ORIGINAL ARTICLE

Comparison of the Effects of Nettle and Alyssum with Q10 Plus and L-Carnitine on Improving Sperm Parameters of Infertile Men

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ABSTRACT

Background

Infertility is one of the most stressful and complicated experiences in a couple's life.

Objective

The aim of this study was comparing the effects of Nettle and Alyssum with Q10 plus and L-Carnitine on improving the sperm parameters of infertile men in Iran.

Materials and Methods

This three-blind randomized clinical trial study conducted on 75 infertile men referred to Jahrom infertility clinic in 2022. The participants selected by simple random method and assigned to two intervention and control groups. The subjects of the intervention group took herbal drugs includes urtidine (Nettle) and Alyssum. The control group took routine treatment consists Q10 plus and l-carnitine for 12 weeks. Data collected through the standard checklist of semen analysis before and the end of the intervention for both groups. Data were analyzed by descriptive (frequency and percentage) and analytical (Fisher-exact, chi-square, independent t-test and Mann-Whitney U) tests.

Results

The results indicated that the positive effectiveness of Nettle and Alyssum on the improvement of some sperm parameters of infertile men, including volume, sperm shape and motility compared to Q10 plus and L-carnitine. In fact, after the intervention, a statistically significant difference observed in the parameters of sperm in in the intervention group compared to the control group ($p<0/05$).***Conclusions****:* consumption of Nettle and Alyssum improves semen volume, sperm motility and morphology in infertile men. Considering the positive effect of herbal remedies on the spermogram of infertile men, the results of this research along with further studies can use in infertility clinics.

Keywords

male; infertility, Nettle; coenzyme Q10; l-Carnitine.

INTRODUCTION

Infertility is one of the most stressful and complicated experiences in a couple's life. It's a real crisis for infertile couples. Infertility is defined by the failure to achieve a natural pregnancy after 12 months or more of regular unprotected sexual intercourse[1]. In the world, the male factor is responsible for 51.2% and in Iran for 50% of infertility cases. Every single couple out of 10 in search of medical health care guidance due to infertility, where in male factor is associated may lead to infertility. Male infertility aspect is typically distinct by atypical results on semen analysis[1,2]. Infertility can cause stress in couples, producing feelings of sadness,

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panic, disappointment and so on[3]. The cost of infertility treatment is very high and most of the insurance organizations do not have any commitment in this regard [4]. Before starting any infertility treatment in infertile men, first assessment includes semen analysis [1]. Currently, in order to improve the seminal fluid parameters in infertile men used various methods such as hormone therapy, medicinal supplements and antioxidants (Coenzyme Q10 and L-carnitine (LC) [5, 6]. Antioxidants can increase sperm motility and concentration [7]. Low levels of Q10 plus have been observed in infertile men [8]. Contradictory results reported regarding the effect of Q10 plus and L-carnitine on semen parameters. For example, the results showed that treatment with Q10 plus improved semen parameters and antioxidant status [9, 10]. but, other studies did not show any positive influence of coenzyme Q10 on testosterone, semen and the improvement of sperm motility [11, 12]. The result of a study showed L-carnitine significantly improves sperm motility, morphology, concentration and levels of testosterone luteal hormone [13]. In another study, no significant improvement shown in sperm motility [14]. In general, these findings require further confirmation by additional research studies.

In recent years, it reported the side effects of many chemical drugs and their influence on the [15]. Because the high cost of infertility treatment with chemical drugs and existing sanctions in Iran, the tendency to use herbal remedies regimens is increasing for easily access and lower cost and side effects [16,17].

Approximately 80% of the population uses herbal remedies in the world [18]. Stinging Nettle with the scientific name Urtica urens has flavonoid compounds, vitamin C, nitrate, potassium and calcium, which stimulates sexual power [19]. In a study, Nettle significantly increased the number, motility and morphology of sperm in male rats [20]. In another study, the number of abnormal and dead sperm reduced and sperm motility increased [21].

Qadomeh (Todari or Tuzrej) with the scientific name Alyssum contains flavonoid compounds, lecithin, vitamin C and mucilage, and its properties include increasing sexual power, semen fluid and sperm count [22-24]. In a case report study, a significant improvement observed in spermogram indicators with use of a traditional combined drug that Alyssum is one of its components [25].

