Role of antioxidant therapy and cessation of smoking in treatment of infertile men.

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الخلاصة

الهدف من الدراسة : لتقييم دور علاج مضادات الأكسدة وتوقف التدخين في مرضى عقم الرجال.

المرضى وطرق إجراء الدراسة : أجريت الدراسة في شهر شباط 2012 إلى شهرايلول2013 . العدد الكلي للمرضى كان 152 مريض ، 35 مريض كانوا مصابين بعقم ثانوي، مدى مدة الزواج كان 1-8 سنوات، وكان مدى التدخين من 15-40 سيجارة في اليوم وعلى فترة من 2-15 سنة، وشملت الدراسة أنواع متعددة من العقم (قلة العدد،ضعف الحيامن،تشوه الحيامن،أو جميعهم). أما متلازمة فقد النطاف الكلي فكان مستبعد عن الدراسة. 90 مريض عولج بالمضادات بدون التوقف من التدخين(رفض ذاتي)، و 62 مريض عولج بالمضادات مع توقف التدخين. كل المرضى اجري لهم تحاليل الهورمونات في الدم.

النتائج : 27 مريض مصاب بضعف النطف أوقفوا التدخين ، وكان متوسط القدرة على الحركة 16,4 بالمئة وبعد العلاج أصبح 30,1 بالمئة ، 53 مريض مصاب بضعف النطف من الذين لم يوقفوا التدخين ، كان متوسط القدرة على الحركة 15,3 بالمئة وبعد العلاج أصبح 31بالمئة . 23 مصاب بقلة عدد النطف أوقفوا التدخين كان متوسط العدد بالمليون 6,3 وبعد العلاج أصبح 15,2. 33 مريض مصابين بقلة عدد النطف لم يوقفوا التدخين كان متوسط العدد بالمليون 6,4 وبعد العلاج أصبح 9,2. أما بالنسبة لمرضى الحيامن المشوهة فكان 5 منهم قد أوقفوا التدخين وكان متوسط نسبة الشكل غير المشوه 1,8 بالمئة وبعد العلاج أصبح 12,4 بالمئة و 11 مريض مصابين بتشوهات الحيامن ممن لم يوقفوا التدخين كان نسبة النطف غير المشوهة 1,7 بالمئة وبعد العلاج أصبح 5,6 بالمئة.

الاستنتاج : استخدام مضادات الأكسدة والتوقف عن التدخين في مرضى العقم ممن اجري لهم هورمونات الجنس وكانت طبيعية يعطي نتائج جيدة بالنسبة لعدد النطف وقدرتها على الحركة.

Abstract

Aim: To assess role of antioxidant therapy and cessation of smoking in infertile men .

Patients and Methods: This study was conducted at infertility unit at Al- Diwaniya gynecological hospital and private clinic from February 2012 to November 2013. Total number of patients was taken in study were 152. Thirty-five patients were secondarily infertile while 117 patients were primarily infertile. Range of duration of marriage was 1-8

years. Each man smoked from 15-40 cigarette per day for 2-15 years. The study was include patients presented with various seminal fluid analytic pictures (oligospermia, teratospermia, asthenospermia, OAT syndrome). Ninety patients were treated by antioxidants without cessation of smoking and 62 patients were treated by antioxidants with cessation of smoking.

Results: Regarding 27 asthenospermic ceased smoking patients (mean motility percentage before treatment is 16.4 and mean motility percentage after treatment is 30.1), 53 asthenospermic non ceased smoking patients (mean motility percentage before treatment is 15.3 and mean motility percentage after treatment is 31), 23 oligospermic ceased smoking patients (mean count per million before treatment is 6.3 and mean count per million after treatment is 15.2), 33 oligospermic non ceased smoking patients (mean count per million is 6.4 and mean count per million after treatment is 9.2). regarding 5 teretospermic ceased smoking patients (mean percentage of abnormal morphology before treatment is 1.8 and mean percentage of abnormal morphology after treatment is 12.4) and 11 teretospermic non ceased smoking patients(mean percentage of abnormal morphology before treatment is 1.7 and mean percentage of abnormal morphology after treatment is 5.6).

