



Improvement of Semen Parameters in a Man With Idiopathic Severe Oligoasthenoteratozoospermia Using Date Palm Pollen (*Phoenix dactylifera* L.) Based on Iranian Traditional Medicine: A Case Report and Literature Preview

Mehrdad Karimi¹, Firoozeh Akbari Asbagh², Roja Rahimi³, Majid Safavi⁴, Gholamreza Pourmand⁴, Fatemeh Sadat Hoseini⁵ and Mohammadreza Mirzaei^{1,*}

¹Department of Iranian Traditional Medicine, School of Traditional Medicine, Tehran University of Medical Sciences, Tehran, IR Iran

²Department of Obstetrics and Gynecology, IVF Unit, Yas Hospital, Tehran University of Medical Sciences, Tehran, IR Iran

³Department of Traditional Pharmacy, School of Traditional Pharmacy, Tehran University of Medical Sciences, Tehran, IR Iran

⁴Urology Research Center, Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran

⁵Yas Hospital, Tehran University of Medical Sciences, Tehran, IR Iran

*Corresponding author: Mohammadreza Mirzaei, Building of the Ahmadiye, No 27, Corner Alley Tabriz, Sarparast Shomali Street, Taleghani Ave, P. O. Box: 1416663361, Tehran, IR Iran. Tel: +98-9143110286, Fax: +98-4135249263, E-mail: dr.mirzaei_m@yahoo.com

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Abstract

Introduction: Almost 50% of infertilities are associated with males and among them 30 to 50% are idiopathic. Empirical treatments are used in idiopathic male infertility, yet not enough scientific evidence is available for the application of such remedies. Date palm pollen (DPP) is one of the drugs suggested for such patients in Iranian traditional medicine (ITM).

Case Presentation: This study was performed on a 35-year-old male patient with idiopathic infertility. He previously had severe oligoasthenoteratozoospermia and was under medical supervision at Yas hospital of the Tehran University of Medical Sciences, Tehran, Iran from August 2016 to February 2017, where he was treated with DPP at a dose of 3 g twice daily, for three months. The second semen analysis was carried out after a quarter of the treatment period, followed by re-analyses after one and three months of finalizing the treatment period. The results obtained showed an impressive improvement in the quality of semen parameters. Within six months, the initial values of normal morphology (1%), total motility (3%), progressive motility (0.0), and sperm concentration (0.1 million) increased to 20%, 60%, 10%, and 10 million, respectively.

Conclusions: Date palm pollen could be helpful in improving semen parameters in such patients. Clinical studies are required to find the exact effect.

Keywords: Date Palm, Infertility, Oligospermia, Pullen, Semen, Spermatozoa, Traditional

1. Introduction

About 15% of couples are infertile (1). Infertility is a common problem, with crucial psychosocial issues. Men are responsible of almost 50% of infertility cases (2). Different causes, such as congenital or acquired urogenital disorders, urinary tract infection, endocrine disorders, systemic diseases, genetic causes, and immunologic and environmental factors are involved in male infertility (3). A fraction of 30% to 50% of male infertility causes are still unknown; this condition is called idiopathic infertility (2). Various types of empirical cures, including hormonal treatments, such as androgens, gonadotropins, anti-estrogens, and antioxidants like zinc, selenium, L-carnitine, vitamin E, and other dietary supplements are used in treating these patients (2, 4), yet scientific evidence of the medical benefits of empirical methods are scarce (2, 4). The use of anti-

estrogens, aromatase inhibitors, gonadotropins, and antioxidants, such as vitamin E, glutathione, and L-carnitine has been reported to improve semen quality, yet there is no statistical evidence to prove the efficacy of such treatments (4). A systematic review by Kumar et al. suggested that sufficient scientific evidence is not available regarding the use of existing relevant medications (5).

Assisted reproductive technology (ART) methods are also used as a final approach in the treatment of such patients. This method is, however, both invasive and expensive, while it is likely to be associated with serious complications, lacking a high treatment response (3).

It seems that the use of traditional medical therapies is more effective and less costly; they cause fewer complications in the treatment of idiopathic male infertility. Several studies have presented evidence of improvements in

semen quality with the use of traditional medicine therapies (6). In ITM, qualitative and quantitative disorders in semen account for some causes of infertility and various treatments are provided in this respect (7, 8). Nevertheless, there have been a limited number of studies in this area.