Effective substances in plants have a biological balance due to the combination with other substances. These substances do not accumulate in the body and do not cause side effects if they used correctly [15]. Nettles and Alyssum probably increase testosterone by inhibiting the activity of aromatase and 5-alpha reductase enzymes due to their flavonoid compounds, vitamin C and antioxidant materials [26]. Despite the effective mechanism of this herbal remedies, no study was found in this field.

The useful impacts of Nettle and Alyssum mentioned in the traditional medicine books. It was limited human studies on the semen parameters. In addition, it is unclear the effect of l-carnitine and Q10 plus on human parameters. According to the mentioned contents and experimental use of this herbal regimes by some women specialist, this study was conducted with the aim of comparing the effects of Nettle and Alyssum with Q10 plus and l-carnitine on sperm parameters of infertile men.

MATERIALS AND METHODS:

This three-blind randomized clinical trial study done from August 2021 to July 2022. In this study, 80 men with a diagnosis of infertility w selected between the people who referred to the women's and infertility clinic of Jahrom city. In this study, a table of random numbers used to assign infertile men to two intervention and control groups. The table of random numbers consists of random numbers 0 to 9, and each of the numbers in this table is repeated the same on average, and there is no recognizable pattern of the number values. The random list was prepared using the random numbers of the table and we assigned each number to a treatment assignment. Now, regarding the two treatments, we assigned the numbers 0-4 for treatment A and the numbers 5-9 for treatment B. We started the list at an optional point of the table that we chose at random. We continued this work until the end of sampling. The sample size estimated based on the study of Mehdiani et al [27] taking into account the confidence interval of 95% and the power of 90% that was 35 people in each group, and considering the dropout rate of 10%, this number was determined to be 40 people in each group. In the next step, after completing the informed consent form, they randomly allocated into two intervention groups (Nettle, Alyssum) and control (Q10 plus, L-carnitine).

Inclusion criteria were complete a written informed consent form, living with a spouse, absence of infertility

in the spouse, Iranian nationality, age 20 to 45 years, disorder in at least one sperm parameter, the absence of pregnancy by the wife after 12 months of sexual intercourse, and the absence of autoimmune diseases, no addiction to alcohol and drugs.

People we excluded from the study if they forgot to take the medicine for two days, possible complications during taking the medicine, and did not want to continue to cooperate.

DATA COLLECTION TOOLS

We used a two-part checklist. The first part: demographic information includes age, weight, height, education level, job, income, type of infertility (primary or secondary), number of children, type of marriage and history of disease, surgery, use of infertility drugs. The second part: spermogram parameters based on Speroff Book Clinical Endocrinology of Gynecology and Obstetrics [28] including: volume, sperm count, sperm motility and sperm morphology.

To perform the procedure, the participants referred to Dr. Houshmand's laboratory located in Jahrom for spermogram after the initial visit by the gynecology and infertility specialist. After receiving the laboratory report and the presence of disturbance in one or more sperm parameters, the participants allocated in two intervention and control groups. Spermogram done for all participants in two stages before and after the implementation of the intervention. The spermogram checklist was completed according spermogram laboratory report before and after the intervention (12 week).

The intervention group received the Nettles in the form of 150 mg Urtidine tablets, 3 time a day and Alyssum in the form of aqueous extract, 1 capsule of 50 mg daily for 12 weeks. In this study control group, received routine treatment includes Q10 plus tablet 100 mg daily and L-carnitine tablet 500 mg daily for 12 weeks. Nettle tablet was available for this research in pharmacies (manufactured by Barij Essan Pharmaceutical Company), but the aqueous extract of Alyssum plant was prepared by the school of Pharmacy in Kerman University of Medical Sciences for this purpose. In relation to the production of Alyssum due to the fact that the seeds of Alyssum contain significant amounts of cyanogenic glycosides that can cause toxic effects, therefore, hot water extract of the plant along with heat was used to remove these compounds. The obtained extract standardized after drying under vacuum and in an oven. Standardization of the plant done by determining major plant compounds (determination of phenolic compounds or mucilage). It noted that the considered dosage for the two herbal remedies Nettle and Alyssum based on the values found in the book of traditional medicine. It is reported there the permissible oral dosage for nettle plant 2-3 grams, twice a day and Alyssum plant 8-12 grams [29, 30]. Authors review other considerations related to the manufacture and use of the drug by Dr. Pharmacognosist (manufacturer of Alyssum drug).