Conclusion: use of antioxidant and cessation of smoking in selected patients (normal serum hormones) gives good improvement regarding motility and count of sperms

Introduction

Infertility is inability of a couple to achieve conception or bring a pregnancy to term after one year or more of regular, unprotected sexual intercourse according to world health organization definition [(1)].

It affected at least one in six couples [(2)]. In about 50% of cases, male factors play a role in couples infertility [(3,4)].

The etiology of abnormal semen quality is poorly understood, and many physiological, anatomical, environmental, and genetic factors have been implicated [(5- 8)].

The oxidative stress is mechanism resulted from these factors which is induced by reactive oxygen species(ROS) or free radicals, excessive ROS (superoxide anion, hydrogen peroxide, hydroxyl radical) can damage sperm by modifying cell functions or endanger cell survival or both [(9)].

ROS are products of normal cellular metabolism. During the enzymatic reduction of O_2 to produce energy, free radicals form as a byproduct [(10)].

The unique cellular structure of spermatozoa renders them particularly sensitive to oxidative stress in that the sperm cells lack significant cytoplasm and therefore contain only minimal amounts of ROS scavenging enzymatic substances(catalase, superoxide dismutase(SOD), and glutathione peroxidase).

Sources of ROS :

1-leukospermia as a result of infection/ inflammation [(11-19)].

2-exposure to industrial compounds(phthalate in plastic material used in food packaging), pesticides(contains lindane) [(20,21)].

3-cigarrete smoking [(22-26)].

4-alcohol intake [(22-26)].

5-high body temperature like fever [(27)] or wearing tight fitting underwear[(28)].

Exposure to cigarette smoke generate high levels of ROS, directly increasing both seminal leukocyte concentration and seminal ROS generation [(22,26)].

Effects of smoking on testicular function: decreasing Semen quality and sperm fertilizing capacity and decreasing seminal levels of antioxidant enzymes [(29)].

In addition to that the smoking increase production of norepinephrine which increases the conversion of testosterone to

estrogen causing decreased testosterone levels [30].

Nicotine-induced suppression of hypothalamic-pituitary-testicular axis that is one of the causes of smoking-induced adverse effects on male infertility through suppression of LH secretion [31].

Antioxidants maintains a steady state of ROS in the seminal plasma(act as free radical scavengers). In addition, semen contain a variety of non-enzymatic antioxidant molecules such as vitamin C, vitamin E, glutathione, selenium, and carnitine [32].These antioxidants compensate for the loss of sperm cytoplasmic enzymes as the cytoplasm is extruded during spermiogenesis, which in turn, diminishes endogenous repair mechanism and enzymatic defenses [33].

Patients and Methods

This prospective clinical trial was conducted at infertility unit at Al- Diwaniya gynecological hospital and private clinic from February 2012 to November 2013.

One hundred fifty two was the total number included in the study. Thirty-five patients were secondarily infertile while 117 patients were primarily infertile. Range of duration of infertility was 1-8 years. Each man smoked from 15-40 cigarette per day for 2-15 years.

The study was include patients presented with various seminal fluid analytic pictures (oligospermia, teratospermia, asthenospermia, OAT syndrome). Azoospermia, varicocele and pyospermia were excluded from the study.

infertility duration / year	**1-8**
Number of cigarettes / day	**15-40**
Duration of smoking / year	**2-15**
Number of primary infertile men	**117**
Number of secondary infertile men	**35**

Table 1 : summarize the above data.

All their wives were consult their gynecologists.

Ninety patients were treated by antioxidants(mixture of zinc, selenium, L-Carnitine, L-arginine and Vitamin E) without cessation of smoking and 62 patients were treated by antioxidants with cessation of smoking.

