Aegean Journal of Obstetrics and Gynecology 5/2

Aegean Journal of Obstetrics and Gynecology

Original Article

The effect of an antioxidant agent-multivitamin complex food supplement on spermiogram in infertile men

Pınar Tuğçe Özer [a, †], Nursen Atasoy [b], Adnan Budak [c], Hatice Öntürk Akyüz [d]

[a] Department of Obstetrics and Gynecology, İzmir Kemalpaşa State Hospital, İzmir, Türkiye

[b] Department of Urology, University of Health Sciences, Tepecik Training and Research Hospital, İzmir, Türkiye

[c] Department of Obstetrics and Gynecology, University of Health Sciences, Tepecik Training and Research Hospital, İzmir, Türkiye

[d] Department of Nursing, Faculty of Health Science, Bitlis Eren University, Bitlis, Türkiye

A B S T R A C T

Objective: Oxidative stress (OS) occurs due to overproduction of reactive oxygen radicals (ROS) or weakening of anti-oxidant mechanisms and may harm fertility. Our study aimed to investigate the effects of combined support therapy containing antioxidant agents and vitamin complexes on fertility.

Materials and methods: In this retrospective case-control study, 300 randomly selected infertile men were included. For four months, the effect of daily intake of an antioxidant-multivitamin complex containing astaxhantin (5mg), Coenzyme Q10 (100mg), L-Arginine (250mg), L-Carnitine (250mg), Selenium (100mcg), Zinc (10mg), Folic acid (400mcg), Vitamin E (100mg) and Vitamin C (100mg) on spermiogram parameters was investigated.

Results: In Semen volume (2.21 ml -3.05 ml; p=.004), sperm concentration (9.60 million/ml -14.10 million/ml; p=.000), progressive motility sperm count (16.50% -26.65%; p=.000), sperm vitality rate (48% -68%; p=.001) in patients receiving nutritional support a statistically significant increase was found. In addition, it was determined that the treatment provided a significant decrease (77% - 61%; p=.002) in the number of patients with abnormal morphology (at least 4% of patients who could not achieve normal morphology according to Kruger criteria).

Conclusion: It was determined that antioxidant-multivitamin-containing nutritional supplements containing Astaxhantin, coenzyme Q10, L-arginine, L-carnitine, selenium, zinc, vitamins E and C provided significant improvement on semen volume, sperm morphology, vitality and motility. In this context, we predict that the antioxidant-multivitamin complex can be used as a food supplement for supportive treatment in male infertility.

Keywords: male infertility; astaxhantin; oxidative stress; spermiogram

A R T I C L E I N F O

Doi: 10.46328/aejog.v5i2.137

Article history:

Received: 23 March 2023

Revision received: 18 May 2023

Accepted: 26 June 2023

Introduction

Infertility is defined as the inability to achieve clinical pregnancy success within 12 months despite regular unprotected sexual intercourse, which is seen in 15% of couples [1,2]. Subfertility is defined as difficulty and delay in spontaneous fertilization [3,4]. The most critical parameter that can predict the possibility of unexpected pregnancy is the time that couples spend without using contraception due to their desire for fertility. The chance of pregnancy with regular intercourse in the first six cycles is approximately 80% [4].

The role of the male in fertility depends on the production of functional spermatozoa [1]. Decreased motility (asthenospermia), abnormal morphology (teratozoospermia), reduced number (oligospermia), or absence of sperm in the ejaculate (azoospermia) reduces the chance of pregnancy [5].

The role of oxidative stress (OS) on female and male fertility has gained importance in recent years and has begun to be studied more closely. OS occurs due to overproduction of reactive oxygen radicals (ROS) or the weakening of antioxidant mechanisms [6,7]. A balanced ratio of ROS; is required for spermatogenesis, capacitation, acrosome reaction and attachment of sperm to the zona pellucida [7]. However, the increasing number of ROSs, which are already unstable, can easily interact with lipids, nucleic acids and proteins in the cell structure and cause damage [8]. As a result of detecting DNA damage with advanced technology, the adverse effects of ROS on reproductive cells have begun to be understood [9].

The efficacy of various antioxidant agents, which increase the fertility capacity of infertile women and men, and nutritional supplements containing vitamins and minerals with known antioxidant activity have been demonstrated. In this context, many studies in the literature report the positive effects of Astaxhantin, Coenzyme Q10, Glutathione, L-Arginine, L-Carnitine, Selenium, Zinc, Vitamin E and Vitamin C on fertility. [7,10-13].