For both groups, to ensure regular and correct medication use, the daily record form provided to the participants and they asked to mark the form every time after taking the medication. In addition, the researcher made telephone calls to the participants of both the intervention and control groups once every 72 hours, in order to answer the questions and check their possible problems, about the regular use of tablets and filling out the daily form. After the completion of the intervention, both groups were re-examined in terms of the imprvoement of Semen parameters by performing a spermogram. The persons including gynecologist and infertility specialist, collecting the spermogram data of the participants and the statistician responsible for data analysis, were unaware of the type of drug used and groups. The data analyzed with SPSS version 24 software and Kolmogorov Smirnoff statistical tests to check the normality of the data, and independent t, Mann-Whitney U, Wilcoxon, chi-square and Fisher. The significance level considered <0.05.

Ethical Clearance

The Ethics Committee of the Rafsanjan University of Medical Science approved the study. (IR.RUMS.REC.1400.05). Patients informed of the purpose of the research. Participants informed of their right to refuse to participate in or to withdraw from the study at any stage. Anonymity and confidentiality of participants maintained.

RESULTS

In this study, out of 80 participants, 75 people completed the study and 5 people were excluded from the study due to not taking the medicine correctly (Figure 1(. The average age of the participants in the intervention group is 32/29 and in the control group 33/76. Infertility period

in the intervention and control group is respectively 34/97and 34/38. Groups did not have statistically significant differences in demographic variables and were homogeneous in this respect (p>0.05) (Table 1). The results indicated that the positive effectiveness of Nettle and Alyssum on the improvement of some sperm parameters of infertile men, including volume, sperm shape and motility compared to Q10 plus and L-carnitine. In fact after the intervention, a statistically significant difference was observed in the parameters of sperm in in the intervention group compared to the control group (Table 2,3).

Table 1: Comparison of the demographic characteristics of the two groups of Intervention and control

Variable		Intervention (38)	control (37)	P value
		N (%)	N (%)	
education	High school	16 (42/10)	14 (37/91)	*0/931
	diploma	14 (36/88)	16 (43/29)	
	Bachelor's degree	7 (18/40)	7 (18/90)	
	Master's degree	1 (2/72)	0 (0)	
Job	Unemployed	1 (2/74)	0 (0)	*0/087
	self-employment	28 (73/73)	34 (91/91)	
	Employee	9 (23/63)	3 (8/19)	
Income	weak	4 (10/519)	8 (21/72)	**0/264
	medium	25 (65/91)	18 (48/65)	
	Good	9 (23/60)	11 (29/63)	
Type of infertility	primitive	26 (68/46)	28(75/64)	**0/609
	Secondary	12 (31/54)	9 (24/46)	
disease History	Yes	2 (5/33)	2 (5/46)	**0/99
	no	36 (94/77)	35 (94/64)	
History of surgery	Yes	9 (23/74)	7 (18/81)	**0/615
	No	29 (76/36)	30 (81/19)	
History use of infertility drugs	Yes	0 (0)	1 (2/76)	*0/232
	No	38 (100)	36 (97/24)	
Type of marriage	family relation	0 (0)	1 (2/77)	**0/308
	No family relation	38 (100)	36 (97/23)	
number of children	0	26 (68/38)	28 (75/79)	*0/199
	1	12 (31/62)	7 (18/81)	
	2	0 (0)	2 (5/40)	