Semen samples were collected by usual way (masterbation)and analyzed under microscopy. Serum Pituitary- Testicular hormones : LH, FSH, Testosterone were measured.

Results

The table below reveals results of the study after prescribing antioxidant treatment with and without cessation of smoking. regarding 27 asthenospermic ceased smoking patients (mean motility percentage[grade A] before treatment is 16.4 and mean motility percentage[grade A] after treatment is 36.1), 53 asthenospermic non ceased smoking patients(mean motility percentage[grade A] before treatment is 15.3 and mean motility percentage [grade A] after treatment is 31), 23 oligospermic ceased smoking patients(mean count per million before treatment is 6.3 and mean count per million after treatment is 15.2), 33 oligospermic non ceased smoking patients (mean count per million is 6.4 and mean count per million after treatment is 9.2). regarding 5 teretospermic ceased smoking patients (mean percentage of normal morphology before treatment is 1.8 and mean percentage of normal morphology after treatment is 12.4)and 11 teretospermic non ceased smoking patients(mean percentage of normal morphology before

treatment is 1.7 and mean percentage of normal morphology after treatment is 5.6).

	Mean	N	Std. Deviatio	P value
Asthenopretreatment cease	16.4074	27	9.26224	<0.001
asthenoposttreatment cease	36.1852	27	11.61245	
asthenopretreatment n ceased	15.3396	53	10.17906	<0.001
asthenopostnonceased	31.0943	53	11.82121	
oligopreceased	6.3348	23	3.57995	<0.001
oligopostceased	15.2609	23	7.57704	
oligoprenonceased	6.4576	33	4.04529	0.001
oligopostnonceased	9.2636	33	5.07068	
nonteratopreceased	1.8000	5	.83666	0.030
nonteratopostceased	12.4000	5	6.58027	
nonteratoprenonceased	1.7273	11	.78625	0.076
nonteratopostnonceased	5.6364	11	6.56160	

Table 2: results after treatment by antioxidant with or without cessation of smoking.