Our study aimed to investigate the effects of combined support therapy containing antioxidant agents and vitamin complexes on fertility.

Material and methods

This study was carried out in the Department of Obstetrics and Gynecology, University of Health Sciences, Tepecik Training and Research Hospital, a tertiary center. In this study, spermiogram data of 300 infertile men randomly selected among the patients treated in our infertility clinic between March and June 2022 were used. The retrospective study we conducted has been approved by the ethics committee on January 11, 2023, under research number 810 and decision number 830.

† Corresponding author.
E-mail: pintugbar@gmail.com
Orcid ID: 0000-0002-3571-8894

In the design and implementation of the study, the articles of the Helsinki Convention were adhered to.
Male patients aged 18-55 years, without any systemic disease, and who had not taken any urological medicine or undergone surgery in the last six months were included in the study.
Sperm samples were taken after at least three days of sexual abstinence. Volume, sperm concentration, total sperm count, total motility percentage, progressive motility percentage, morphology and vitality parameters were evaluated according to WHO 2010 criteria [14].
First and foremost, our study focused on examining the impact of a daily intake of an antioxidant-multivitamin complex on spermiogram parameters among our 150 patients. This complex contains astaxhantin (5mg), Coenzyme Q10 (100mg), L-Arginine (250mg), L-Carnitine (250mg), Selenium (100mcg), Zinc (10mg), Folic acid (400mcg), Vitamin E (100mg), and Vitamin C (100mg). Our primary aim was to observe potential improvements in sperm quality over a four-month period. We comparatively analyzed volume, concentration, total motility, progressive motility, abnormal morphology, and vitality parameters in spermiogram tests. These tests were taken from patients at the beginning and again at the end of the 4th month.
On the other hand, 150 patients whose mean age was similar to the study group and who did not want to use nutritional supplements were included in the control group. At the end of the 4th month, the volume, concentration, total motility and progressive motility parameters in the spermiogram tests taken from 300 patients, 150 of whom were from the study group and 150 from the control group, were ranked according to their numerical values. The patients were divided into two groups according to the median value of each parameter. The group of 150 people below the median value was called GROUP I, and the group of 150 people above the median value was called GROUP II. The proportions of patients using antioxidant-multivitamin complex in both groups were calculated and the statistical significance of the distribution was analyzed.

Statistical analysis

Statistical Package for Social Sciences (SPSS) 26.0 software program was used to analyze the data of the patients included in the study. Wilcoxon Signed Ranks Test was applied to examine the effect of the patients on the values before and after the drug. Pearson Chi-Square test was used to examine the relationship between the groups.

Results

In this study, it was determined that using antioxidant agent-multivitamin complex for 4 months significantly improved spermiogram parameters. In Semen volume (2.21 ml -3.05 ml; p=.004), sperm concentration (9.60 million/ml -14.10 million/ml; p=.000), progressive motility sperm count (16.50% -26.65%; p=.000), sperm vitality rate (48% -68%; p=.001) in patients receiving nutritional support a statistically significant increase was found. There was an increase in the total motile sperm count (36.65% -37.50%; p=.006). In addition, it was found that the treatment provided a significant decrease (77% - 61%; p=.002) in the number of patients with abnormal morphology (patients who could not achieve at least 4% normal morphology according to Kruger criteria) (Table 1).
Table 2 compares those who take nutritional supplements and those who do not. Accordingly, a statistically significant association was found between dietary supplement intake and increased sperm volume, concentration, progressive and total motile sperm count. According to this, 65% (n=97; p=.000) of the patients whose sperm volume was above the median value, 70% (n=105; p=.000) of the patients whose sperm concentration was above the median value and respectively 72% (n=108; p= .000) and 80% (n=120; p=.001) of the patients whose total and progressively mobile sperm count was above the median value were found to use antioxidant agent-multivitamin complex (Table 2).

