



## STUDY OF THE FERTILITY POTENTIAL IN OLIGOSPERMIA WITH HERBAL DOSAGE FORM DESIGN

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### ABSTRACT

Background - Men worldwide are confronted with oligospermia which is seriously disturbing factor and requires preference of treatment. The Department of Clinical Sciences, Faculty of Eastern Medicine has undertaken a task to conduct the research with Unani Medicine on clinical evaluation of male infertility. Methods -We conducted a Case control direct, uni-centre, prospective, randomized authentic herbal controlled, two arm parallel group clinical trial at multi-ceterr clinics in Karachi, Pakistan. Patients (25 years and 45 years) with clinical diagnosis of idiopathic oligospermia (n=50) were randomly assigned to receive 3gm B.D. powder of Spermogen twice a day and ProXeed B.D. twice daily. The study period was 3 years with a window for the follow up visit every month accounting for variable for semen analysis outcome measure.

Results-Comparison of showed highly significant differences between test and control groups in total count of sperm and live count of sperm ( $p < 0.001$ ,  $p < 0.000$ ) respectively. Whereas, in rapid linear progression of motility was observed equal in both treatment group ( $p > 0.05$ ). All these data were analyzed by Chi-square test and Fisher's Exact Test and obtained p values and the level of significance were applied.

Conclusion-Spermogen is as effective as the ProXeed in the treatment of Idiopathic of Oligospermia. There was no untoward manifestation associated with the use of Spermogen and found a good acceptability by all treated patients.

**Key words:** Idiopathic Oligospermia, Herbal medicine, ProXeed

### INTRODUCTION

Idiopathic oligospermia is one of the major cause in male infertility. Despite the broad use of Unani Medicine treatment there is relative paucity of data available to demonstrate convincingly the safety, efficacy, effectiveness of these Unani practices. Therefore, systematic analysis of alternative treatment male infertility will be targeted and rigorous clinical investigation of Unani Medicine as compared to alternative medicine has been conducted. Specific objective for the current research was undertaken an intervention to facilitate the design and conduct of randomized, control trial. The focus was on research methodology, biostatistics, clinical trial design and laboratory methods that relate to Unani and alternative medicine. Significance of the research on male oligospermia is to address problems *vis a vis* Unani and alternative medicine covering study design and procedures, clinical trials, outcome measure, inclusion and exclusion criteria and data analysis of the ailment.

The literature search obtained from NAPALERT data (Natural Product Alert Database, University of Illinois at Chicago) revealed that many plants are used for the treatment of

male infertility. Out of the list plants *Cheiranthus cheiri*, *Withania somnifera*, *Tribulus terrestris*, *Orachis litifolia Orachis*, *Sida cordifolia*, and *Sesamum indicum Linn* has been selected to formulate a coded herbal formulation designated as Spermogen.

*Cheiranthus cheiri* has a long history of usage to treat spermatorrhoea and increases semen production<sup>1</sup>. In the literature study of *Withania somnifera* concluded that the essence used as an effective herbal drug for spermatorrhoea<sup>2</sup>. *Tribulus terrestris* is also prescribed for the same<sup>3</sup>. Protodioscin, an active principle in *Tribulus terrestris*, is converted to DHEA (De-Hydro-Epi-Androsterone), which is a precursor of testosterone, and thus improves sexual desire and sperm production. Studies show that adequate levels of testosterone stimulate the production of vasoactive substances like nitric oxide, resulting in satisfactory erection<sup>4</sup>. A study showed that treatment with this herb increased the intracavernous pressure in the penis and enhanced sexual behaviour. This is possibly due to the herb's ability to increase androgen (testosterone) levels and the subsequent release of nitric oxide from the nerve endings innervating the corpus cavernosum, resulting in improved blood flow to the penis and in

turn improvement in the functioning of the musculature in the penile region<sup>5</sup>.

*Orachis litifolia Orachis* has long been known for its value in cases of sexual weakness<sup>6</sup>. *Sida cordifolia* have fertility enhancing functions and it helps balance proper amounts of the male hormone, testosterone, and increases sexual desire<sup>7</sup>. *Sesamum indicum* medicinally the seeds is valued on account of its aphrodisiac nature have male fertility activity<sup>8</sup>.

ProXeed is a male fertility dietary supplement clinically recommended by thousands of physicians for optimizing sperm quality. The Ingredients of ProXeed® Plus: Supporting Male Fertility by Optimizing Sperm Health and fertile men<sup>9</sup>.

### Material and Method

#### Study design

This was a case control direct multi-center prospective examination based study, conducted in Karachi, on the patients living in urban areas and belonging to good socio-economic middle and upper middle class.

Patients were randomly assigned to one of two treatment groups: those receiving coded herbal formulation spermogen labeled as Test group, while those administered dietary supplement dosage form design ProXeed marked as Control group.

Detailed history was taken from every patient and only those were selected who were willing to give their written consent and would fulfill the inclusion criteria. Study was approved by the medical ethics committee of Faculty of Medicine, Hamdard University. The study period include 3 years time October 2006 to October 2009.

