



The Therapeutic Effects of a Medicinal Plant Mixture in Capsule Form on Catalase Levels in the Semen of Men with Oligospermia

Hasti Alizadeh¹, Arash Khaki¹, Laya Farzadi^{1*}, Mohammad Nourri², Yadoulah Ahmadi-Asrbadr³, Giti Seyed-Ghiasi¹, Vahideh Shahnazi¹

Abstract

Objective: In the present study, the therapeutic effects of mixed herbs (onion, ginger, basil, cinnamon, orange peel, yellow and red watermelon seeds, and carrot seed) on catalase levels in the semen of men with oligospermia were evaluated. About 50% of recognized infertility factors are male-related factors, and are mainly the result of oligospermia, astenospermia, and teratozoospermia.

Materials and Methods: The study participants included 40 males with oligospermia and infertility. The studied medicine were 700 mg capsules containing onion, ginger, basil, cinnamon, orange peel, yellow and red watermelon seeds, and carrot seed (100 mg of each). Catalase activity was measured by Aebi method.

Results: A significant increase was observed in catalase level in semen as a result of using the medicinal plant mixture ($P < 0.001$).

Conclusion: Free radicals play an important role in male infertility. Antioxidants can prevent the damaging effects they have on sperm. Oxidative stress reduction can increase the chances of natural fertility or assisted reproductive technology (ART). Medicinal plants have low costs, complications, and easy availability, and cause an increase in semen plasma antioxidants and subsequent improvement in semen parameters. Thus, they can be the source of new hopes for the treatment of infertility.

Keywords: Antioxidants, Infertility, Oligospermia, Oxidative Stress

Introduction

One of the main issues in medicine is infertility. The cause of infertility in 40% of infertile couples is considered to be male infertility. Since sperm production disorders are the leading cause of male infertility, correcting these disorders to make fertility possible for many couples is of great importance (1,2). Oxidative damage caused by free radicals is a major cause of idiopathic oligospermia and even has adverse effects on sperm structure and produces sperm abnormalities (3-5). There are

two antioxidant systems in the human body (antioxidant defense system), containing proteins such as albumin and ceruloplasmin which bind to metal ions and prevent the formation of active species, and thus, prevent a chain reaction of reactive oxygen species (ROS). While scanning the system, antioxidants like vitamin E, vitamin C, glutathione peroxidase, eliminate produced ROS in order to inhibit plasma membrane lipid peroxidation (6). Assisted reproductive technology (ART), such as intracytoplasmic sperm injection

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¹ Women's Reproductive Health Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

² Women's Reproductive Health Research Center AND Department of Biochemistry, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

³ Department of Urology, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

*Corresponding Author: Laya Farzadi, Women's Reproductive Health Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

Tel: +98 9141153712, Email: farzadl_29@yahoo.com

(ICSI), zygote intrafallopian transfer (ZIFT), and in vitro fertilisation (IVF), can lead to fertilization of the egg and sperm and have solved many infertility problems. Nevertheless, these treatment methods are extremely costly procedures. Low-cost medical treatments are also available for a wide range of couples. Much attention has been paid to the bioactivity of plant extracts because they are derived from natural resources and are compatible with the vital systems. Medicinal plants have a positive impact on the increasing of fertility and to resolving of issues such as hormonal imbalances, oligospermia, sperm motility, prostatitis, and varicocele, and thus, have long been studied. Previous studies conducted on laboratory animals have proven the beneficial properties of onion (7), ginger (8), basil (9), cinnamon, orange peel (10), yellow and red watermelon seeds, and carrot seed (11) as rich sources of vitamins, flavonoids, and minerals. Based on the results of these studies, each of these plants has dramatic effects on infertility factors. Orange peel extract can improve sperm motility and cinnamon affects testosterone levels more than others. On the other hand, red watermelon seed extract and orange peel extract further reduce the amount of malondialdehyde (MDA) and increase the amount of superoxide dismutase (SOD). Based on previous studies, yellow watermelon seeds have a greater effect on SOD and cause an increase in its amount. Therefore, these herbs have a more significant effect on oligospermia in comparison to other infertility factors. The complex combinations of these extracts can have different effects and often show significantly greater effects than each compound of the plants. Therefore, the aim of this study was to investigate the effect of mixed herbs on the improvement of the standards of abnormal sperm and male infertility. In case of positive results, this herbal mixture can be beneficial and may be used before ART as a booster containing natural antioxidants to increase the fertility of sperm.

