

ORIGINAL

## Associations between oxidative stress biomarkers in different body fluids and reproductive parameters in male partners of subfertile couples



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Received 23 March 2015; accepted 26 January 2016

Available online 8 April 2016

### KEYWORDS

Oxidative stress;  
Reproductive hormones;  
Semen quality;  
Total antioxidant capacity

### Abstract

**Objective:** To evaluate the relationships between oxidative stress (OS) biomarkers and total antioxidant capacity (TAC) in blood serum and seminal plasma, and their associations with semen quality and serum reproductive hormone concentrations in potential subfertile men.

**Material and method:** A cross-sectional study was conducted on men ( $n = 122$ ) attending an infertility clinic in the Murcia Region (Southern Spain) between 2012 and 2013. Concentrations of malondialdehyde (MDA), nitric oxide (NO) and TAC were measured in blood and semen. Follicle-stimulating hormone, luteinising hormone, testosterone, prolactin and oestradiol concentrations were measured in serum. Semen analyses were performed according to World Health Organization criteria. Correlation analysis and multiple linear regression models were performed, controlling for important covariates.

**Results:** There was a significant inverse association between serum MDA concentrations and all sperm parameters, except for seminal volume. Serum TAC concentrations were positively related to sperm count and motility. A positive association was observed between seminal plasma NO levels and the percentage of morphologically normal sperm. With regard to reproductive hormones, serum MDA concentrations were positively related to FSH and LH levels, and TAC inversely associated with FSH levels.

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**Conclusions:** Our results suggest that oxidative stress may be associated with semen parameters and reproductive hormone levels in male partners of couples seeking infertility treatment. However, further studies are needed to confirm and extend these findings, in particular, with regard to serum reproductive hormones.

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## PALABRAS CLAVE

Estrés oxidativo;  
Hormonas reproductivas;  
Calidad seminal;  
Capacidad antioxidante total

## Asociaciones entre biomarcadores de estrés oxidativo en diferentes fluidos biológicos y parámetros reproductivos en varones de parejas subfértiles

### Resumen

**Objetivo:** Evaluar las correlaciones entre marcadores de estrés oxidativo (OS) y capacidad antioxidante total (TAC) en suero sanguíneo y plasma seminal, y sus asociaciones con calidad seminal y hormonas reproductivas en varones potencialmente subfértiles.

**Material y método:** Estudio transversal realizado en varones (n = 122) que acudían a un servicio de infertilidad de Murcia entre 2012-2013. Las concentraciones de malondialdehído (MDA), óxido nítrico (NO) y TAC se midieron en sangre y semen. Se analizaron los niveles séricos de las hormonas foliculoestimulante, luteinizante, testosterona, prolactina y estradiol. Los análisis espermáticos se llevaron a cabo siguiendo las normas de la Organización Mundial de la Salud. Se utilizaron análisis de correlación y modelos de regresión lineal múltiple ajustando por covariables importantes.

**Resultados:** Se mostró una asociación inversa significativa entre las concentraciones séricas de MDA y todos los parámetros espermáticos, excepto el volumen seminal. Las concentraciones séricas de TAC se relacionaron positivamente con el recuento y la movilidad espermática. Los niveles de NO en plasma seminal se asociaron directamente con el porcentaje de espermatozoides morfológicamente normales. Con respecto a las hormonas reproductivas, las concentraciones séricas de MDA se asociaron positivamente con los niveles de FSH y LH, y las de TAC se asociaron inversamente con los niveles de FSH.

**Conclusiones:** Nuestros resultados sugieren que el estrés oxidativo estaría asociado con los parámetros seminales y hormonales en varones de parejas que consultan por problemas de infertilidad. Sin embargo, son necesarios más estudios para confirmar estos hallazgos, en particular con respecto al papel de las hormonas reproductivas.

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## Introduction

Male factor infertility accounts for approximately 25% of consultations to infertility clinics and is a contributing factor in an additional 30%–40%.<sup>1</sup> In recent years oxidative stress (OS) has been identified as an underlying etiological factor in the mechanism leading to sperm dysfunction and male infertility.<sup>1–3</sup> Several animal and human studies have revealed generation of reactive oxygen species (ROS) by spermatozoa and leukocytes.<sup>2</sup> A number of studies have also reported associations between pathological levels of ROS, male infertility and impaired seminal quality,<sup>3</sup> including sperm concentration, motility, and morphology.<sup>4–8</sup> ROS react with and modify lipids, carbohydrates, proteins and DNA and may result in cytotoxicity and dysfunction.<sup>9,10</sup> For example, ROS reacts with polyunsaturated fatty acids present in the plasma membrane of the spermatozoa,<sup>3</sup> producing lipid peroxidation – measured by malondialdehyde (MDA) levels – and changes in fluidity and integrity of the membrane,

which leads to a decrease of sperm motility and changes in sperm morphology.<sup>6–9</sup> Another ROS, the nitric oxide (NO) has been negatively correlated with sperm function, including motility<sup>10</sup> or vitality.<sup>11</sup> Nevertheless, there is a balance between ROS production and antioxidant scavenging activities in the male reproductive tract.<sup>12</sup> Total antioxidant capacity (TAC) is a well-known tool to assess the overall antioxidant status. Low levels of TAC have been found in seminal plasma of infertile men,<sup>2,12</sup> while high levels were positively associated to traditional criteria for good semen quality.<sup>13</sup> Little is known about the role of OS markers in potential subfertile men from Southern Spain.

The role of reproductive hormones on male fertility is well documented,<sup>14</sup> and the main pathways refer to hormonal imbalance affecting spermatogenesis. However, there are reasons to believe that sex hormones may have another pathway through which male fertility may be hampered. There is increasing evidence that hormones can modulate the antioxidant system, at least in some disorders or

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