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Consumption of Iranian Herbal Medicine by Infertile Men Can Improve Pregnancy Outcome

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ABSTRACT

The main goal was to evaluate the impact of herbal formula TOPALAF powdered herbs including **T**ribulus terrestris, **O**rchis mascula, **P**hoenix dactylifera, **A**llium ampeloprasum, **L**epidium sativus, **A**mygdalus communis and **F**icus carica on sperm parameters of infertile men and pregnancy outcomes. Sixty-two men were divided into treated (32 men) and control groups (30 men). The treated group was asked to consume packages of herbal medicine TOPALAF and control group took placebo three times a week for three months. The effect of TOPALAF was determined on sperm parameters before and after consumption, then compared to control group. Also the rate of pregnancy was determined in treated group after three months of TOPALAF consumption. There was significant increase in sperm count (42.91±9.29 to 51.05±8.32, $P < 0.05$) and progressive motility (36.93±3.2 to 52.23±5.7, $p<0.001$) in treated compared to control group, respectively. There was insignificant difference in sperm normal morphology before and after treatment. The rates of clinical pregnancies were 18.75% and 3.3% in treated and control groups, respectively. It seems TOPALAF would be useful for treatment of male infertility problem if consumed for one spermatogenesis period. However, more studies are required to elucidate probable mechanisms on fertility potential of infertile men.

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INTRODUCTION

Infertility is defined as ability to achieve pregnancy after one year of unprotected intercourse [17]. Inability to have child is one of the most important problems for couples and male factor infertility is considered as a cause up to 30% of the infertile couples [16]. Numerous methods have been used for treatment of infertility problems in men. In this regards, herbal medicine has been applied in order to treat different aspects of male infertility, such as improvement of libido, erectile dysfunction, and also spermatogenesis [18]. Large numbers of herbals have been used in order to investigate probable effects on reproductive system and male infertility. However; there are no any reports regarding scientific and pharmacological effects of beneficial therapeutic agents [18]. According to World Health Organization (WHO), more than 80% of people use traditional medicine for their primary treatment [4]. Also, researchers were invited to determine herbal medicines as a new source for infertility treatment [18].

Heidary *et al* (2008) enrolled 52 nonsmoker infertile men whose problem could not be solved surgically. They were treated by saffron for 3 months (50 mg, 3 times a week). They reported an increase of 7.4% in normal sperm morphology. Significant increases were also detected in the percentages of class A to C sperm motility. However, they detected a significant increase in sperm count with saffron therapy [14].

Another study was involved thirty male subjects diagnosed with oligoasthenoteratozoospermia[10]. Patients from treated group were administered purified Tribulus terrestris L. extract 250 mg tablets, three times per day for two months which were compared with placebo tablets in control group. It was shown that Tribulus terrestris L. did not show any improvements in spermatozoa normal morphology. But, acrosome reactions as well as slow and non-progressive motility were increased [24]. Also in animal studies, oral administration of this extract to

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laboratory animals resulted in the stimulation of spermatogenesis and the proliferation of the spermatogonia, which involved cell divisions of the spermatocytes and spermatids. In addition, the number of Sertoli cells, sperm viability and survival rate were also significantly increased [12].

TOPALAF is one of the herbal medicines including Tribulus terrestris, Orchis mascula, Phoenix dactylifera, Allium ampeloprasum, Lepidium sativus, Amygdalus communis and Ficus carica (Table 1). The effect of herbal medicine TOPALAF has not been studied yet, but Pharmacological effects of these herbs have been investigated separately [7-2-26-8-28-22-9].Our aim was to investigate the probable influence of TOPALAF on sperm count, motility and morphology and the potentials of this drug on male reproductive system.

Table 1: Names of the herbs used in the TOPALAF.

Herb	Percentage
Powdered fruit of Tribulusterrestris	20
Powdered root of Orchismascula	20
Phoenix dactylifera pollen	20
Powdered seed of Allium ampeloprasum	10
Powdered seed of Lepidiumsativus seed	10
Powdered seed of Amygdaluscommunis	10
Powdered fruit of Ficuscarica	10

MATERIALS AND METHODS

Patients:

This case control study evaluated infertile men referred to our urology department. Only infertile couples with male factor etiology met the inclusion criteria. Semen analysis was performed for infertile male, suffering from primary or secondary infertility. Individuals who had varicocele, azoospermia, history of testicular torsion, or any type of inflammations as well as smokers were excluded. Men with oligozoospermia, asthenozoospermia, teratozoospermia or oligoasthenoteratozoospermia were included in this study. The patients were asked not to use any drugs for infertility treatment during three months. Sixty-two volunteers were divided into treated (32 men) and control groups (30 men). This study was approved at the author's institute ethics committee (Ref no.: 1382).

