Original Article

The Effect of Palm Pollen and Black Seed Pollen on Male Sex Hormones and Sperm Quality: A Single-Blind, Placebo-Controlled Clinical Trial Study

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Abstract

Background: Nowadays, using medicinal properties is a good alternative for infertility treatment to use them is increasing in the world. The aim of this study was to determine the effects of Herbal oral capsules included palm pollen extract (DPP) and Nigella Sativa extract (NS) on sex hormones in adult infertile men.

Materials and Methods: In this a single-blind, placebo-controlled clinical trial study, a total of 62 infertile men between 22 and 42 years of age were randomly selected and tested for sex hormones and prolactin. Thirty people in the case group received two 500 mg/kg capsules on a daily basis containing an herbal composition of palm pollen extract (350 mg) and black seed powder extract (250 mg) and the 20 in the control group received a placebo in the morning and at night for 3 months. The herbal composition capsules were manufactured by the Golbadistan Company. At the end of the three -month period, blood and semen tests were performed before and after the intervention in the case group that was compared with the control group. Hormonal assays were performed by Immunoradiometric Assay (IRMA) method. The data entered SPSS statistical software and the level of significance was set at $P \leq 0.05$.

Results: The spermiogram test results showed significant changes in the sperm count, progressive motility and rapid progressivity of the case group at the end of a quarterly period after consuming plant composition except for morphology (P=0.001, P=0.001, P=0.02, P=0.23). In addition, in the case group, the concentration of testosterone, follicle stimulating hormone (FSH), luteinizing hormone (LH) was significantly increased compared to the control group (P=0.000, P=0.004, P=0.012).

Conclusion: It seems that taking one 500 mg/kg capsule of DPP and NS extract can significantly increase sperm parameters and testosterone (registration number: IRCT2015020120895N1).

Keywords: Infertile Men, Prolactin, Sex Hormones

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Introduction

Infertility is defined as the inability to conceive after one year of unprotected intercourse. In 25-50% of cases, infertility is explained by male factors (1). Infertility is one of the medical problems of couples that according to the statistics of the World Health Organization (WHO), about 10% of couples have infertility problems, of which about 40 to 50% of infertility factors is in men and the most important reasons are related to low sperm quality. Therefore, paying attention to these problems and trying to solve them is very important (2). Studies on the effects of herbs on sperm parameters and sex hormones have shown that many of them are effective in reducing infertility (3). The aim of this study was to investigate the effect of plant composition on sperm parameters, sex hormones and prolactin. A combination of date pollen powder (Phoenix dactylifera pollen) and black seed (Nigella Sativa) has been traditionally used in Iran. However, so far, its combined effects on fertility has not been scientifically studied. The plant composition used is palm pollen powder (Phoenix dactylifera pollen) and black seed plant (Nigella Sativa) produced by Gulbestan Company. Phoenix dactylifera Date Palm Pollen (DPP) is widely used today as a topical remedy for infertility in traditional medicine. Previous studies have shown that the use of Phenix dactylifera pollen suspension

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increases testicular and epididymal weight as well as sperm parameters such as sperm count, motility, morphology (4).

In addition, DPP consumption in rats showed a significant increase in their serum testosterone levels (5). Also, increased testosterone levels on the one hand, increased sperm concentration, motility and increased natural morphology on the other hand have been observed in studies with palm pollen (6). In addition, date pollen contains gonadal stimulating estrogen compounds, and sterols that can contribute to the treatment of male infertility (7). Linolenic acid and oleic acid in black seed increase sperm parameters such as sperm count and motility,but reduce abnormal sperm (8). Phenolic and alkaloids black seed compounds stimulate the secretion of testosterone and follicle stimulating hormone (FSH) (9). Thymoquinone in black seed improves semen quality (10). Although small amounts of reactive oxygen species (ROS) are essential for sperm activity such as capacity, acrosomal reaction, and oocyte adhesion (11), high concentrations damage sperm cells, reducing sperm motility and ultimately inhibiting sperm fertility (12). Extensive research has been conducted on the antioxidant properties of plants as a substance that reduces oxidative stress (13). The results of investigating palm pollen have shown that the presence of phenolic compounds in this plant induces oxidative stress andimproves sperm quality that increases sex hormones (14). The present clinical trial study, investigated the combined effect of palm pollen and black seed pollen on male sex hormones and prolactin.