* Fisher-exact** chi-square *** Independent t-test **** Mann-Whitney U

DISCUSSION

This research is the first study that evaluate the comparison of the effects of Nettle and Alyssum with Q10 plus and L-Carnitine on improving sperm parameters of human samples. The results indicated that the positive effectiveness of herbal remedies on the improvement of some sperm parameters of infertile men, including volume, sperm shape and motility. In the books of traditional medicine, there are positive effects of Nettles and Alyssum on fertility, especially males. The results of a study showed that Nettle plant extract significantly reduced the number of abnormal and dead sperm in diabetic rats and increases sperm motility [21]. The results of the case report study indicated a significant improvement in the spermogram indicators (number, motility and morphology) with use of a traditional combined medicine, which Alyssum was one of its ingredients [25]. Nettle and Alyssum probably increase testosterone hormone in men, due to flavonoid compounds, vitamin C and antioxidant properties [26, 31].

One study aimed to determine the effect of Mucuna pruriens seed extract on the sperm quality in mice exposed to cigarette smoke. All groups were exposed to cigarette smoke. Parameters of sperm quality included concentration, morphology, motility and viability. Post hoc tests showed there were significant differences among treatment groups. The use of Mucuna pruriens seed extract containing antioxidants and L-dopa is expected to improve the quality of sperm after exposure to cigarette smoke[32].

Probably the reason for the positive results of our study

Table 2: Inter-group comparison of sperm parameters of infertile men, before and after intervention in the both groups

Time		Before intervention		After intervention		P value Before	P value After
Variable		intervention N (%)	control N (%)	intervention N (%)	Control N (%)		
Liquid volume Seaman	Abnormal (less than 2 ml)	6 (15/80)	10 (27)	0 (0)	12 (32/35)	*0/235 x^2=1/41	* <0/001 x^2=1/46
	Normal (2-6 milliliters)	32 (84/20)	27 (73)	38 (100)	25 (67/65)		
Total sperm count	abnormal (less than 20 million per milliliter)	11 (28/81)	6 (16/20)	5 (13/29)	3 (8/19)	*0/188 x^2=1/73	*0/479 F =0/50
	normal (between 20-80 million per milliliter)	27 (71/19)	31 (83/80)	33 (86/71)	34 (91/81)		
sperm morphology	Abnormal (equal to or less than 4%)	28 (73/73)	20 (54)	8 (21)	16 (43/24)	*0/095 x^2=3/13	*0/039 x^2=4/24
	Normal (more than 4%)	10 (26/27)	17 (46)	30 (79)	21 (56/76)		
Sperm motility	Good (more than 60percent)	2 (5/36)	1 (2/71)	9 (23/77)	4 (10/85)	*0/99 F =0/49	*0/047 F =0/55
	medium (30-50 percent)	26(68/40)	27 (73)	29 (76/23)	29 (78/44)		
	Weak (0-30%)	10 (26/24)	9 (24/39)	0 (0)	4 (10/81)		

* Fisher-exact

Table 3: Intra-group comparison of sperm parameters of infertile men, before and after intervention in the both groups

group		intervention		P value	Control		P value
time		Before intervention N (%)	After intervention N (%)		Before intervention N (%)	After intervention N (%)	
Variable							
Liquid volume Seaman	Abnormal (less than 2 ml)	6 (15/80)	0 (0)	*0.003 F =0/83	10 (27)	12 (32/45)	*0/611 x^2 =0/25
	Normal (2-6 ml)	32 (84/19)	38 (100)		27 (73)	25 (67/55)	
Total sperm count	abnormal (less than 20 million per milliliter)	11 (28/86)	5 (13/21)	*0.103 x^2 =2/66	6 (16/20)	3 (8/18)	*0.282 F =1/15
	normal (between 20-80 million per milliliter)	27 (71/14)	33 (86/79)		31 (83/80)	34 (91/82)	
sperm morphology	Abnormal (equal to or less than 4%)	28 (73/73)	8 (21)	*0.001 x^2 =2/12	20 (54)	16 (43/23)	*0.352 x^2 =0/86
	Normal (more than 4%)	10 (26/27)	30 (79)		17 (46)	21 (56/77)	
Sperm motility	Good (more than 60percent)	2 (5/30)	9 (23/75)	0.001 x^2 =1/46	1 (2/72)	4 (10/82)	0.162 F =3/58
	medium (30-50 percent)	26 (68/41)	29 (76/25)		27 (731)	29 (78/45)	
	Weak (0-30%)	10 (26/39)	0 (0)		9(24/37)	4(10/83)	

* Fisher-exact

with other studies is the combined use of antioxidants, their synergistic effect and the difference in the dosage and duration of the drugs usage. The results of this study can use as a basis course in university education, infertility fellowships and the pharmaceutical industry. One of the important goals of any research is to use its results in practice, to improve the current situation and solve existing problems. The results of this research can use in infertility clinics. Moreover, more studies needed in this field.