Preparation of TOPALAF:

TOPALAF was prepared by blending the powdered herbs including Tribulus terrestris, root of Orchis mascula, Phoenix dactylifera pollen, Allium ampeloprasum seed, Lepidium sativus seed, Amygdalus communis and Ficus carica. A package for a complete period of consumption was included 45 bags (each was 25 g). Bags for treated group were included powdered herbal medicine TOPALAF and in control group were placebo instead. Packages were supplied by Golbedastan Company (Yazd, Iran).Treated group was asked to consume TOPALAF three times a week for three months; while, control group consumed placebo. Both groups did not receive other treatments during the study period and were followed during treatment course.

Semen analysis:

Before starting the treatment, semen analysis was performed according to WHO criteria [27]. Sperm count, motility, normal morphology and volume of semen were recorded for each sample. Three months after TOPALAF consumption, semen analysis was done again for both groups. Abstinence period was between 2- 7 days. Semen samples were collected in sterile container and evaluated after liquefaction. Only samples that had sperm concentration of 5-19 $\times 10^6$/ml, progressive motility less than 50%, and normal morphology below 30% were included in this study [27]. Semen analysis was performed in a double blind manner. In case of abnormal semen parameters, the specimens were checked again.

The sperm count was done by Mackler chamber. Sperm motility was evaluated in four classes of A: quick progressive, B: slow progressive, C: non progressive, and D: immotile [27]. Sperm morphology was examined using Papanicolaou staining and phase contrast microscope. At least, 200 spermatozoa were counted for sperm motility and morphology analysis. In order to record the pregnancy outcomes, the couples were followed for 3 months during consumption and 3 months after TOPALAF consumption.

Statistical analysis:

The data were shown as mean ± SD. Paired t-test and independent sample test were used for statistical analysis wherever appropriate. All data were dealt with SPSS software version 16.0 (Chicago, USA). Data were considered statistically significant when $p \leq 0.05$.

Results:

Sperm parameters:

The data showed that mean age had no significant differences between treated and control groups (32.22±5.2 and 33.79±3.7, respectively). There were insignificant differences on sperm count, motility and

morphology in control group before and after placebo consumption. There was significant increase (12.9%) in progressive motility and decrease in non-progressive motility and immotile sperm after treatment in treated group when compared to control group. However, there was insignificant increase in normal morphology (Fig 1). Also, there was insignificant differences in the rates of sperm normal morphology in treated compared to control groups (Fig 2).

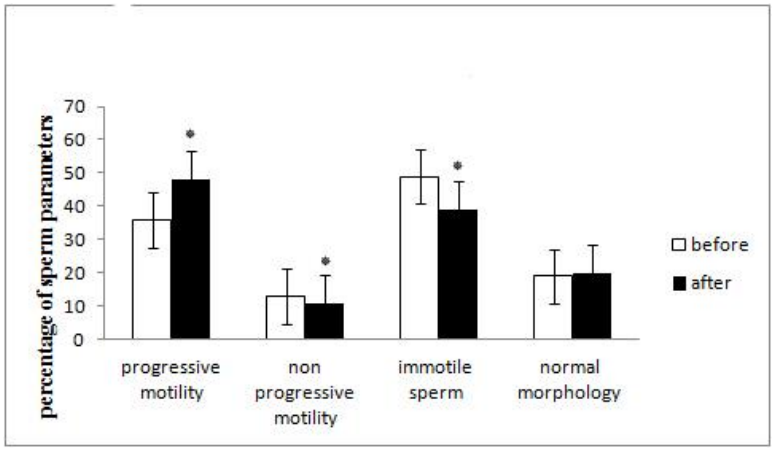

Fig. 1: Effect of TOPALAF treatment in treated group (n=32) (p≤0.001*).