Materials and Methods

Study design

In this single-blind, placebo-controlled clinical trial study, 62 infertile men, between 22 and 42 years of age were randomly selected in 2015 (January) -22 (June) in the infertility center of Umm Leila Hospital, Bandar Abbas (Fig.1). Patients were included after consulting a urologist and their infertility was confirmed. Sperm samples with a total count of <15 million per milliliter, morphology <4% and progressive motility <40% were included in this study. All participants were screened through a checklist of sexual behaviors, history of infertility, history of radiation exposure, smoking and hookah and alcohol, adult diseases as well as systemic diseases and acute infections such as mumps, varicocele, trauma and a history of drug use. Those not meeting the exclusion criteria were excluded. Twelve patients were excluded from the study due to smoking or illness after completing the checklist, and finally, after obtaining a written consent, 50 patients remained until the end of the study. Placement of people in each of the new treatment (intervention) and common treatment and plasebo (control) groups was done by simple random method. Patients in the intervention group, in addition to the standard medical treatment of infertility (the same drug prescribed by a specialist for all patient participants), received two 500 mg/kg capsules of the plant composition of date pollen extract (350 mg) and black seed powder extract (250 mg) in the morning and evening for 3 months. Also besides the standard infertility medical treatment, Subjects in the control group received two 500 mg/kg capsules containing a placebo in the morning and night for 3 months. At the end of the three-month period, blood and semen tests were given before and after the intervention in the case group and was compared with the control group. Semen analysis (volume, sperm count, sperm motility, sperm morphology and progressive motility) was determined by routine laboratory methods and performed by sperm quality analysis (SQAIIC-P, America) (15). Hormonal assays including luteinizing hormone (LH), FSH and PRL were performed by Immunoradiometric Assay (IRMA) method and serum testosterone levels were measured by radioimmunoassay. This study was approved by the Ethics Committee of Hormozgan University of Medical Sciences and registered with the ethical code of IR.HUMS.REC.1394.201 in the clinical trial system (IRCT2015020120895N1).

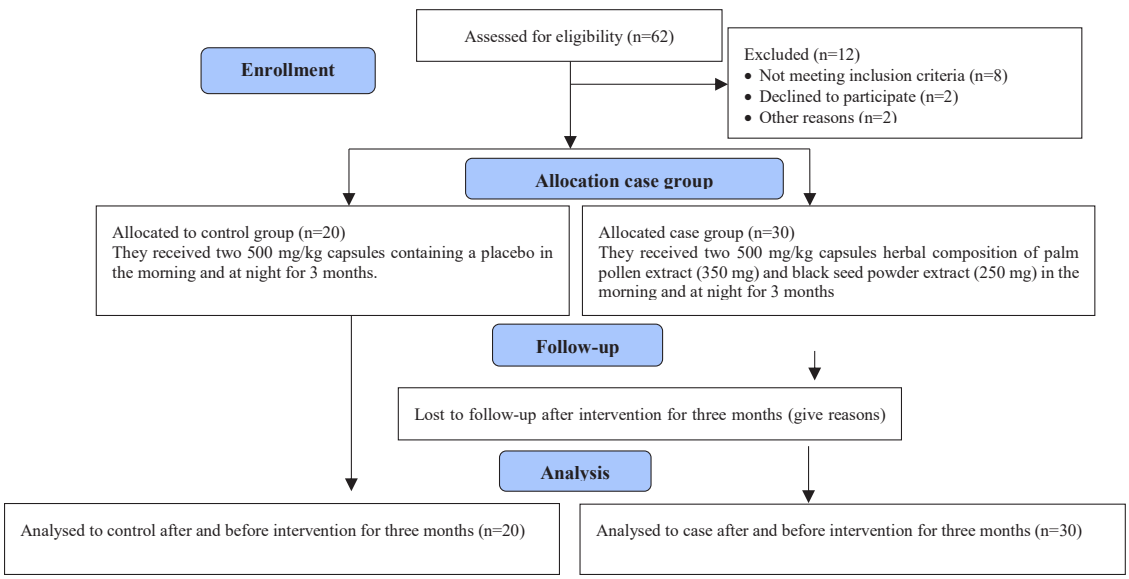

Fig.1: Single-blind, and comparative controlled clinical trial Consort flow chart.

Blood sampling and analysis of hormones

Peripheral blood samples for 5 ml were collected from all the subjects in two times before and after treatment). Once the serum was segregated by centrifuge (Sigma 4-10, USA, 2000 rpm, 15 minutes), the serum level for testosterone, estradiol, progesterone, LH, FSH and porlolactin hormones was double checked by proper ELISA kits (Labsystems Ltd., Finland).