Date palm pollen (DPP) is a drug included in ITM and recommended for boosting fertility and sexual performance. Furthermore, DPP is male reproductive cells of palm flowers, which has long been used traditionally in the treatment of infertility, particularly in Egypt, Iran, and other Southeast Asian countries. Several animal studies have reported improvement in semen parameters with use of this drug. In most studies, improved motility and sperm count are of main effects of this drug. In an investigation of healthy male rabbits, motility and sperm count were improved by the drug. In another study prescribing different doses of suspension on male rats resulted in improvement of motility, sperm count, and normal morphology. Also improvements in sperm count, motility, and normal morphology in mice were reported in other studies. The improved motility of sperm has also been reported in vitro under the effect of this drug (9).

The subject of this study was a man with idiopathic infertility with severe oligoasthenoteratozoospermia. Idiopathic oligoasthenoteratozoospermia, especially in its severe forms, is one main reason for male infertility (1). According to the knowledge of ITM, the patient was treated with the DPP drug, which resulted in improved semen parameters.

2. Case Presentation

This study was a retrospective observation. The ethical approval of this study was issued by the ethics committee of Tehran University of Medical Sciences (Ethic number: IR.TUMS.REC.1394.146559). The subject was a 35-year-old male, who was under medical supervision at Yas hospital, which was a referral center of infertility of the government, managed by Tehran University of Medical Sciences from August 2016 to February 2017. The patient got married eight years prior to the study and had been unsuccessful at impregnating his wife for the last three years. The patient's wife was healthy and had no infertility-related problems. The patient had no records of varicocele, urologic diseases, urologic surgeries, and no history of smoking, alcohol, and drug abuse. His medical history and examinations revealed no known conditions, such as endocrine disorders, chronic diseases of the liver or kidneys and other systemic disorders, no mumps during his childhood or other conditions that may have led to infertility or impaired semen parameters. A physical examination showed

normal-sized testes with normal levels of serum follicle-stimulating hormone (FSH), luteinizing hormone (LH), thyroid-stimulating hormone, testosterone, and prolactin at in vitro evaluations. The patient had frequently visited several urologists in the past and been diagnosed with idiopathic infertility and severe oligoasthenoteratozoospermia. The subject had been given medications, such as vitamin E, zinc, pentoxifylline, L-carnitine, and injectable human chorionic gonadotropin, yet had not been administered any medication for almost four months prior to the intervention. The patient had no history of using ART.

First, after obtaining the patient's informed consent before the intervention, the semen was analyzed again and indicated severe oligoasthenoteratozoospermia (Table 1). In this study, the patient's semen was analyzed at all stages based on the world health organization standards (2010) (10).

The patient was advised to maintain three days of sexual abstinence prior to semen analysis. The interval of the time of abstinence was recorded when the sample was handed in. The semen sample was collected at the hospital by masturbation directly in a 50-mL polyethylene jar. The Semen sample was analyzed within one hour after ejaculation. After liquefaction, semen volume was measured in a graded tube with a 0.1-mL accuracy. Macroscopic (volume, appearance, viscosity, and liquefaction) and microscopic (concentration, motility, and morphology) analyses were performed. All assessments were performed by a single technician in an in vitro fertilization (IVF) laboratory at Yas hospital, a specialized infertility laboratory, Tehran, Iran. Sperm concentration was counted in a Neubauer hemocytometer counting chamber at a magnification of $\times 200$ or $\times 400$. Only intact spermatozoa were counted for sperm concentration (defined as having a head and a tail). The researchers prepared a wet preparation, approximately 20 micrometers deep, and waited for the sample to stop drifting (within 60 seconds). Then, the researchers examined the slide with phase-contrast optics (Nikon, Japan) at $\times 200$ or $\times 400$ magnification. Next, approximately 200 spermatozoa per replicate were assessed for the percentage of different motile categories. The previous edition of this manual recommended that progressively motile spermatozoa should be categorized as rapid or slow, with a speed of > 25 -m/sec at 37°C defining "grade a" spermatozoa. However, it is difficult for technicians to define the forward progression accurately and without bias.

In this study, the motility of each spermatozoon was graded as follows (10):

Progressive motility (PR): spermatozoa were moving actively, either linearly or in a large circle, regardless of speed.

Non-Progressive motility (NP): all other patterns of

Table 1. Effects of Date Palm Pollen on Semen Parameters

Semen Parameters	Before Treatment	3 Month After	4 Month After	6 Month After
Volume (mL)	5	5	3	5
Sperm concentration (million/mL)	0.1	0.5	1	10
Total sperm count (million)	0.5	2.5	3	50
Normal morphology (%)	1	10	5	20
Total motility (%)	3	50	10	60
Progressive motility (%)	0	0	0	10
Non progressive motility (%)	3	50	10	50
Immotile (%)	97	50	90	40

motility with an absence of progression, e.g., swimming in small circles, the flagellar force hardly displacing the head, or when only a flagellar beat can be observed.