Materials and Methods

The study participants consisted of 40 males with infertility and oligospermia. They were enrolled in the study after obtaining informed consents from each one and in the absence of any specific drug used during the past 6 months. First, the initial semen samples, after a minimum of 2 and a maximum of 7 days of abstinence from sexual contact, were obtained to assess the baseline levels of semen catalase. Then, they received medication for 6 months. The studied medicine were 700 mg capsules containing onions, ginger, basil, cinnamon, orange peel, superoxide dismutase, yellow and red watermelon seeds, and carrot seeds. An equal amount of each element (100 mg) was used in the capsules. The patients used one capsule daily. The antioxidant that was studied was catalase.

Catalase activity was estimated using the Aebi

method (12). Catalase can degrade hydrogen peroxide, which can be measured directly through the decrease in the absorbance at 240 nm. Hydrogen peroxide was diluted with phosphate buffer at pH: 7.0 and its initial absorption was adjusted between 0.5-0.6 absorbance units in 240 nm. The decrease in absorbance was measured. A unite of catalase activity was defined as the amount of catalase adsorbed within 30 seconds at 25 °C. Catalase activity was then calculated by the change in absorbance and expressed as u/ml (12).

Results

This was a clinical trial on 40 male participants with infertility and oligospermia.

Participant's characteristics

The mean age of the participants was 34.1 ± 9.16 years. The youngest was 21 years old and the oldest was 80 years old. The mean of the infertility years of the patients was 3 years; maximum 13 years and minimum 1 year. Due to the abnormal distribution, the mean and standard deviation were not reported (Table 1).

Table 1. Demographic characteristics of the participants

Variable	Mean \pm SD
Age (year)	34.1 ± 9.16
Occupation	
Self-employed	17.0 ± 42.5
Worker	10.0 ± 25.0
Driver	6.0 ± 15.0
Employed	3.0 ± 7.5
Farmer	1.0 ± 2.5
Retired	1.0 ± 2.5
Chef	1.0 ± 2.5
Data not available	1.0 ± 2.5
Smoking	
Yes	5.0 ± 12.5
No	35.0 ± 87.5
Alcohol	
Yes	0 ± 0
No	40.0 ± 100
Drugs	
Yes	0 ± 0
No	40.0 ± 100
Side effects	
Diarrhea	2.0 ± 5.0
Tenesmus	2.0 ± 5.0
Nausea	1.0 ± 2.5
Gastrointestinal bleeding	1.0 ± 2.5

Determining the changes in semen catalase

Using the Kolmogorov-Smirnov test and descriptive evidence, the normality of data related to the semen catalase variable was evaluated; it followed a normal distribution. Paired t-test analysis was performed, and P values of less than 0.05 were considered significant. Semen catalase changes as a result of medication use were significant ($P < 0.001$) (Table 2).

Table 2. The relationship between using the medicinal plant combination (onions, ginger, basil, cinnamon, orange peel, yellow and red watermelon seeds, and carrot seeds) and semen catalase

Variable	Before (Mean ± SD)	After (Mean ± SD)	MD (CI 95%)	P
Semen catalase	14.10 ± 0.418	15.97 ± 1.070	-1.87 (-2.18 to -1.56)	< 0.001

MD: Mean difference; CI: Confidence interval; P < 0.05 is significant; P value based on paired t-test

Discussion

There is growing evidence about spermatozoa damage caused by oxygen free radicals (ROS) (13). Oxidative stress has a basic role in male infertility and poor sperm quality and performance. The overall level of antioxidants and vitamin E concentrations in plasma of infertile men, compared to fertile men, were clearly lower. There was a direct relationship between catalase activity and superoxide dismutase in seminal plasma of malondialdehyde (MDA) spermatozoa levels in men with normospermia. Furthermore, there was a direct connection between overall catalase activities and overall MDA level in seminal plasma (14).

The purpose of this study was to investigate the relationship between nutritional supplements rich in antioxidants and antioxidant levels in semen. In the present study, a strong relationship was observed between diet rich in antioxidants and improved plasma antioxidant parameters of semen. Nevertheless, further studies are necessary in this regard. Infertile men with or without varicocele have higher seminal plasma MDA levels and lower levels of antioxidants compared with fertile men with or without varicocele. Increased oxidative stress has a direct correlation with reduced semen parameters (15). In recent years, the widespread use of herbal medicines has encouraged scientists to improve health through their use (16).