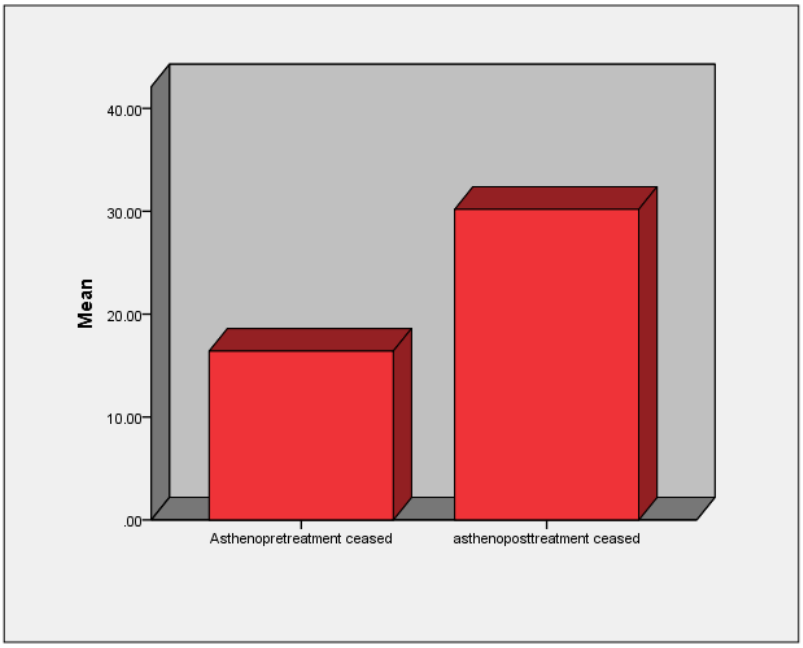

Figure1: improvement of motility(grade A) in patients stop smoking

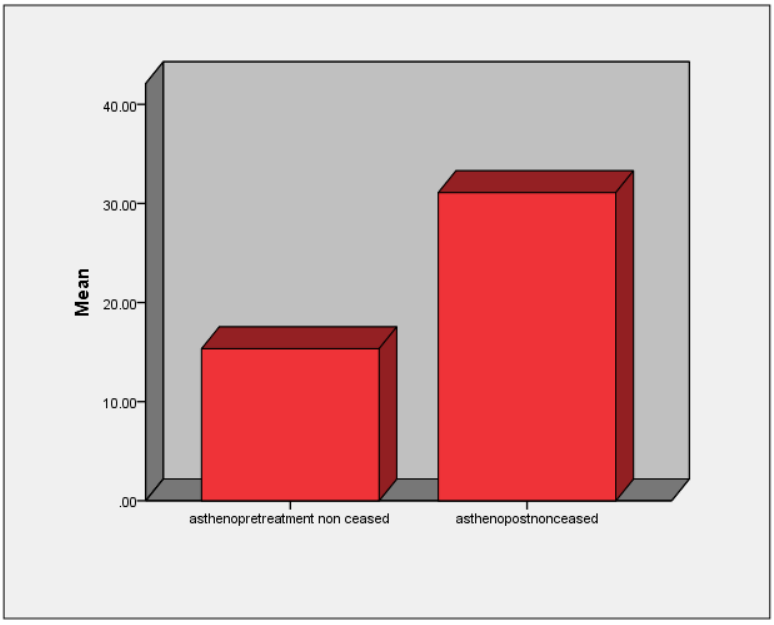

Figure2: improvement of motility(grade A) in patients not stop smoking

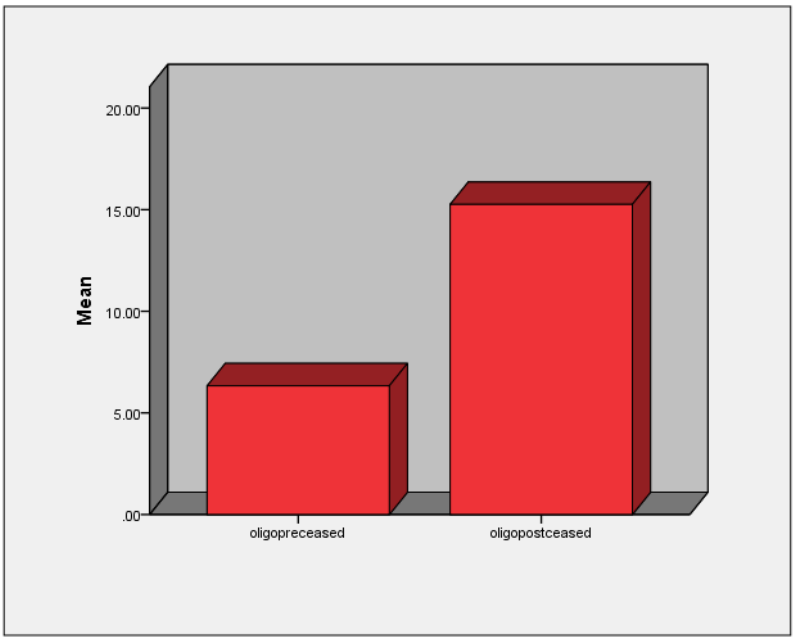

Figure3: improvement of sperm count in patients stop smoking

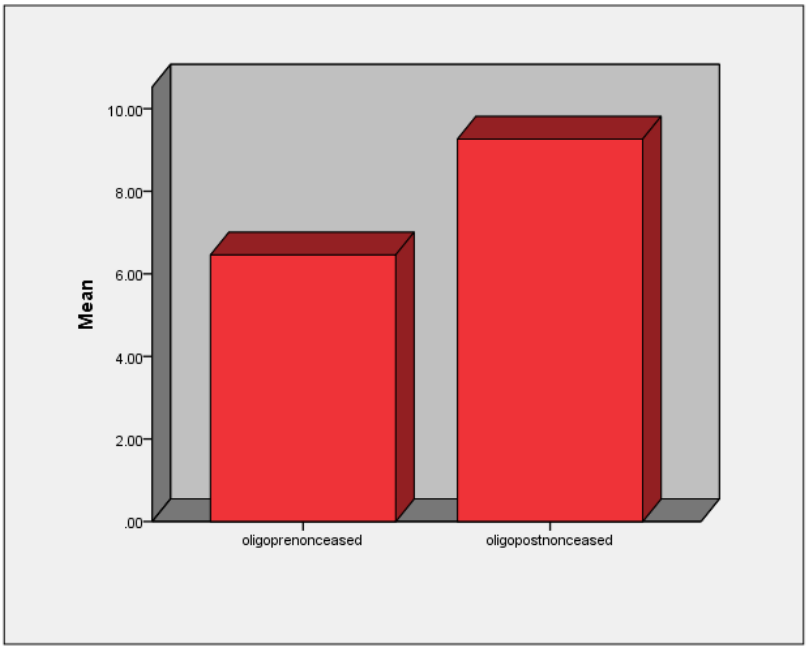

Figure4: improvement of sperm count in patients not stop smoking

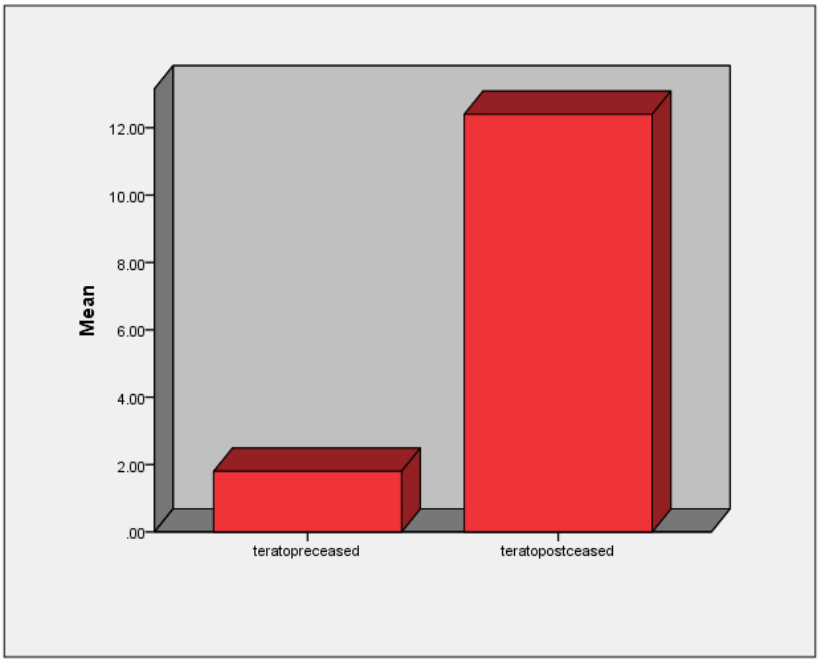

Figure5: improvement of sperm morphology in patients stop smoking

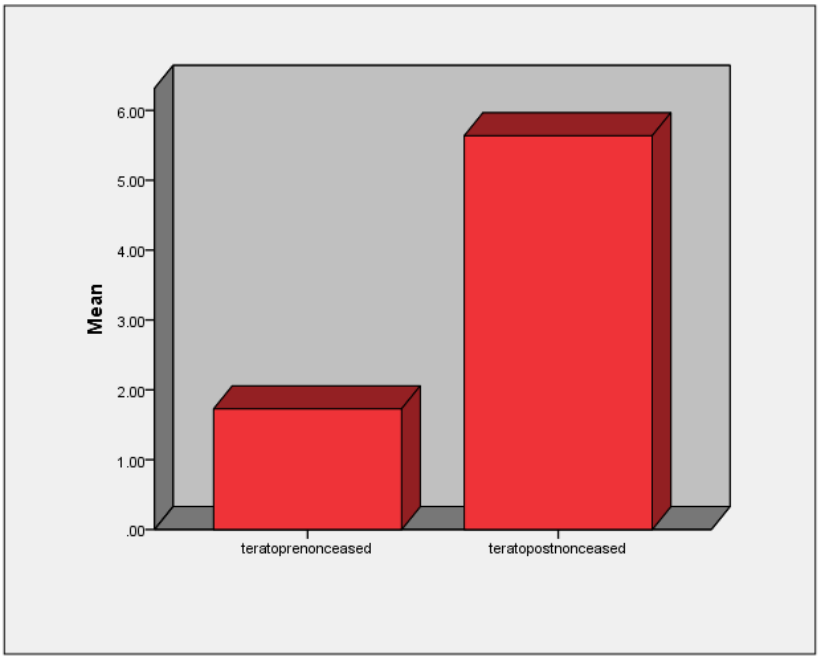

Figure6: improvement of sperm morphology in patient not stop smokin

Discussion

As we know, infertility is inability to get pregnancy after one year or more of regular sexual intercourse without contraceptive procedures and this is may be due to a lot of reasons (genetic , environmental , physiological causes) or may be idiopathic [34-37].

From the environmental factors is oxidative stress and smoking as they mentioned in many studies like (Agarwal et al , Saleh et al, Chen H et al) [23, 38,39].

Oxidative stress is due to increased level of reactive oxygen species or antioxidant disability within semen [40].

Sperms are susceptible to oxidative stress for 2 reasons, firstly high polyunsaturated fatty acids and secondly deficiency of intracellular antioxidant enzymatic protection , and this is lead to DNA damage.