Immotility (IM): no movement.

Total motility was considered as PR + NP motility.

Diff -Quick staining was used for evaluating sperm morphology according to the strict (Kruger classification) criteria (11).

The lower reference limit was considered 15, 40%, 32%, and 4% for sperm concentration (106 per mL), progressive motility (PR), total motility (PR + NP), and sperm morphology, respectively (10). After preparing the first spermogram, the patient was treated with the powder of DPP (3 g, twice a day) for three months. The patient was provided with DPP in the form of sachets (3 g). The DPP drug used in this study was obtained from the palm groves of Jahrom city, Southern Iran, and standardized based on total steroids (0.044 mg/g DDP). The patient was visited and examined monthly, especially for side effects, which were measured according to the common toxicity criteria table. No side effects were observed during the treatment. At the end of the quarter, the patient's semen was analyzed again and thereafter one and three months, respectively, after completion of treatment (Table 1). The subject received no medication from three months after completion of the treatment until the end of the sixth-month test. In the current study, parameters including sperm count, motility, and normal morphology were considered as specific characters. The results obtained showed an impressive improvement in the quality of semen parameters, including sperm count, motility, and morphology, yet no increase in semen volume (Table 1). Within six months, the initial values of normal morphology (1%), total motility (3%), progressive motility (0.0), and sperm concentration (0.1 million) increased to levels of 20%, 60%, 10%, and 10 million, respectively. Also, immotile sperm decreased from 97% to 40% in six months. As expected, pregnancy did not occur in this case until the end of the sixth month and the final test.

3. Discussion

The present research reports on a male with idiopathic infertility with severe oligoasthenoteratozoospermia that was cured with the DPP drug, administered according to the knowledge of ITM, which led to improved semen quality. The administration of a daily 6-gram dose of DPP is much more effective in promoting semen parameters in terms of sperm concentration, total sperm count, total motility, progressive motility, non-progressive motility, normal morphology, and decreased immotile sperm.

In ITM, DPP is one of the herbal monographs used in the treatment of male infertility. From the perspective of ITM, as the drug can increase male fertility, it is regarded as a strong sexual performance enhancer (9).

The results of this study are consistent with findings from previous studies conducted on the effects of the medication on improving semen parameters.

An in vitro study demonstrated increased motility as an effect of this drug (9). Elevated sperm count and motility have also been reported in several animal studies, whereas normal morphology improvement has been reported only in some studies (9). In a research conducted on mice by Mattar and Adaay, DPP increased the normal morphology, sperm count, and motility (12). Administration of this drug at doses of 30, 60, 120, and 240 mg/kg to healthy male rats for 35 days, yielded normal morphology only at doses of 120 and 240 mg/kg, yet sperm count and motility increased significantly in all groups. They also reported elevation of serum testosterone and estradiol, as well as weight gain in the testes and epididymis (9, 13). A study on male rabbits given doses of 5 and 25 mg.kg⁻¹ for eight weeks recorded increases in sperm count and motility (9). It seems that the use of effective therapeutic doses of the drug has marked impacts, particularly on the betterment of normal morphology.

In one study, DPP powder at a daily dose of 120 mg/kg (500 mg capsules) was administrated to 40 patients

with idiopathic infertility with oligoteratozoospermia or oligoasthenoteratozoospermia for two months, which led to significant rises in motility, sperm count, and normal morphology. In the present research, the average value of motility increased from 16.80 to 21.40, sperm count from 12.54 to 19.07, and normal morphology from 16.45 to 18.32 (14), however, it seems that administration of this drug at a dose of 120 mg/kg daily in the form of 500 mg capsules is impractical because in this case, for example, a person weighing 75 kg should consume 18 capsules daily for two months, which seems not feasible.

Comparison of the current study with others highlights its value. The mentioned animal studies were carried out solely on animals with normal spermatogenesis and fertility, and most have reported improvement in motility and sperm count. This was while the current patient had severe oligoasthenoteratozoospermia and was under different drug treatments before the study and had no improvement in his semen parameters. The therapeutic outcomes of this study are much more significant. The results showed that an initial sperm concentration of 0.1 million reached 0.5 million after three months, 1.0 million at the end of the fourth month, and 10 million two months later. Normal morphology also increased from 1% to 20% in six months. Total motility went up from 3% to 60%, and progressive motility rose from zero to 10% after six months. Also, immotile sperm decreased from 97% to 40% in six months. Comparison of the current results with others revealed a very significant finding in a way that the current utilized drug dosage and medication time span could be a basis for further future studies.