#### Patients

Patient with decreased sperm count < 20 Million/ml presenting Oligospermia as cause of infertility with the age 25-45 included in the study. Total 50 patients screened 25 patients in each group.

#### Setting

The sample was selected from the out patient enrolled in at Matab Hamdard on the basis of preliminary clinical examination. Each subject was asked to abstain for 48 – 72 hour prior to their visit to the infertility center and was asked to collect the semen sample in glass container. The sample was then analyzed for physical

examination and microscopic examination. Blood sample were taken only at the initial visit for the hormonal level of FSH, LH, Prolactin and testosterone.

**Clinical Assessment**

The main outcome measures were: It includes total sperm counts, live counts, motility and rapid linear progression. Data collected for this study included filling of clinical trial proforma through counseling, personal observation, use of case record, file and documents. The clinical trial proforma attached here which clearly specifies the clinical feature and information. Calculation of the class interval from the formula  $(1 + 3.3 \log (n))$  and find out the range from the formula (largest observation – Smallest observation) and to find out the class size from the formula (Range / Class Interval). This article will define sperm quality, summarize fertility research for men using various nutritional supplements, then compare the industry standard nutritional supplement - ProXeed™ - with coded herbal formulation spermogen.

**Statistical Analysis**

Statistical analysis were performed using SPSS using excel software, the Chi Square Test. Test were employed. All differences were considered statistically significant by generating a p value from test statistics. The significant result with p value less than 0.05 was defined as statistically significant.

**Study Limitations**

The data was adjusted based on the number of cases in the light of demographic factor using statistical methods like multinomial logistic regression. The data were composed in separate group. These groups were compared after random selection of subject in equal proportion using SPSS software. The subject were divided into two groups the case and the control groups.

**Ethical Issues**

Ethical committee clearance and permission was obtained

**Investigations**

Hormonal level in blood sample was analyzed by using standard procedure for some of the patients as required. Hormones that were taken in to account were FSH, LH, Testosterone and Prolactin. Physical examination and Microscopic examination of semen sample were performed in routine laboratory before and after treatment.

**Inclusion Criteria**

Following protocols were observed as inclusion criteria;

1. Infertile patient having oligospermia (Sperm count < 20 Million/ml).
2. Healthy, men aged 25–45 years living in a stable relationship and desiring fertility.
3. Male partner was asked to submit the pathological report of female partner prior to entry in study.
4. Patient willing to provide written consent.

**Exclusion Criteria**

The major exclusion criteria for this trial were:

1. Patient having history of undescended testicles and teruma to testis, excessive radiation to testis and uncorrected bilat cryptorchidism.

2. Patient on cytotoxic drugs, alcohol and spiro lactone.
3. Patient of alpha blockers and on Anti tuberculosis treatment.
4. Patient suffering from autoimmune diseases or paraplegia.
5. Patient hooked on hormonal treatment
6. Any pathology with female partner.

**Results and Discussion**

This study was under taken as clinical evaluation of effect of herbal medicine on quantity and quality of sperm male idiopathic oligospermia. An attempt has been made to explore the performance of unani (test drug) and authentic (control) medicine so as to asses their efficacy.

**Patient's Recruitment**

The intent-to-treat population consisted of 70 patients enrolled: 25 were treated with coded herbal formulation Spermogen, and 25 were treated with ProXeed. 10 (in test group) and 10 in the (control group) were lost to follow-up and therefore not evaluable. To find out the therapeutic evaluations of these medicines 50 patients were examined clinically and laboratory investigations of semen analysis are taken during the course of treatment.

**Table 1: distribution of age group**

| Age Group     | Treatment Group |         | Total |
|---------------|-----------------|---------|-------|
|               | Test            | Control |       |
| 25 – 28 Years | 3               | 2       | 5     |
| 28 – 31 Years | 6               | 7       | 13    |
| 31 – 34 Years | 13              | 2       | 15    |
| 34 – 37 Years | 0               | 6       | 6     |
| 37 – 40 Years | 1               | 5       | 6     |
| 40 – 43 Years | 2               | 3       | 5     |
| 43 – 45 Years | 0               | 0       | 0     |
| Total         | 25              | 25      | 50    |

**Demographic Characteristics of Patients**

All the patients were clearly categorized as having idiopathic oligospermia. The demographic and baseline characteristics of the patients included in the groups evaluable for efficacy were found to be similar for the two treatment groups and were comparable to those of the intent-to-treat population as  $p > 0.05$ . All of the patients recruited in this study were categorized in different class interval ranging from 25 years of age to 45 years of age. All patients had married and having no child, which were almost same in both treatment groups as  $p > 0.05$

**Clinical Response Before and After Treatment**

All patients were examined for different semen parameters as semen quantity, total sperm counts, live counts, sperm per ejaculate, and rapid linear progression semen color, semen transparency, semen viscosity on physical examination and in semen fructose on chemical assessment as delineated in table 2-6. All variables were equally balance in both treatment groups before treatment.

