The Role Folic Acid and Zinc Sulphate in the Treatment of Idiopathic Infertility (A Local Study)

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ABSTRACT
Objective: to evaluate the affect zinc sulphate and folic acid handling on the seminal fluid factor in patients with idiopathic male infertility.

Patients and methods: From February 2013 to February 2020, 700 patients with idiopathic primary infertility, presented to Al Yarmouk teaching hospital and Al Ramadi teaching hospital in addition to 3 private clinics were enrolled in this prospective study, their age ranged from 17 to 56 years, Semen evaluation done for all patients at the start of study (baseline) and after three months of treatment. The patients received folic acid 5 mg and zinc sulphate 60 mg prepared in special capsules once daily for 3 months.

Results: Seven hundreds patients completed the treatment period for 3 months. The age of patients ranged from 17 to 56 years, there was statistically significant difference in the sperm concentration after treatment compared to baseline and also statistically significant difference in the perm motility after 3 months treatment period (p value < 0.05). The increment in the percentage of normal morphology was statistically non-significant, and also the slight increase in the seminal fluid volume was non-significant (p value > 0.05).

Conclusion: Handling of idiopathic male infertility with combination of zinc sulphate and folic acid was safe and effective in improving seminal fluid parameters.

Key words: folate, zinc, idiopathic, infertility

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INTRODUCTION
Infertility is failure to get pregnancy after one year of unprotected sexual intercourse. Men contribute equally to women as a cause of infertility123.

The infertility is idiopathic when no cause can be identified despite great efforts in searching for the underlying cause4. Most studies demonstrate the critical role of nutrition in the normal function of the reproductive system56. There is increasing evidence that indicates the detrimental effect of nutrition in poor sperm quality56. Nutrition is an important factor in the synthesis of DNA, as most of the essential components of DNA are derived from the dietary sources. Also most of the enzymes utilized the synthesis of DNA are vitamin B and zinc dependent and certainly the DNA synthesis is significant for the improvement of sperms56.

Folate (vitamin B9) is found naturally in different types of foods, including legumes, leafy green vegetables, beef liver, beets, eggs, and yeast. Folate is significant for the synthesis of DNA, transfer RNA and the amino acids methionine and cysteine. Folic acid which is the synthetic form of folate, is effective scavenger of oxidizing radicals free and can be considered anti-oxidant57.

Zinc is a trace microelement needed in the body and it is found in Shellfish, meat, poultry, fish, legumes, eggs and whole grains56. More than two hundred enzymes involved in several biochemical methods in the body are reliant on zinc56. Too because of the concentration of zinc is too great in male genital organs similar prostate, testes and in the sperms theme self, its role in male reproduction cannot be denied56.

The synthesis of DNA has crucial part in the development of the germ cells, and therefore, it is obvious that folic acid and zinc are important for male reproduction and they part in the empirical therapy of idiopathic man infertility should not be forgotten so we performed this study to highlight the effect of folic acid and zinc in the therapy of idiopathic man infertility.

PATIENTS AND METHODS
From February 2013 to February 2020, 700 patients with idiopathic primary infertility, presented to Al Yarmouk teaching hospital and Al Ramadi teaching hospital in addition to 3 private clinics were enrolled in this prospective study, their age ranged from 17 to 56 years, baseline evaluation done for all patients including history and general physical examination and focused genital examination, also endocrine evaluation was done to exclude hormonal abnormalities in addition to scrotal duplex ultrasonography in selected cases. Semen evaluation done for totally patients at the start of study (baseline) and after 3 months of treatment with abstinence period of 3 days, and the results evaluated according to the fifth edition of the WHO laboratory manual123.

Patients with varicoceles, abnormal hormonal evaluation, B12 deficiency, chronic drug use, drug allergy, history of cryptorchism, scrotal surgery, hypospadias, and trauma were excluded from this study. And all patients should have no medical for three months before starting the study treatment. The patients received folic acid 5 mg and zinc sulphate 60 mg prepared in special capsules for 3 months, the dose of zinc was carefully selected, because undue raised level of plasma seminal zinc decreases sperm motility123. The changes in the seminal fluid parameters before and after treatment were evaluated.

Informed consent signed by each patient, and study ratified via the moral committee in the college of medicine. Analysis of result was loading out utilizing the obtainable statistical parcel of SPSS-25. result was approaching in...
measures simple of mean, range and standard deviation. Statistical importance was look whenever the value P was equal or lower than 0.05.

RESULTS
From total of 850 patients screened for this study, 700 patients fulfilled the inclusion criteria and completed the treatment. The age of patients raged from 17 to 56 years, they wear statistically important variance in the sperm concentration after treatment compared to baseline (p value <0.05).

There was statistically significant difference in the perm motility after 3 months treatment period (p value <0.05). The increment in the percentage of normal morphology after receiving treatment for 3 months was statistically non significant, and also the slight increase in the seminal fluid volume was non significant (p value >0.05). Table 1 and figure 1

Table 1: The changes in the seminal fluid parameters before and after treatment

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>After treatment for 3 months</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sperm concentration (10^6/ml)</td>
<td>13±14.1 (10-75)</td>
<td>20±22.9 (14-120)</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Motility (%)</td>
<td>25±6.7 (0-31)</td>
<td>34±7.9 (10-50)</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Morphology (%) strict criteria</td>
<td>9.98±13.97 (4-16)</td>
<td>11.95±14.09 (4-18)</td>
<td>0.23</td>
</tr>
<tr>
<td>Volume (ml)</td>
<td>2.99±0.66 (1-4)</td>
<td>3.63±0.34 (1-4)</td>
<td>0.98</td>
</tr>
</tbody>
</table>

- Data were presented as Mean±SD (Range)

*Highly significant difference between two dependent means using Paired-t-test at 0.05 level

DISCUSSION

There are many findings indicate that nutrition is one of the most ecological parameter affecting the health of the generative method, so it looks worthy to include dietary supplements in the therapy protocols of man infertility. Zinc is vital for the processes of spermatogenesis. It shows an important part in the testes improvement and spermatogenic physiological functions. Zinc has anti-apoptotic properties. Folate is important for DNA synthesis and deficiency folate increases apoptosis. Both folic acid and zinc have antioxidant activity by which these nutrients can affect apoptosis. Apoptosis is also related to some forms of man parameter infertility. The therapy of idiopathic infertility is usually empirical as no underlying cause is identified. The use of combination of folic acid and zinc in our study resulted in significant improvement in the seminal fluid parameters including the sperm count and motility, and these findings are consistent of that of Wong et al. who demonstrated important rise in the sperm count in sub fertile group receiving zinc and folic acid also increase in the motility although this increase was statistically non-significant. And also consistent with results of Jawad HM who reported that the treatment with zinc sulphate decrease the antisperm antibodies and increases the seminal fluid parameters including the concentration and motility but the study used only zinc and in patients with increased antisperm antibodies.

There are several studies appeared that folate has a part in spermatogenesis supporting our finding. Several studies demonstrate that zinc enhances sperm mobility through ATP system and phospholipid, reduce the incidence of anti-sperm antibodies and improves the sperm...
quality and fertilization capacity, these results support our findings.\textsuperscript{19-21} The observations of these studies support the results of the current study. The treatment course was uneventful and treatment was tolerable with no serious side effects. More studies are required to assess whether these improvement in the seminal fluid parameter has positive effect on the rate of conception.

**CONCLUSION**

Handling of idiopathic man infertility with permutation of zinc sulphate and folic acid was effective in improving seminal fluid parameters and also safe as there was no serious side effects.

**REFERENCES**


