13	1.6%	1.03 [0.04, 26.70]	
Azizollahi 2013 (2)	2	40	0	13	1.8%	1.75 [0.08, 38.88]	
Balercia 2005 (1)	2	15	1	5	2.4%	0.62 [0.04, 8.70]	
Balercia 2005 (2)	2	15	1	5	2.4%	0.62 [0.04, 8.70]	
Balercia 2005 (3)	5	15	1	5	2.8%	2.00 [0.17, 22.95]	
Balercia 2009	6	30	3	30	6.4%	2.25 [0.51, 9.99]	
Barekat 2016	5	20	2	20	4.8%	3.00 [0.51, 17.74]	
Busetto 2017	10	45	2	49	5.8%	6.71 [1.38, 32.60]	
Busetto 2018	10	45	10	49	11.2%	1.11 [0.41, 2.99]	
Gopinath 2013 (1)	7	43	2	36	5.5%	3.31 [0.64, 17.04]	
Gopinath 2013 (2)	6	46	2	36	5.4%	2.55 [0.48, 13.47]	
Kizilay 2019 (1)	18	64	5	29	9.7%	1.88 [0.62, 5.68]	
Kopets 2020	10	42	2	41	5.8%	6.09 [1.24, 29.84]	
Omu 1998	11	49	2	48	5.9%	6.66 [1.39, 31.90]	
Paradiso Galatioto 2008	1	20	0	22	1.6%	3.46 [0.13, 89.95]	
Scott 1998 (1)	5	46	0	18	2.0%	4.90 [0.26, 93.36]	
Steiner 2020	15	85	22	86	15.1%	0.62 [0.30, 1.30]	
Stenqvist 2018	3	37	4	40	5.9%	0.79 [0.17, 3.81]	
Suleiman 1996	11	52	0	35	2.1%	19.67 [1.12, 345.85]	
Zavaczki 2003	1	12	0	14	1.6%	3.78 [0.14, 101.83]	
Total (95% CI)		761		594	100.0%	1.97 [1.28, 3.04]	◆
Total events	131		59				
Heterogeneity: Tau ² = 0.18	3; Chi ² = 2	3.83, df	f = 19 (P = 0.20); l	²= 20%			
Test for overall effect: Z = 3.09 (P = 0.002) 10 10 100 100 Test for overall effect: Z = 3.09 (P = 0.002) Favours Placebo/No Treatm Favours AOX Favours Placebo/No Treatm Favours AOX							