Semen analysis and isolation of spermatozoa from seminal fluid

The subjects had to abstain from intercourse 3-5 days prior to the test. The test involved the collection of fresh semen samples in sterile containers acquired through masturbation. Thirty minutes was allocated to the liquification of samples. Then the semen was analyzed based on WHO instructions (Edition, 2010).

Statistical analysis

The data were statistically analyzed in SPSS. To examine the normal distribution of data, the Kolmograph-Smirnov test was used. Independent-samples t test was used to analyze the data with normal distribution and Mann-Whitney U-test was used for the data with abnormal distribution and the significant statistical level was considered as P=0.05. In this study, there was no missing data and the continuous variables were described as mean ± standard deviation (SD).

Results

Fifty people participated in this study, of whom 30 in the case group used herbal powder and 20 in the control group took placebo for three months. The average age of people in the case group was 33.31 and, in the control, group was 32.28 which did not differ significantly. At the beginning of the comparison of parameters and hormones in both groups under study did not show a significant difference (Table 1), but at the end of the quarter and the second phase of the study Comparison of the mean sperm count in the case group after consumption of plant powder 52.07 ± 33.80 increased which showed a significant relationship (P=0.001). Also, the mean progressive motility (total fast and slow motility) which is an indicator for assessing sperm strength increased by 16.80 ± 12.01 (0.001). The natural morphology of sperms also increased by about 19 ± 13.03 which did not show significant difference in the samples before and after (P=0.23, Table 2).

Comparing sperm parameters of case and control groups at the end of the quarterly period of palm and black seed pollen consumption showed significant changes. Sperm quality indices were increased in all parameters) sperm count, progressive motility, rapid progressive) except for morphology in the case group (P=0.001, P=0.001, P=0.02, P=0.23, Table 2). Moreover, hormonal status of the samples serum levels of testosterone, FSH, LH, prolactin and estradiol showed that the concentration of testosterone, FSH, LH was significantly increased in the case group (P=0.000, P=0.004, P=0.012, Table 2). Also, a significant decrease was found in the concentration of progesterone and prolactin in the case group (P=0.001, P=0.000, Table 2). It should be noted that the number of samples at the beginning of the study was 62 and some were excluded from the study for different reasons: not completing the three-month course of treatment, not using the drug correctly and not going to the infertility center.

Table 1: Comparison of the mean values between the two groups before taking treatment in infertile men

Variable	Before taking a placebo in the control group	Before taking the herbal composition in the case group	P value
FSH (mIU/ml)	4.08 ± 3.40	4.23 ± 3.72	0.981
LH (mIU/ml)	4.91 ± 2.15	5.21 ± 2.67	0.840
Testesteron (ng/ml)	4.35 ± 3.03	4.74 ± 3.10	0.195
Esteradiol (ng/ml)	28.81 ± 18	30.01 ± 17.12	0.820
Progesteron (ng/ml)	0.19 ± 1.05	0.93 ± 0.99	0.842
Prolactin (ng/ml)	227.12 ± 75.32	225.38 ± 68.95	0.491
Sperm count	46.3 ± 25.46	43.93 ± 30.93	0.631
Progressive motility	8.52 ± 6.51	8.53 ± 5.80	0.974
Rapid progressive	40.9 ± 20.05	39.63 ± 16.15	0.947
Morphology	20.03 ± 13.98	17.50 ± 11.10	0.205

Data are presented as mean ± SD. Paired t test. FSH; Follicle stimulating hormone and LH; Luteinizing hormone.

Table 2: Comparison of the mean values between the two groups after taking treatment in infertile men

Variable	Control	Case	P value
FSH (mIU/ml)	4.88 ± 3.67	5.22 ± 4.16	0.004*
LH (mIU/ml)	5.69 ± 2.59	6.29 ± 3.01	0.012*
Testesteron (ng/ml)	3.83 ± 1.77	4.86 ± 1.94	0.000*
Esteradiol (ng/ml)	31.62 ± 19.68	30.87 ± 17.37	0.877
Progesteron (ng/ml)	1.03 ± 1.02	0.81 ± 0.87	0.001*
Prolactin (ng/ml)	221.52 ± 77.51	198.99 ± 71.94	0.000*
Sperm count	43.20 ± 40.01	52.07 ± 33.80	0.001*
Progressive motility	6.70 ± 5.90	16.80 ± 12.01	0.001*
Rapid Progressive	37.16 ± 19.76	52.56 ± 16.13	0.020
Morphology	17.50 ± 11	19 ± 13.03	0.234

Data are presented as mean ± SD. Paired t test. FSH; Follicle stimulating hormone, LH; Luteinizing hormone, and *; Significance level P=0.05.

