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Male infertility: Decreased levels of selenium, zinc and antioxidants

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ABSTRACT

In this study, we aimed to compare the level of zinc, selenium, glutathione peroxidase activity and antioxidant status in following populations of men: severe inflammation in prostate (>10^6 white blood cells in prostate secretion; $n = 29$), severe leukocytospermia, (>10^6 white blood cells in semen; $n = 31$), mild inflammation, (0.2–1 M white blood cells in semen or prostate secretion; $n = 24$), non-inflammatory oligozoospermia ($n = 32$) and healthy controls ($n = 27$). Male partners of infertile couples had reduced level of antioxidative activity, selenium and zinc in their seminal plasma. Most importantly, reduced selenium levels were evident in all patient groups regardless of inflammation status. Therefore, these patients might gain some benefit from selenium supplementation.

Introduction

Our previous studies have thoroughly characterized the decrease of antioxidant activity in man's organism [1,2] and we identified toxic trace elements associating with oxidative stress [1].

Prostatitis is one of the diseases that may reduce semen quality. In addition to obstructive and immunologic mechanisms, also the prostatitis-associated OxS may cause DNA damage in spermatozoa and affect sperm motility, sperm number, and sperm–oocyte fusion [3–6].

It has been investigated whether antioxidant supplementation influences the pregnancy rates. Six out of ten studies showed that there was a positive effect (reviewed by [7]), as if indicating a marginal to modest positive effect.

Infertility represents an increasing medical problem affecting approximately 15% of couples around the world while its treatment is stressful, invasive, and costly. Male factor accounts for almost 50% cases of infertility. Extensive research in the last decade has led to the identification of oxidative stress (OxS) as a possible cause of male infertility. Oxidative stress is a shift of redox balance towards oxidation. OxS has been shown to affect both standard semen parameters and fertilizing capacity. Elevated levels of reactive oxygen species (ROS) are seen in up to 30–80% of men with male infertility [8].

In the present study, we aimed to reveal the level of antioxidant status in male partners of infertile couples displaying different inflammation patterns in their upper genital tract with or without oligozoospermia.

Materials and methods

Ethics

The study was approved by local ethics review board.

Study group

The study was carried out at the Andrology Centre of Tartu University Hospital from May 2009 to March 2010 and included 143 men (aged 18–53 years) who participated in a prospective study of causes of male infertility.

The study subjects (excl. control group) consulted andrologist due to couple infertility (trying to conceive >1 year) while the female partners had been investigated for causes of infertility at the same time. Invitation to participate in the present study was given first to the subjects with oligozoospermia and second to the men with leukocytospermia in their first semen sample. Majority of these men had inflammation in their upper genital tract, therefore they were grouped according to inflammation in their semen, expressed prostatic secretion (EPS) and/or post-prostate-massage

Abbreviations: GPx, glutathione peroxidase; OxS, oxidative stress; WBC, white blood cells; TAC, total antioxidant capacity; TAA, total antioxidant activity.

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Table 1
Clinical parameters of the study subjects.

	Group I (n = 29) Severe inflammation in semen	Group II (n = 31) Severe inflammation in EPS and/or post-M	Group III (n = 24) Mild inflammation in semen, EPS and/or post-M	Group IV (n = 32) Oligozoospermia without inflammation	Group V (n = 27) Controls	p values
Age (y)	**31** (28–39)	**30** (28–34)	**31.5** (27–34)	**31** (29–35)	**31** (25–33)	NS
Period of abstinence (d)	**3** (3–4)	**3** (3–4)	**3** (3–4)	**4** (3–4)	**4** (3–5)	NS
hsCRP in blood serum (mg/L)	**0.90** (0.47–2.64)	**0.84** (0.39–2.41)	**0.65** (0.43–0.93)[1]	**1.12** (0.50–2.29)[1]	**0.68** (0.34–1.13)	0.045[1]
Total sperm count (M)	**38** (25–85)([1–3]	**21** (9–66)[4,5]	**17** (6–43)[1,6,7]	**6** (2–12)[2,4,6,8]	**385** (269–509)[3,5,7,8]	0.021[1] <0.001[2–8] 0.004[6]
Semen volume (mL)	**4.3** (3.1–5.3)	**4.4** (3.4–5.3)	**4.3** (3.3–4.9)	**4.1** (2.9–5.1)	**4.2** (3.0–5.4)	NS
Motility A + B (%)	**37** (31–47)[1,2]	**34** (23–46)[3,4]	**35** (22–50)[5,6]	**21** (15–40)[1,3,5,7]	**55** (40–57)[2,6,7]	0.020[1] 0.002[2,6] 0.043[3] <0.001[4,7] 0.047[5]
Morphologically normal sperms (%)	**5** (2–9)[1]	**6** (2–8)[2]	**5** (2–9)[3]	**3** (1–6)[4]	**12** (8–18)[1–4]	<0.001[1–4]
WBCs in semen (M/mL)	**2.1** (1.4–2.9)[1–4]	**0.2** (0.1–0.4)[1,5,6]	**0.3** (0.2–0.4)[2,7,8]	**0.0** (0.0–0.1)[3,5,7]	**0.0** (0.0–0.0)[4,6,8]	<0.001[1–8]
IL-6 in semen (pg/mL)	**85** (46–236)([1–4]	**27** (18–51)[1,5,6]	**25** (14–39)[2]	**17** (13–30)[3,5]	**20** (12–28)[4,6]	<0.001[1–4] 0.037[5] 0.031[6]
WBCs in EPS (M/mL)	**1.2** (0.2–2.4)[1–3]	**2.1** (1.3–5.8)[1,4,5]	**0.4** (0.0–0.6)[2,4,6]	**0.0** (0.0–0.1)[3,5,6]	nd	0.030[1] 0.010[2] <0.001[3–5] 0.005[6]
WBCs in post-M by haemocytometer (WBC/mm^3)	**3** (0–100)[1,2]	**25** (0–100)[3,4]	**0** (0–0)[1,3]	**0** (0–0)[2,4]	nd	0.002[1] 0.005[2] <0.001[3] 0.001[4]
IL-6 in EPS (pg/mL)	**109** (63–318)[1,2]	**91** (50–177)[3,4]	**21** (7–67)[1,3]	**33** (25–51)[2,4]	nd	0.010[1,2] 0.007[3] 0.008[4]

