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Original article

Ozone decreases sperm quality in systemic lupus erythematosus patients

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ABSTRACT

Objective: To investigate the deleterious effects of air pollutants exposure in the Sao Paulo metropolitan region on semen quality in systemic lupus erythematosus (SLE).
Methods: A seven-years longitudinal repeated-measures panel study was performed at the Laboratory of Experimental Air Pollution and Rheumatology Division. Two semen samples from 28 post-pubertal SLE patients were analyzed. Daily concentrations of air pollutants exposure: PM_{10}, SO_2, NO_2, ozone, CO, and meteorological variables were evaluated on 90 days before each semen collection dates using generalized estimating equation models.
Results: Intravenous cyclophosphamide (IVCYC) and ozone had an association with a decrease in sperm quality of SLE patients. IVCYC was associated with decreases of 64.3 million of spermatozoa/mL (95% CI 39.01–89.65; $p = 0.0001$) and 149.14 million of spermatozoa/ejaculate (95% CI 81.93–216.38; $p = 0.017$). With regard to ozone, the most relevant adverse effects were observed from lags 80–88, when the exposure to an interquartile range increase in ozone 9-day moving average concentration led to decreases of 22.9 million of spermatozoa/mL (95% CI 5.8–40.0; $p = 0.009$) and 70.5 million of spermatozoa/ejaculate (95% CI 12.3–128.7; $p = 0.016$). Further analysis of 17 patients that never used IVCYC showed association between exposure to ozone (80–88 days) and decrease of 30.0 million of spermatozoa/mL (95% CI 7.0–53.0; $p = 0.011$) and 79.0 million of spermatozoa/ejaculate (95% CI 2.1–155.9; $p = 0.044$).
Conclusion: Ozone and IVCYC had a consistent adverse effect on semen quality of SLE patients during spermatogenesis. Minimizing exposure to air pollution should be taken into account, especially for patients with chronic systemic inflammatory diseases living in large cities.

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O ozônio diminui a qualidade do sêmen em pacientes com lúpus eritematoso sistêmico

Palavras-chave:
Lúpus eritematoso sistêmico
Poluição do ar
Qualidade do sêmen
Fertilidade
Ciclofosfamida

RESUMO

Objetivo: Investigar os efeitos deletérios da exposição aos poluentes do ar na Região Metropolitana de São Paulo sobre a qualidade do sêmen de pacientes com lúpus eritematoso sistêmico (LES).

Métodos: Foi feito um estudo longitudinal de painel com medidas repetidas de sete anos no Laboratório de Poluição Atmosférica Experimental e Reumatologia. Foram analisadas duas amostras de sêmen de 28 pacientes com LES pós-púberes. Foram avaliadas as concentrações diárias de exposição aos poluentes do ar PM_{10}, SO_2, NO2, ozônio e CO e variáveis meteorológicas 90 dias antes de cada data de coleta de sêmen com o uso do método de equações de estimativas generalizadas.

Resultados: A ciclofosfamida intravenosa (CICIV) e o ozônio estiveram associados a uma diminuição na qualidade do sêmen dos pacientes com LES. A CICIV esteve associada a um decréscimo de 64,3 milhões de espermatozoides/mL (IC 95% 39,01-89,65; p = 0,0001) e 149,14 milhões de espermatozoides/ejaculado (IC 95% 81,93-216,38; p = 0,017). Em relação ao ozônio, os efeitos adversos mais relevantes foram observados entre os lags (intervalo de tempo) 80 e 88, quando a exposição a uma concentração média de ozônio um intervalo interquartil maior em nove dias móveis levou a um decréscimo de 22,9 milhões de espermatozoides/mL (IC 95% 5,8-40; p = 0,009) e 70,5 milhões de espermatozoides/ejaculado (IC 95% 12,3-128,7; p = 0,016). Uma análise mais aprofundada dos 17 pacientes que nunca usaram CICIV mostrou associação entre a exposição ao ozônio (80-88 dias) e o decréscimo de 30 milhões de espermatozoides/mL (IC 95% 7-53; p = 0,011) e 79 milhões de espermatozoides/ejaculado (IC 95% 2,1-155,9; p = 0,044).

Conclusão: O ozônio e a CICIV tiveram um efeito adverso consistente sobre a qualidade do sêmen de pacientes com LES durante a espermatogênese. Deve-se considerar a minimização da exposição à poluição do ar, especialmente para pacientes com doenças inflamatórias sistêmicas crônicas que vivem nas grandes cidades.

Introduction

Gonad function is severely affected in male SLE patients. Recently, severe sperm abnormalities with testicular atrophy, high follicle-stimulating hormone (FSH) levels and testicular Sertoli cell dysfunction associated with intravenous cyclophosphamide (IVCYC) treatment were reported by our group in systemic lupus erythematosus (SLE).[1–3]

Exposure to air pollutants has also been correlated with male reproductive outcomes, especially sperm quality,[4–9] however this environmental factor was not studied in male SLE population with gonadal function assessment.

In fact, air pollution is composed of a heterogeneous mixture of gases and particles that include ozone (O_3), particulate matter (PM_{10}), nitrates (NO), sulfur dioxide (SO_2), toxic by-product of tobacco smoke and carbon monoxide (CO) and may trigger systemic inflammation and autoimmunity in SLE.[10,11]

Therefore, the objective of this study was to investigate prospectively the correlation of air pollutants exposure concentrations and semen quality in Sao Paulo metropolitan region in SLE patients.

Material and methods

A longitudinal repeated-measures panel study was performed with 35 nonsmokers post-pubertal male SLE patients regularly followed at the Pediatric Rheumatology Unit and the Lupus Clinics of the Rheumatology Division. All patients fulfilled the American College of Rheumatology classification criteria for SLE.[12] None of them had cryptorchidism, hydrocele, hypospadia, testicular infection (e.g., mumps), orchitis, testicular vasculitis, testicular cancer, ureteral impairment and previous history of any scrotal or inguinal surgery (e.g., varicocelectomy, vasectomy and hernia repair). Nine SLE patients were excluded since they did not reside within the metropolitan region of the city of Sao Paulo, presented azoospermia or had only one sample of sperm collected. Therefore, from January 2000 to January 2006, 26 SLE patients resident of Sao Paulo metropolitan region performed a global reproductive health evaluation including two sperm samples of each patient with a median interval of 1 month (range 0.7–8 months).

The Ethics Committee of our University Hospital approved this study and an informed consent was obtained from all participants.