Discussion

The results of this study showed that date palm and black seed have a positive effect on the performance of sex hormones as well as sperm parameters of infertile men. The combined effect also managed to improve sperm quality. A significant increase was observed in sperm parameters in men treated with palm and black seed pollen compared to the control group. Dcunha et al. (16) showed that using the herbal drug SPEMAN for three months in men with oligosperm improved sperm quality and sex hormones.

Oluwasina Banga et al. (17) also reported that 120-

240 mg/kg of date pollen had a positive effect on the number, motility and morphology of rat sperm. In addition, the saponin in palm pollen increased the serum concentrations of FSH and LH hormones and increased testosterone concentration. Elevated serum testosterone levels indicated that palm pollen altered steroidogenesis in Leydig cells. But the exact mechanism of this action was not clear. Moreover, estradiol had a direct effect on sperm production and maturation.

Furthermore, palmitic acid and stearic acid compounds in palm pollen have inhibitory properties of 5-alpha-reductase enzyme activity. Inhibition of this enzyme reduces the conversion of testosterone to dihydrotestosterone in the tissue. As a result, less testosterone is converted to dihydrotestosterone. The concentration of testosterone is increased in the blood (18).

Ghasemi et al. (19) studied the effect of alcoholic black seed extract on fertility in rats. These researchers found that black seed increases variables including body weight, reproductive parameters (thickness and diameter of sperm tubes, number of spermatogonia, primary and secondary spermatocytes, spermatids, number of Sertoli and Leydig cells, diameter of Leydig cells, total height of sperm cells, hormones testosterone, follicle stimulating hormone) and also protein concentration. Alkaloids and black seed phenols also stimulate the secretion of FSH and testosterone (20). The increase in sperm concentration was due to increased levels of testosterone and FSH in testicular tissue; Because these two hormones were responsible for spermatocytogenesis and spermiogenesis in the fallopian tubes, testosterone is responsible for epididymal function in sperm maturation (21). On the other hand, increased prolactin has a negative effect on male reproduction. This affects sexual desire in men and plays a major role in male infertility (22, 23). The findings of the present study showed a significant decrease in the levels of prolactin, progesterone and estradiol after a three-month period of treatment with plant powder, while increasing the concentrations of testosterone, FSH and LH. It also seems that this plant powder has been able to regulate the balance of estrogen and androgen.

Conclusion

It seems that the combination of palm pollen and black seed in infertile men improves the quality of sperm parameters and can also increase sex hormones after a three-month consumption. Also, the results showed that this combination has an effective role in reducing the prolactin level.

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Authors' Contributions

A.H.; Participated in the collection of the data, research study design, and wrote the manuscript. Z.S.; Performed the statistical analysis, methodology, and discussion writer. R.A., A.N.; Data collection, methodology, and helped to draft the manuscript. M.M.; Data analysis and interpretation, and helped to draft the manuscript. M.L.; Methodology, review and editing. S.F.; Substantial contributor to conception and design the study, interpretation of data, revising the manuscript critically, and has given final approval of the version to be published. All authors read and approved the final manuscript.