Previous studies on ginger showed that it reduced blood sugar levels and MDA, and increased the weight of reproductive organs and testosterone levels. It also increased sperm quality and motility, and superoxide dismutase, catalase, and glutathione peroxidase levels (17). In this study, the medicinal plant mixture that included ginger also significantly increased catalase. Superoxide dismutase is an important compound of the antioxidant defense system and plays an important role in spermatozoa protection against oxidative damage (18). Previous studies have shown the important role of onion (*Allium cepa*) in reducing oxidative stress and inhibiting apoptosis in cardiovascular system and reproductive system protection (19). The present study results were in agreement with this finding. In this study, the medicinal plant mixture, which also included onions, significantly improved the level of catalase in semen.

In a study conducted by Alpsoy et al., treatment with basil (*Ocimum basilicum*), resulted in histological changes and immunohistochemical enhancement, which was created due to the effect of cadmium heavy metal resulting in testicular toxicity (19). This effect was the result of the antioxidant effect of the plant (20). In this study, the consumption of the combination of medicinal plants, which also contained basil, also resulted in an increase in catalase levels.

In a study conducted by Aleissa in Saudi Arabia, ginger illustrated antioxidant and androgenic activity, and also had positive effects on spermatogenesis and improvement of sperm parameters and reproductive behavior in rats (17). In a study conducted in 2012 by Al-Kadir Mares and Najam at the University of Tikrit, Iraq, a significant increase was observed in sperm count in infertile men after treatment with ginger (P < 0.01) (21). Another study was conducted by Hafez in Greece on the effect of a ginger and cinnamon combination on infertile diabetic rats. They showed that this combination increased the weight of testicles and seminal vesicles, improved the quality and quantity of semen, decreased glucose levels, and increased insulin levels. It also improved the degenerative lesions in the testis of diabetic rats. In the study by Hafez, it was suggested that ginger or cinnamon extracts can increase fertility in diabetic rats (22).

In a study by Abo-Ghanema et al., the treatment of infertile rats with a ginger and L-carnitine mixture showed more desirable results in terms of sperm parameters (including count, motility, and viability), semen antioxidant enzymes, and testosterone levels, in comparison to treatment with either of these two alone (23). The present study also illustrated a statistically significant increase in semen catalase levels as a result of the treatment with a combination of antioxidant supplements. This was in agreement with the findings of the abovementioned studies.

Conclusion

Free radicals play an important role in male infertility and antioxidants can prevent their harmful effects on the sperm. Each antioxidant improves at least one of the semen parameters. However, they had the greatest impact on sperm motility. The optimal doses of most antioxidants have not been determined. Oxidative stress reduction can increase the possibility of a natural fertility or ART.

Today, medicinal plants have a special place in the treatment of infertility. They are cost-effective, have very few side effects, and are accessible. They improve semen parameters, increase semen plasma antioxidant level, and prevent oxidative damage to spermatozoa caused by inevitable contact with free radicals of the body and the environment of the present industrialized life. It can also be the cause of new hope in the treatment and prevention of infertility, and reduce the costs associated with their treatment.

Ethical issues

We have no ethical issues to declare.

Conflict of interests

We declare that we have no conflict of interests.