Normally epididymis contain enzymatic and non-enzymatic antioxidants protect sperms, enzymatic like dismutase, catalase, non-enzymatic like vitamin C , E , and many.

A lot of studies have carried out to establish beneficial effects of antioxidant in improving sperm quality and quantity.

From these studies: Fraga et al were used Vitamin C, Kodama et al were used Glutathione, Keskes-Amma et al were used Selenium, Costa et al were used L-carnitine, Kynaston et al were used Zinc, Giovenco et al were used Vitamin E .

Semen of smoker patient contain high proportion of malformed sperm [41-43].

By-product of nicotine present in the semen of smokers have been found to reduce motility of sperm and their fertilization capacity [43].

In our study, we found that abnormal sperm count and motility in infertile smoker whether ceased or not were improved after treatment with antioxidant and this is due to the opposite effect on oxidative stress on sperm count and motility where p value is significant in asthenospermic and oligospermic patients after treatment especially more in patients where ceased smoking.

Most of urologists think that presence of reactive oxygen species is existing normally in every man but because of imbalance between them and scavengers , the reactive oxygen species will offend and cause jeopardy to sperms [38,44].

In our study, were we use antioxidants inform of Vitamin E (α-tocopherol), Vitamin C, selenium , L-carnitine , to every patient and as we know effects of these antioxidants (suppress lipid peroxidation in testicular mitochondria and reverse the harmful effect of oxidative stress and then maintain spermatogenesis and maturation of the sperms.

In our study, were we instruct all patients to cease smoking but from 152 patients only 55 patients cease and those were got better improvement due to dangerous effect of smoking because smoking increase oxidative stress and cause more lipid peroxidation and inhibition of DNA synthesis (34,39,45-47).

In teratospermic patients , were we found that p value is insignificant and this may be due to little number of patients and this lead to more standard errors.

We recommend from our study : to use of antioxidant and cessation of smoking in selected patients (normal serum hormones) may get good improvement regarding motility and count of sperms and also recommend selection of large number of teratospermic patients to get better results in future studies.

Conclusion

use of antioxidant and cessation of smoking in selected patients (normal serum hormones) gives good improvement regarding motility and count of sperms

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