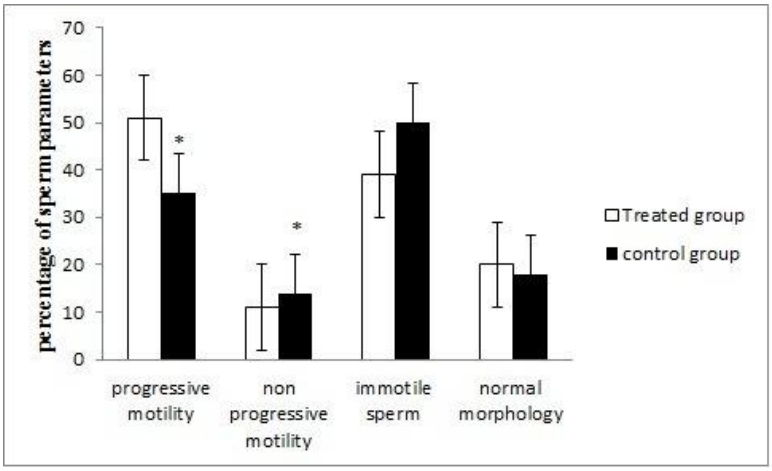

Fig. 2: Sperm parameters of treated group after treatment when compared to control group (p≤0.001*).

There was no significant increase in sperm count and volume of ejaculates in control group after placebo treatment; while, it showed an increase to 8.14% in treated group. The ejaculate volume showed significant increase in treated group after consumption compared to before (p<0.001). Also, sperm count was significantly increased in treated group compared to controls (Table 2).

Table 2: Sperm Count& Ejaculate Volume in control, treated & pregnancy group.

	Before treatment		After treatment	
	Sperm count($\times 10^6$/mL)	Ejaculate volume(ml)	Sperm count($\times 10^6$/mL)	Ejaculate volume(ml)
Control group(n=30)	45.33±34.4	2.18±.7	42.23±39.0*	2.00±.6*
Treated group(n=32)	42.91±29.9	2.80±.7	3.63±1.1**	51.05±32.8**
Pregnant group(n=6)	41.8±26.5	3.4±1.5	80.44±48.1*	4.6±.8*

* (P < 0.05), ** (P<0.001)

Pregnancy outcome:

A total of 6 wives became pregnant (18.75%) after consumption of herbal TOPALAF by their partners. This rate was only 3.3 % in control group. Data showed that sperm count and ejaculate volume significantly were increased after consumption of TOPALAF in pregnant group (Table2). Also, the rates of progressive motility were increased significantly (P<0.001). However, no significant changes in non-progressive motility and normal morphology were seen (Fig 3).

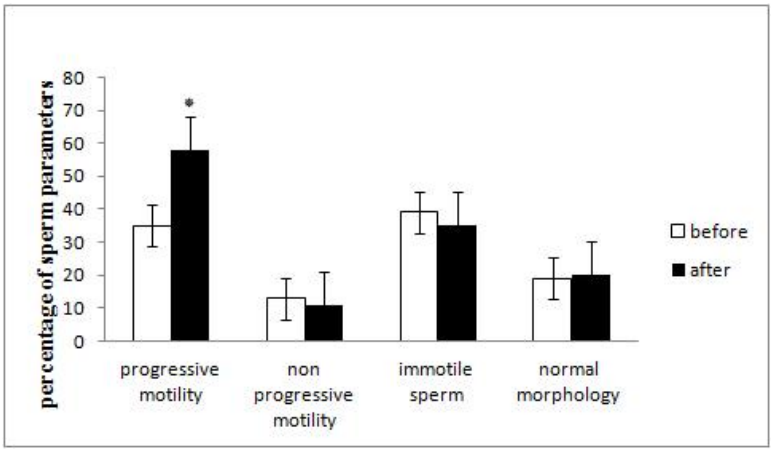

Fig. 3: Effect of TOPALAF treatment in pregnant group ($p \leq 0.001$).

Discussion:

This study investigated the effect of TOPALAF on sperm parameters of infertile men. Our data showed that sperm count and progressive motility was increased, while no significant change was noticed on normal sperm morphology in treated group. Also, 18.75% pregnancies were observed in wives of treated group.