Table 1. Effect of antioxidant agent-multivitamin food complex on spermiogram

Semen analysis	Before Treatment	After Medication	p
Age/year	33		
Volume/ml	2.21	3.05	0,004
Concentration/10^6 ml	9.6	14.1	<0,001
Total Motility/%	36.65	37.5	0,006
Progressive Motility/%	16.5	26.65	<0,001
Abnormal Morphology/%	77	61	0,002
Vitality/%	48	68	0,001

Table 2. Antioxidant agent-multivitamin complex usage rate between groups

Variable	Group I (n=150)	Group II (n=150)	p
Volume (n)	53(35%)	97(65%)	<0,001
Concentration (n)	45(30%)	105(70%)	<0,001
Total Motility (n)	42(28%)	108(72%)	<0,001
Progressive Motility (n)	30(20%)	120(80%)	0,001

Discussion

Although the exact cause of suboptimal semen quality is not clearly understood, environmental factors, mainly caused by oxidative stress, are blamed as well as genetic factors [15]. Studies have reported a negative correlation between the amount of ROS and the proportion of sperm with normal and borderline morphology [16, 18].
Assisted reproductive techniques can overcome infertility due to tubal factors or low sperm count. However, little progress has been made regarding the adverse effects of advancing age on ovarian function [1]. There are theories stating that this change in oocytes occurs secondary to increased oxidative stress and ROS imbalance secondary to abnormal vascularization and decreased perfusion [19]. PCOS, hyperglycemia, obesity, and endometriosis increase ROS in women [6,20].
There are many studies in the literature on the positive effects of antioxidant agents on fertility. Evaluated as a powerful antioxidant, Astaxhantin is a yellow-orange oil-soluble natural carotenoid. In addition to its antioxidant effect, it has attracted wide attention with its anti-inflammatory, anti-apoptotic and immunomodulatory properties. It has been used as a multi-purpose pharmacological agent in various diseases [21]. It has been reported to protect against oxidative stress by supporting the mitochondrial redox system [22]. It has been reported that astaxhantin protects sperm capacitation and has a protective and beneficial effect on sperm quality [23-25]. Studies have reported that astaxhantin supports blastocyst development and protects the oocyte against oxidative stress [26].
Coenzyme Q10, which has an antioxidant effect, improved the number of motile sperm and increased fertilization with

spontaneous and assisted reproductive treatment methods. Similarly, a positive impact on fertility was found in women by increasing serum inhibin B levels and decreasing FSH levels [7,27-29].

Studies on subfertile men have reported improvement in sperm parameters with daily use of arginine, a semi-essential amino acid [7,30,31].

L-carnitine has a strong antioxidant effect as well as an energy support for the cell. It effects on motility by taking part in the transition of transportable fatty acids from the cytosol to the mitochondria. The use of carnitine has been associated with increased sperm motility and decreased ROS levels. It has been reported to have beneficial effects in treating female infertility [7,32-34].

Selenium is an antioxidant trace element that acts on glutathione peroxidase, by using its which Increased sperm motility has been reported [7,35,36].

Zinc is an essential micromineral found in the body, especially in the prostate gland, 2-4 mg. It is involved in repairing DNA damage. It is involved in testicular development and spermiogenesis. Its deficiency causes hypogonadism, testicular-seminiferous tubule atrophy, and retardation in developing secondary sexual character. [7,37,38] Seminal zinc deficiency may be a risk factor for sperm abnormalities and idiopathic male infertility. Infertile men who smoke are at risk for zinc deficiency. Zinc acts as an antioxidant against oxidative stress, which increases in smoking men. Poor nutritional status from zinc is a risk factor for poor sperm quality and idiopathic infertility [39].

Vitamin E and Vitamin C are water-soluble antioxidants. Degeneration of testicular germinal epithelium is detected in vitamin C deficiency. Ascorbic acids increase the effectiveness of gonadotropin treatments. It is recommended to use 90 mg daily. A reduction in sperm DNA damage has been reported with the combined use of vitamins C and E for two months [7,40]. Adequate intake of folic acid, vitamin C, vitamin E and selenium have been reported to have a protective effect on fertility [41].

Improvement in sperm parameters was observed in infertile men with supportive treatment consisting of L-carnitine, coenzyme Q-10, selenium, vitamins C and E, zinc and folic acid; It has been determined that it provides an increase in fertility by strengthening the antioxidative system in infertile women. It also increased the likelihood of spontaneous or ICSI pregnancy [7,42–44].