References

1. Practice Committee of the American Society for Reproductive Medicine. Definitions of infertility and recurrent pregnancy loss: a committee opinion. Fertil Steril. 2013; 99(1): 63.
2. Martin-Hidalgo D, Bragado MJ, Batista AR, Oliveira PF, Alves MG. Antioxidants and male fertility: from molecular studies to clinical evidence. Antioxidants (Basel). 2019; 8(4): 89.
3. Del Giudice F, Kasman AM, De Berardinis E, Busetto GM, Belladelli F, Eisenberg ML. Association between male infertility and male-specific malignancies: systematic review and meta-analysis of population-based retrospective cohort studies. Fertil Steril. 2020; 114(5): 984-996.
4. Fallahi S, Rajaei M, Hesam MJ, Koolivand M, Malekzadeh K. The effect of Phoenix dactylifera pollen on the expression of NRF2, SOD2, CAT, and GPX4 genes, and sperm parameters of fertile and infertile men: a controlled clinical trial. Int J Reprod Biomed. 2021; 19(6): 545-558.
5. Shehzad M, Rasheed H, Naqvi SA, Al-Khayri JM, Lorenzo JM, Alaghbari MA, et al. Therapeutic potential of date palm against human infertility: a review. Metabolites. 2021; 11(6): 408.
6. Sampannang A, Arun S, Burawat J, Sukhorum W, Iamsaard S. Comparison of male reproductive parameters in mice with type 1 and type 2 diabetes. Clin Exp Reprod Med. 2020; 47(1): 20-33.
7. Ubah SA, Agbonu OA, Columbus PK, Abah KO, Chibuogwu IC, Abalaka SE, et al. Effects of date fruit (Phoenix dactylifera) on sperm cell morphology and reproductive hormonal profiles in cypermethrin-induced male infertility in Wister rats. Sci Afr. 2021; 11: e00713.
8. Leisegang K, Almaghrawi W, Henkel R. The effect of Nigella sativa oil and metformin on male seminal parameters and testosterone in Wistar rats exposed to an obesogenic diet. Biomed Pharmacother. 2021; 133: 111085.
9. Adedara IA, Lawal TA, Adesina AA, Oyebiyi OO, Ebokaiwe AP, Farombi EO. Sperm functional parameters and erythrocytes oxidant-antioxidant imbalance during municipal landfill leachate treatment withdrawal in rats. Environ Toxicol Pharmacol. 2014; 37(1): 460-467.
10. Rosli FD, Hashim NH, Osman K, Ibrahim SF, Kabir N. Ameliorative effects of thymoquinone on sperm parameters and testosterone level of nicotine-treated sprague dawley rats. Braz Arch Biol Technol. 2019; 62.
11. O'Flaherty C. Reactive oxygen species and male fertility. Antioxidants (Basel). 2020; 9(4): 287.
12. Signorini C, Moretti E, Collodel G. Role of isoprostanes in human male infertility. Syst Biol Reprod Med. 2020; 66(5): 291-299.
13. Garcia-Perez P, Xiao J, Munekata PE, Lorenzo JM, Barba FJ, Rajoka MSR, et al. Revalorization of almond by-products for the design of novel functional foods: an updated review. Foods. 2021; 10(8): 1823.
14. Leisegang K, Finelli R. Alternative medicine and herbal remedies in the treatment of erectile dysfunction: a systematic review. Arab J

Urol. 2021; 19(3): 323-339.
15. Lu JC, Huang YF, Lü NQ. WHO laboratory manual for the examination and processing of human semen: its applicability to andrology laboratories in China. Zhonghua Nan Ke Xue. 2010; 16(10): 867-871.
16. Dcunha R, Hussein RS, Ananda H, Kumari S, Adiga SK, Kannan N, et al. Current insights and latest updates in sperm motility and associated applications in assisted reproduction. Reprod Sci. 2022; 29(1): 7-25.
17. Oluwasina OO, Demehin BF, Awolu OO, Igbe FO. Optimization of starch-based candy supplemented with date palm (Phoenix dactylifera) and tamarind (Tamarindus indica L.). Arab J Chem. 2020; 13(11): 8039-8050.
18. Turner KA, Rambhatla A, Schon S, Agarwal A, Krawetz SA, Dupree JM, et al. Male infertility is a women's health issue—research and clinical evaluation of male infertility is needed. Cells. 2020; 9(4): 990.
19. Ghasemi R, Mir Mohammad Rezaei F, Nasri S, Nili Ahmadabadi A. The effects of hydro-alcoholic extract of Nigella sativa seed on sperm parameters and spermatogenesis in toxicity induced by diazinon in male rats. Armaghane Danesh. 2017; 22(4): 486-498.
20. Marefati N, Ghorani V, Shakeri F, Boskabady M, Kianian F, Rezaee R, et al. A review of anti-inflammatory, antioxidant, and immunomodulatory effects of Allium cepa and its main constituents. Pharm Biol. 2021; 59(1): 287-302.
21. Recchia K, Jorge AS, Pessôa LVdF, Botigelli RC, Zugaib VC, de Souza AF, et al. Actions and roles of FSH in germinative cells. Int J Mol Med Sci. 2021; 22(18): 10110.
22. Gangwar PK, Sankhwar SN, Pant S, Krishna A, Singh BP, Mahdi AA, et al. Increased Gonadotropins and prolactin are linked to infertility in males. Bioinformation. 2020; 16(2): 176-182.
23. Green KI, Amadi C. Status of serum prolactin levels among male cohort in infertile couples. Int J Appl Basic Med Res. 2020; 10(4): 245-251.