A number of animal studies have shown the effect of this drug on the male reproductive system, resulting in hormonal changes and enhancement of sexual behavior; for example several animal studies observed weight gain in sexual organs and spermatogenesis augmentation resulting from DPP use (9).

Although there is no full explanation for the pharmacological effects of the drug on the male reproductive system and enhancement of quality and quantity of semen, the results of some studies, as well as the phytochemical components of DPP, signify that the drug can have hormonal and antioxidant efficacy.

Increases in serum and intra-testicular levels of testosterone as a result of taking this drug have been reported in several animal studies (9). A study also showed gonadotropic activities of this drug (15). Another study indicated the presence of LH and FSH hormones in DPP (9). The effects of DPP on the male reproductive system may be related to the presence of an active substance with gonadotropic actions.

DPP contains steroidal compounds such as estradiol,

cholesterol, estrogen, estrone, and estriol (15). A study on animals reported rises in estradiol levels with this drug. They also found increased motility and weight gain of the sexual organs and attributed the impacts to the stimulation of the antioxidant system by the drug (16). Some studies also linked the antioxidant properties of DPP to phytosterols (9).

The drug contains other components such as saponins, tannins, carotenoids, flavonoids, and alkaloids, which have antioxidant properties (9). A study relates the effects of DPP on spermatogenesis boost to these antioxidant contents (17). This medicine contains salts and minerals, including zinc, selenium, iron, copper, cobalt, manganese and nickel as well as vitamins such as B1, B2, B12, A, E, and C (9), many of which have antioxidant properties. Vitamins E and C and minerals, such as zinc and selenium, are also widely used as dietary antioxidant supplements in the empirical treatment of such patients (2, 4). In fact, the drug is a dietary supplement rich in antioxidants.

Date palm pollen contains types of amino acids, which contain the main components of the drug. Arginine, one of the main amino acids in the drug (9), acts as an antioxidant in the empirical treatment of idiopathic male infertility (4). A systematic review has highlighted its effects on improving semen parameters caused by the impact on the antioxidant system (18).

From the perspective of ITM, nutrition is the main part of the treatment of male infertility (8). Besides, the impact of nutritional deficiencies in both spermatogenesis and male idiopathic infertility disorders is well known (19). Some studies presented evidence that combination therapy may have a greater impact on semen parameters and increased fertility in such patients (4). Given the presence of various vitamins, micronutrients, and in particular, amino acids in the drug, it is considered to be a natural dietary supplement for the patients. In fact, DPP, as a dietary supplement, with its hormonal functions and antioxidant effects, may account for an appropriate and natural remedy for combination therapy in the patients.

The current study can be considered as a valuable research, and the first case report of a male with severe oligoasthenoteratozoospermia that was treated with DPP and has shown remarkable improvements in semen parameters. Semen quality has a significant role in male's fertility. Semen analysis is the main predictor of male's infertility. Most infertility cases of the male's idiopathic infertility are diagnosed to be oligoasthenoteratozoospermia (1). Therefore, improving semen parameters among males with idiopathic infertility is a target of medicinal therapies. Sperm quality is a determining factor in selecting ART type and has a great role in the success of this method. Therefore, in case of ART as a final treatment, improvement

in sperm parameters leads to the selection of better types of ART and increases the level of success of the method in patients. This issue is more highlighted in patients with severe oligoasthenoteratozoospermia, in which responsiveness level is still low even in the ART method (3). If the ART method was chosen before the interventional treatment in the studied patient, then regarding sperm quality, ICSI/IVF ought to be used that is invasive with high costs and might bring severe side effects and would have less probable success due to the low level of motility and normal morphology. However, after medical intervention and improvement of sperm parameters, better and low-cost methods could be used with less severe side effects, including IUI. Therefore, the effects of this drug on improving semen quality are very important.

The study also had some limitations. The current researchers prescribed unprocessed and natural drugs to the patient; therefore, it is not clear, which ingredient was the most effective and thus prevents further discussions about drug mechanism. A triple-staged semen analysis with one- and two-month intervals and also using a natural drug to treat the patient were the strengths of this study. This study also had some weaknesses. The study was not a comparative one and the researchers did not study the hormonal profile after treatment.

In conclusion, the results of this study indicate that the administration of DPP in an appropriate dosage and treatment duration may have significant and very impressive effects on the improvement of semen parameters in men with idiopathic infertility. Thus, more clinical studies are required to evaluate the effects of DPP medication on boosting semen parameters in patients.

Footnote

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