Herbal medicine as an aphrodisiac can improve sperm parameters in men [23]. Tribulus terrestris has been used as an aphrodisiac drug due to enhance the quality of sperm parameters and spermatogenesis [18-19]. Also, Phoenix dactylifera is used for male infertility in traditional medicine [5]. It was shown that Phoenix dactylifera may improve sperm parameters, also increase the weight of testis and epididymis [26]. The therapeutic effects may be related to estradiol and flavenoid components that would affect sperm parameters [19].Tribulus terrestris and pollen of Phoenix dactylifera contain steroid, flavonoid, alkaloids, saponins and lipid that can affect sperm parameters [19-15]. Consumption of these herbal medicines will increase the plasma level of luteinizing hormone (LH), follicular stimulating hormone (FSH) and testosterone (T) hormone [23]. Alkaloid agents have estrogenic properties and T can increase estradiol by enhancing LH and FSH levels [19]. T also enhances sexual desire, libido and sexual performance [1]. Orchis mascula is consumed as a restorative and tonic aphrodisiac in conditions associated with weakness or reduced sexual activity [2]. Spermatogenesis is controlled by hypothalamus-hypophysis-gonad access. Since, TOPALAF may increase the plasma level of gonadotropins, it may affect spermatogenesis.

In recent years, a large number of reports have been shown improvement in semen parameters and testicular function with Speman administration which is comprised of eight herbal extracts [11]. In Agrawal et al study, subjects were given 2 tablets, twice per day. After three months of treatment, significant improvement in sperm count and motility were observed in 40% of the men. In addition, improved gland functions including prostatic fluid parameters with no effect on hypothalamic-pituitary axis were detected. The wives of thirteen patients (16.2%) became pregnant after treatment with Speman [2]. Though, duration of TOPALAF administration was similar to Speman, but pregnancy outcome was noticed to be more than Speman administration.

Shukla *et al* determined the role of Mucuna pruriens in infertile men who were under psychological stress. 60 subjects who were infertile and 60 healthy men having normal semen parameters with history of at least one pregnancy were considered as treatment and control groups, respectively. Infertile subjects were consumed M. pruriens seed powder (5 gr per day) orally for three months. Treatment with M. pruriens significantly ameliorated psychological stress and seminal plasma lipid peroxide levels along with improvement in sperm parameters. On the basis of their results, it may be concluded that M. pruriens not only reactivates the antioxidant defense system of infertile men, but it also helps in the management of stress and may improve semen quality [25].

Low concentration of Reactive Oxygen Species (ROS) is necessary for sperm functions, but high concentration may damage the lipids, proteins and membrane and decrease normal sperm parameters [3]. Zini and colleagues showed that the level of ROS is increased in semen of infertile men up to more than 40% [29]. However, high concentrations of ROS can directly damage the sperm membrane and motility [3]. Exposure to ROS may cause ATP depletion and lowering sperm motility. This is directly related to the level of lipid peroxidation experienced by the spermatozoa of infertile men [13]. It is assumed that TOPALAF has the potential to increase the sperm motility due to its antioxidant capacity. The beneficial effects of herbal medicine are related to antioxidant capacities and improvement of spermatogenesis [23]. Rich diet of herbal as antioxidants can protect cells against ROS, which may have positive effects on sperm parameters [20]. It seems TOPALAF may increase the quality of sperm and enhance the chance of natural pregnancy in patients with

subnormal semen analysis. Phoenix dactylifera pollen [26], Allium ampeloprasum seed [8], Lepidium sativus seed [28], Amygdalus communis [22] and Ficus carica [9] attributed to various components of antioxidants due to the presence of phenolic and flavonoid. These agents inhibit significantly the lipid peroxidation and protein oxidation; while, can increase the plasma levels of vitamins C, E and A, β-carotene [26]. To the best of our knowledge, this is the first study evaluating the effect of consumption of herbal TOPALAF on male factor couples and following the pregnancy outcomes. Our limitations were, however, the lack of hormonal determinations before and after consumption as well as patients follow-up until delivery. In addition, assessment of sperm DNA integrity of aforesaid patients could be suggested.

Conclusion:

Our data showed that TOPALAF can improve progressive motility and pregnancy outcomes. This effect may be due to the presence of alkaloids, saponins and flavonoids through central and peripheral pathways. Therefore, TOPALAF can improve fertility potentials in men, but more studies are required for proving this hypothesis.

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