In modern societies, the age of becoming a parent is increasing daily. Increasing ROS due to factors such as smoking and alcohol use, improper diet rich in fat-obesity, exposure to radiation, exposure to UV rays, chemical agents-pesticides, and plastic waste threatens the human body. The adverse effects of OS on fertility are inevitable [6,8].

Although exposure to risk factors for ROS can be controlled in some cases, it often develops against our will. For this reason, dietary and lifestyle changes, as well as nutritional supplements with antioxidant content, are gaining importance.

In our study, daily astaxhantin (5 mg), coenzyme Q10 (100mg), L-Arginine (250mg), L-Carnitine (250mg), Selenium (100mcg), Zinc (10mg), Folic acid (400mcg), Vitamin E (100mg) and Vitamin C (100mg) antioxidant-multivitamin supplement, we found significant improvement in semen volume, sperm count, progressively motile sperm ratio, morphology and viability parameters at the end of the 4th month in infertile men. In addition, an increase in the number of motile sperm was observed. According to our other data; When compared to the group that did not take nutritional supplements, it was determined that the use of antioxidant-multivitamin complex was accompanied by increased semen volume, sperm concentration, and total and progressively motile sperm count, which was statistically significant. Our results were similar to the relevant literature.

Conclusion

It was determined that antioxidant-multivitamin-containing nutritional supplements containing Astaxhantin, coenzyme Q10, L-arginine, L-carnitine, selenium, zinc, and vitamins E and C provided significant improvement in semen volume, sperm morphology, vitality and motility. In this context, we predict that the antioxidant-multivitamin complex can be used as a food supplement for the supportive treatment of male infertility. Prospective or randomized studies should be done for getting better outcomes in this subject.

Disclosure

Authors have no potential conflicts of interest to disclose.

References

[1] Farquhar CM, Bhattacharya S, Repping S. female subfertility. Nat Rev Dis Primers .2019;(5):7 https://doi.org/10.1038/s41572-018-0058-8

[2] Salas-Huetos A, Bulló M, Salas-Salvadó J. Dietary patterns, foods and nutrients in male fertility parameters and fecundability: a systematic review of observational studies. Hum Reprod Update. 2017;23(4):371-389. doi: 10.1093/humupd/dmx006.

[3] Ahrenfeldt LJ, Möller S, Wensink M, Jensen TK, Christensen K, Lindahl-Jacobsen R. Heritability of subfertility among Danish twins. Fertile Sterile. 2020 Sep;114(3):618-627. doi: 10.1016/j.fertnstert.2020.03.014. Epub 2020 Jul 2. Erratum in: Fertile Sterile. 2021;116(2):608.

[4] Gnoth C, Godehardt E, Frank-Herrmann P, Friol K, Tigges J, Freundl G. Definition and prevalence of subfertility and infertility. Hum Reprod. 2005;20(5):1144-7. doi: 10.1093/humrep/deh870. Epub 2005 Mar 31. https://pubmed.ncbi.nlm.nih.gov/15802321/

[5] Visser L, Repping S. Unraveling the genetics of spermatogenic failure. reproduction. 2010;139(2):303-7. doi: 10.1530/REP-09-0229. Epub 2009 Sep 23.

[6] Lu J, Wang Z, Cao J, Chen Y, Dong Y. A novel and compact review on the role of oxidative stress in female reproduction. Reprod Biol Endocrinol. 2018;16(1):80. doi: 10.1186/s12958-018-0391-5. https://pubmed.ncbi.nlm.nih.gov/30126412/

[7] Çayan S, Özdemir A, Orhan I, Altay B, Kadıoğlu A. The effect of oxidative stress on fertility and the role of anti-oxidant therapy in infertile men. Andrology Bulletin . 2015; 17 (61):118-124.

[8] Büyükuslu N, Yigitbasi T. Reactive oxygen species and oxidative stress in obesity. Clinical and Experimental Health Sciences .2015; 5 (3):197.

[9] The Optimal Evaluation of the Infertile Male: American Urological Society Best Practice Statement. AUA, Education and Research, 2010

[10] Chan AC. Partners in defense, vitamin E and vitamin C. Can J Physiol Pharmacol. 1993;71(9):725-31. doi: 10.1139/y93-109. https://cdnsciencepub.com/doi/10.1139/y93-109?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed

[11] Pierce JD, Cackler AB, Arnett MG. Why should you care about free radicals? RN. 2004;67(1):38-42.