Among the limitations of our study, there was a possibility of dropping participants due to the use of drugs for 12 weeks, and in order to eliminate or reduce this limitation, the drug use checklist provided to the participants and the researcher contacted them by phone. Another limitation of this plan was the impossibility of having a third group (placebo). Because this plan is a clinical and human trial plan, and depriving the participants of the existing and routine treatment and using a placebo is beyond the scope of ethical considerations.

CONCLUSION

consumption of Nettle and Alyssum improves semen volume, sperm motility and morphology in infertile men. Considering the observed effect of herbal remedies on the process of improving the spermogram of infertile men, the results of this research along with further studies can use in infertility clinics.

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Conflict of Interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

Author contribution

Data gathering and idea owner of this study: MK, AR

Study design: MK, AR, ML

Writing and submitting manuscript: MK

Editing and approval of final draft: MK, AR

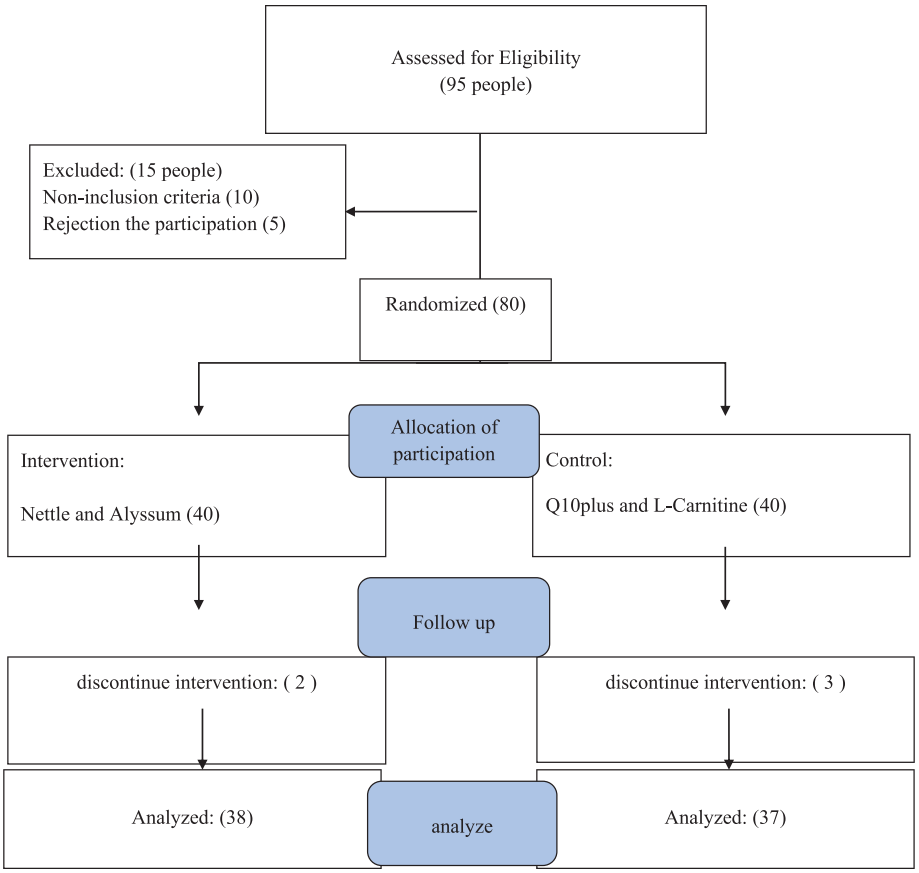

Figure 1: Consort chart study

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