All the data are presented as median (quartiles).
NS – not significant; nd – not detected; EPS – expressed prostatic secretion; WBC – white blood cells; post-M – post-massage urine; IL-6 – interleukin-6; hsCRP – highly sensitive C-reactive protein.
The superscript numbers in last columns of rows, if any, designate p-values of a comparison, and two same superscript numbers in two alternate columns of the same row designate the two sets of data that were compared.

urine (post-M) thus forming Groups I–III (Table 1). In all these men NIH IV category prostatitis (asymptomatic inflammatory prostatitis) [9] was diagnosed. Oligozoospermic men without signs of genital inflammation formed separate group (Group IV).

Group I (n = 29) contained men with severe inflammation in their semen (>1 M white blood cells (WBC)/mL) irrespective of inflammatory status of the prostate specific materials. Among them 17, 6 and 6 subjects show severe (>1 M WBC/mL in EPS and/or >10 WBC/mm^3 in post-M), borderline (0.5–1 M WBC/mL in EPS and/or 5–9 WBC/mm^3 in post-M) and missing inflammatory reaction (<0.5 M WBC/mL in EPS and/or <5 WBC/mm^3 in post-M) in prostate specific materials, respectively. In 7 men of this group sperm concentration was <20 M sperm/mL.

Group II (n = 31) contained men with severe inflammation in their EPS (>1 M WBC/mL) and/or post-M (>10 WBC/mm^3). Among them 20 subjects showed additionally borderline (0.2–0.99 M WBC/mL) inflammatory reaction in semen. In 17 men in this group the sperm concentration was <20 M sperm/mL.

Group III (n = 24) contained men with mild inflammation (see also [10]) in their semen (0.2–0.9 M WBC/mL, n = 20) or EPS (0.5–0.9 M WBC/mL, n = 9). No WBCs in post-M were detected in the patients of this group. In 13 men the sperm concentrations was <20 M sperm/mL.

Group IV men (n = 32) had oligozoospermia (sperm concentrations of <20 M sperm/mL) while no inflammation neither in semen, EPS nor post-M.

The control group (Group V, n = 27) was formed of asymptomatic inflammation-free fertile men – partners of pregnant women.

Exclusion criteria for the whole study group were stated according to the suggestions of the NIH workshop on chronic prostatitis in Bethesda, MD, USA, 1995 (NIH/NIDDKD Workshop on Chronic Prostatitis, 1995). None of these men had received anti-microbial therapy within 3 months and anti-inflammatory medications for at least 1 month before evaluations. We excluded all subjects with signs suggestive to urethritis and/or balanoposthitis.

Participation in the study was voluntary. All subjects were at least 18 years old. Informed consent was obtained from all study subjects. The study was approved by the Ethics Review Committee on Human Research of the Tartu University, Estonia.

Specimens

Blood samples were obtained by venipuncture, serum was obtained by centrifugation at 3000 × g by 5 min and analyzed immediately for high-sensitivity C-reactive protein (hsCRP).

Semen and urine samples were collected by patients in a private room near laboratories after they washed their glans penis with soap and water. The first-catch urine was collected into a sterile collection tube. The semen samples were obtained after urinating by masturbation and were ejaculated into a sterile collection tube. After ejaculation, the semen was incubated at 37 °C for 25–45 min for liquefaction.

Four to five days after semen analysis, EPS was obtained by digital massage approximately 5 min after voiding and collected into a sterile polypropylene container. After the digital massage, subjects were told to collect the first 20 mL of urine (post-M).