[12] Szczepańska M, Koźlik J, Skrzypczak J, Mikołajczyk M. Oxidative stress may be a piece in the endometriosis puzzle. Fertile Sterile. 2003;79(6):1288-93. doi: 10.1016/s0015-0282(03)00266-8.

[13] Van Langendonckt A, Casanas-Roux F, Donnez J. Oxidative stress and peritoneal endometriosis. Fertile Sterile.

2002;77(5):861-70. doi: 10.1016/s0015-0282(02)02959-x.
[14] Grunewald S, Paasch U. Basic diagnostics in andrology. J Dtsch Dermatol Ges. 2013;11(9):799-814; quiz 815. doi: 10.1111/ddg.12177.
https://onlinelibrary.wiley.com/doi/10.1111/ddg.12177
[15] Jungwirth A, Giwercman A, Tournaye H, Diemer T, Kopa Z, Dohle G, et al. European Association of Urology Working Group on Male Infertility. European Association of Urology guidelines on Male Infertility: the 2012 update. EuroUrol. 2012;62(2):324-32. doi: 10.1016/j.eururo.2012.04.048.
[16] Aziz N, Saleh RA, Sharma RK, Lewis-Jones I, Esfandiari N, Thomas AJ Jr, et al. Novel association between sperm reactive oxygen species production, sperm morphological defects, and the sperm deformity index. Fertile Sterile. 2004;81(2):349-54. doi: 10.1016/j.fertnstert.2003.06.026.
[17] Hammadeh ME, Al Hasani S, Rosenbaum P, Schmidt W, Fischer Hammadeh C. Reactive oxygen species, total antioxidant concentration of seminal plasma and their effect on sperm parameters and outcome of IVF/ICSI patients. Arch Gynecol Obstet. 2008;277(6):515-26. doi: 10.1007/s00404-007-0507-1.
https://link.springer.com/article/10.1007/s00404-007-0507-1
[18] Athayde KS, Cocuzza M, Agarwal A, Krajcir N, Lucon AM, Srougi M, et al. Development of normal reference values for seminal reactive oxygen species and their correlation with leukocytes and semen parameters in a fertile population. J Androl. 2007;28(4):613-20. doi: 10.2164/jandrol.106.001966.
[19] Szafarowska M, Jerzak M. Procesy starzenia sie komórki jajowej a niepłodność [Ovarian aging and infertility]. Ginekol Pol. 2013;84(4):298-304. Polish. doi: 10.17772/gp/1580.
[20] Dubey P, Reddy S, Boyd S, Bracamontes C, Sanchez S, Chattopadhyay M, et al. Effect of Nutritional Supplementation on Oxidative Stress and Hormonal and Lipid Profiles in PCOS-Affected Females. Nutrients. 2021;13(9):2938. doi: 10.3390/nu13092938.
[21] Chang MX, Xiong F. Astaxanthin and its Effects in Inflammatory Responses and Inflammation-Associated Diseases: Recent Advances and Future Directions. molecules 2020;25(22):5342. doi: 10.3390/molecules25225342.
[22] Wolf AM, Asoh S, Hiranuma H, Ohsawa I, Iio K, Satou A, et al. Astaxanthin protects mitochondrial redox state and functional integrity against oxidative stress. J Nutr Biochem. 2010;21(5):381-9. doi: 10.1016/j.jnutbio.2009.01.011.
[23] Andrisani A, Donà G, Tibaldi E, Brunati AM, Sabbadin C, Armanini D, et al. Astaxanthin Improves Human Sperm Capacitation by Inducing Lyn Displacement and Activation. Mar Drugs. 2015;13(9):5533-51. doi: 10.3390/md13095533.
[24] Basioura A, Boscos CM, Parrilla I, Tsousis G, Tsakmakidis IA. Effect of astaxanthin on the quality of boar sperm stored at 17°C, incubated at 37°C or under in vitro conditions. Reprod Domest Anim. 2018;53(2):463-471. doi: 10.1111/rda.13133.
[25] Liu W, Kang XF, Shang XJ. [Astaxanthin in male reproduction: Advances in studies]. Zhonghua Nan KeXue. 2016;22(10):938-943.