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References

1. Wright C, Milne S, Leeson H. Sperm DNA damage caused by oxidative stress: modifiable clinical, lifestyle and nutritional factors in male infertility. *Reprod Biomed Online* 2014; 28: 684-703.
2. Rowe PJ, Comhaire FH. WHO Manual for the Standardized Investigation, Diagnosis and Management of the Infertile Male. Cambridge, UK: Cambridge University Press; 2000.
3. Benitez A, Perez DJ. Effect of streptozotocin-diabetes and insulin treatment on regulation of Leydig cell function in the rat. *Horm Metab Res* 1985; 17: 5-7.
4. Chandel A, Dhindsa S, Topiwala S, Chaudhuri A, Dandona P. Testosterone concentration in young patients with diabetes. *Diabetes Care* 2008; 31: 2013-7.
5. Coskun O, Kanter M, Korkmaz A, Oter S. Quercetin, a flavonoid antioxidant, prevents and protects streptozotocin-induced oxidative stress and beta-cell damage in rat pancreas. *Pharmacol Res* 2005; 51: 117-23.
6. Agarwal A, Prabakaran SA, Said TM. Prevention of oxidative stress injury to sperm. *J Androl* 2005; 26: 654-60.
7. Khaki A, Fathiazad F, Nouri M, Khaki AA, Khamenehi HJ, Hamadeh M. Evaluation of androgenic activity of allium cepa on spermatogenesis in the rat. *Folia Morphol (Warsz)* 2009; 68: 45-51.
8. Khaki A, Fathiazad F, Nouri M, Khaki AA, Ozanci CC, Ghafari-Novin M, et al. The effects of Ginger on spermatogenesis and sperm parameters of rat. *Iranian Journal of Reproductive Medicine* 2009; 7: 7-12.
9. Khaki A, Fathi Azad F, Nouri M, Khaki AA. Effects of basil, *Ocimum basilicum* on spermatogenesis in rats. *J Med Plants Res* 2011; 5: 4601-4.
10. Kanaze FI, Termentzi A, Gabrieli C, Niopas I, Georgarakis M, Kokkalou E. The phytochemical analysis and antioxidant activity assessment of orange peel (*Citrus sinensis*) cultivated in Greece-Crete indicates a new commercial source of hesperidin. *Biomed Chromatogr* 2009; 23: 239-49.
11. Alasalvar C, Grigor JM, Zhang D, Quantick PC, Shahidi F. Comparison of volatiles, phenolics, sugars, antioxidant vitamins, and sensory quality of different colored carrot varieties. *J Agric Food Chem* 2001; 49: 1410-6.
12. Aebi H. Catalase in vitro. *Methods Enzymol* 1984; 105: 121-6.
13. Khosrowbeygi A, Zarghami N. Levels of oxidative stress biomarkers in seminal plasma and their relationship with seminal parameters. *BMC Clin Pathol* 2007; 7: 6.
14. Tavilani H, Goodarzi MT, Vaisi-raygani A, Salimi S, Hassanzadeh T. Activity of antioxidant enzymes in seminal plasma and their relationship with lipid peroxidation of spermatozoa. *Int Braz J Urol* 2008; 34: 485-91.
15. Tawadrous GA, Aziz AA, Mostafa T. Seminal soluble fas relationship with oxidative stress in infertile men with varicocele. *Urology* 2013; 82: 820-3.
16. Zini A, Garrels K, Phang D. Antioxidant activity in the semen of fertile and infertile men. *Urology* 2000; 55: 922-6.
17. Aleissa MS. Effect of ginger supplements on some reproductive parameters and spermatogenesis of mice. *Indian Journal of Fundamental and Applied Life Sciences* 2014; 4: 271-7.
18. Faure C, Leveille P, Dupont C, Julia C, Chavatte-Palmer P, Sutton A, et al. Are superoxide dismutase 2 and nitric oxide synthase polymorphisms associated with idiopathic infertility? *Antioxid Redox Signal* 2014; 21: 565-9.
19. Alpsyoy S, Kanter M, Aktas C, Erboğa M, Akyuz A, Akkoyun DC, et al. Protective effects of onion extract on cadmium-induced oxidative stress, histological damage, and apoptosis in rat heart. *Biol Trace Elem Res* 2014; 159: 297-303.
20. Sakr SA, Nooh HZ. Effect of *Ocimum basilicum* extract on cadmium-induced testicular histomorphometric and immunohistochemical alterations in albino rats. *Anat Cell Biol* 2013; 46: 122-30.
21. Al-Kadir Mares WA, Najam WS. The effect of Ginger on semen parameters and serum FSH, LH & testosterone of infertile men. *Tikrit Medical Journal* 2012; 18: 322-9.
22. Hafez DA. Effect of Extracts of Ginger Goots and Cinnamon Bark on Fertility of Male Diabetic Rats. *Journal of American Science* 2010; 6: 940-7.
23. Abo-Ghanema II, El-Nasharty MA, El-Far AH, Ghonium HA. Effect of Ginger and L-Carnitine on the Reproductive Performance of Male Rats. *World Academy of Science* 2012; 6: 971-7.

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