[26] Kuroki T, Ikeda S, Okada T, Maoka T, Kitamura A, Sugimoto M, et al. Astaxanthin ameliorates heat stress-induced impairment of blastocyst development in vitro:--astaxanthin colocalization with and action on mitochondria--. J Assist Reprod Genet. 2013;30(5):623-31. doi: 10.1007/s10815-013-9987-z.
[27] Shetty RA, Ikonne US, Forster MJ, Sumien N. Coenzyme Q10 and α-tocopherol reversed age-associated functional impairments in mice. Exp Gerontol. 2014;58:208-18. doi: 10.1016/j.exger.2014.08.007.
[28] Safarinejad MR. Efficacy of coenzyme Q10 on semen parameters, sperm function and reproductive hormones in infertile men. J Urol. 2009;182(1):237-48. doi: 10.1016/j.juro.2009.02.121.
[29] Ben-Meir A, Kim K, McQuaid R, Esfandiari N, Bentov Y, Casper RF, et al. Co-Enzyme Q10 Supplementation Rescues Cumulus Cells Dysfunction in a Maternal Aging Model. Antioxidants (Basel). 2019;8(3):58. doi: 10.3390/antiox8030058.
[30] Özer Kaya Ş, Gür S, Kaya E. Effect of l-arginine addition on long-term storability of ram semen. andrology 2017. doi: 10.1111/and.12945. Epub ahead of print.
[31] Appleton J. Arginine: Clinical potential of a semi-essential amino acid. Alter Med Rev. 2002;7(6):512–22
[32] Balercia G, Regoli F, Armeni T, Koverech A, Mantero F, Boscaro M. Placebo-controlled double-blind randomized trial on the use of L-carnitine , L-acetylcarnitine, or combined L-Carnitine and L-acetylcarnitine in men with idiopathic asthenozoospermia. Fertile Sterile. 2005;84:662–71
[33] Lenzi A, Lombardo F, Sgro P, Caponecchia L, Dondero F, Gandini L. Use of carnitine therapy in selected cases of male factor infertility: a doubleblind crossover trial. Fertile Sterile. 2003;79(2):292–300.
[34] Agarwal A, Sengupta P, Durairajanayagam D. Role of L-carnitine in female infertility. Reprod Biol Endocrinol. 2018;16(1):5. doi: 10.1186/s12958-018-0323-4.
[35] Mojadadi A, Au A, Salah W, Witting P, Ahmad G. Role for Selenium in Metabolic Homeostasis and Human Reproduction. Nutrients. 2021;13(9):3256. doi: 10.3390/nu13093256.
[36] Scott R, MacPherson A, Yates RW, Hussain B, Dixon J. The effect of oral selenium supplementation on human sperm motility. BrJUrol. 1998l;82(1):76-80. doi: 10.1046/j.1464-410x.1998.00683.x.
[37] Colagar AH, Marzony ET, Chaichi MJ. Zinc levels in seminal plasma are associated with sperm quality in fertile and infertile men. Nutr Res. 2009;29(2):82-8. doi: 10.1016/j.nutres.2008.11.007.
[38] Omu AE, Al-Azemi MK, Kehinde EO, Anim JT, Oriowo MA, Mathew TC. Indications of the mechanisms involved in improved sperm parameters by zinc therapy. Med Prince Pract. 2008;17(2):108-16. doi: 10.1159/000112963.
[39] https://www.eu-openscience.europeanurology.com/article/S1569-9056(09)74942-5/pdf
[40] Wayner DD, Burton GW, Ingold KU. The antioxidant efficiency of vitamin C is concentration-dependent. Biochim Biophys Acta. 1986;884(1):119–2
[41] González-Rodríguez LG, López-Sobaler AM, Perea Sánchez JM, Ortega RM. Nutrición y fertilidad [Nutrition and fertility]. Nutr Hosp. 2018;35(6):7-10. spanish doi: 10.20960/nh.2279.
[42] Agarwal A, Durairajanayagam D, du Plessis SS. Utility of antioxidants during assisted reproductive techniques: an evidence based review. Reprod Biol Endocrinol. 2014;12:112. doi: 10.1186/1477-7827-12-112.
[43] Pierce JD, Cackler AB, Arnett MG: Why should you care about free radicals? RN 2004, 67:38-42.
[44] Van Langendonckt A, Casanas-Roux F, Donnez J: Oxidative stress and peritoneal endometriosis. Fertil Sterile 2002, 77:861-870