Both medications caused a significant improvement in all the variables after treatment. Improvement seen in both treatment groups after therapy (Table 2-6). The rates of Improvement were equal in both treatment group at all times after treatment ( $p > 0.05$ ) in all variables except in total sperm count which was higher in test group ( $p < 0.05$ ).

**Table 2: Semen Quantity in Total Patients.**

| Semen Quantity | Treatment Group  |                   | Total | p value |
|----------------|------------------|-------------------|-------|---------|
|                | Test (Spermogen) | Control (ProXeed) |       |         |
| Baseline       | < 2ml            | 07                | 07    | 0.723   |
|                | 2ml - 4ml        | 13                | 15    |         |
|                | > 4ml            | 05                | 08    |         |

|                 |           |    |    |    |       |
|-----------------|-----------|----|----|----|-------|
|                 | Total     | 25 | 25 | 50 |       |
| After Treatment | < 2ml     | 05 | 04 | 09 | 0.459 |
|                 | 2ml - 4ml | 18 | 16 | 34 |       |
|                 | > 4ml     | 02 | 05 | 07 |       |
|                 | Total     | 25 | 25 | 50 |       |

Table 3: Total Counts in All Patients.

| Total Counts    | Treatment Group  |                   | Total(n) | p value |      |
|-----------------|------------------|-------------------|----------|---------|------|
|                 | Test (Spermogen) | Control (ProXeed) |          |         |      |
| Baseline        | < 20millions/ml  | 09                | 10       | 19      | 0.77 |
|                 | >= 20millions/ml | 16                | 15       |         |      |
|                 | Total            | 25                | 25       |         |      |
| After Treatment | < 20millions/ml  | 00                | 07       | 07      | 0.01 |
|                 | >= 20millions/ml | 25                | 18       |         |      |
|                 | Total            | 25                | 25       |         |      |

Table 4: Live Counts in Total Patients line.

| Live Counts     | Treatment Group  |                   | Total(n) | p value |      |
|-----------------|------------------|-------------------|----------|---------|------|
|                 | Test (Spermogen) | Control (ProXeed) |          |         |      |
| Baseline        | < 20millions/ml  | 15                | 18       | 33      | 0.37 |
|                 | >= 20millions/ml | 10                | 07       |         |      |
|                 | Total            | 25                | 25       |         |      |
| After Treatment | < 20millions/ml  | 01                | 12       | 13      | 0.00 |
|                 | >= 20millions/ml | 24                | 13       |         |      |
|                 | Total            | 25                | 25       |         |      |

Table 5: Sperm per Ejaculate in Total Patients.

| Sperm Per Ejaculate | Treatment Group         |                  | Total(n) | p value |      |
|---------------------|-------------------------|------------------|----------|---------|------|
|                     | Test (Spermogen)        | Control(ProXeed) |          |         |      |
| Baseline            | <40 Millions/Ejaculate  | 05               | 08       | 13      | 0.33 |
|                     | >=40 Millions/Ejaculate | 20               | 17       |         |      |
|                     | Total                   | 25               | 25       |         |      |
| After Treatment     | <40 Millions/Ejaculate  | 03               | 05       | 08      | 0.43 |
|                     | >=40 Millions/Ejaculate | 22               | 20       |         |      |
|                     | Total                   | 25               | 25       |         |      |

Table 6: Rapid Linear Progression in Total Patients.

| Rapid Linear Progression | Treatment Group  |                   | Total (n) | p value |       |
|--------------------------|------------------|-------------------|-----------|---------|-------|
|                          | Test (Spermogen) | Control (ProXeed) |           |         |       |
| Baseline                 | < 25%            | 24                | 24        | 48      | 1.00  |
|                          | >=25%            | 01                | 01        |         |       |
|                          | Total            | 25                | 25        |         |       |
| After Treatment          | < 25%            | 09                | 15        | 24      | 0.088 |
|                          | >=25%            | 16                | 10        |         |       |
|                          | Total            | 25                | 25        |         |       |

The outcome from this research demonstrated that there was no statistically significant difference when comparing the effectiveness of Spermogen for idiopathic oligospermia to ProXeed treatment for the same type of disorder. This is clearly evident that Spermogen proved to have a therapeutic value for the treatment of idiopathic oligospermia leading to increase in sperm count. The objective of Spermogen (test drug) was compared to ProXeed (control drug) to determine that it can be beneficial in addressing the infertility in males. This is an exercise of applying herbal medicine as a clinical design to prove its usefulness in conception to bear child by female partner. The efficacy of Spermogen formulation is characteristic of many chemical compounds of different classes present in different medicinal material formulated and used as multiple dosage form design.

## CONCLUSION

Spermogen is as effective as the ProXeed in the treatment of Idiopathic of Oligospermia. There was no untoward manifestation associated with the use of Spermogen and found a good acceptability by all treated patients.

## REFERENCES

1. Usmanghani K, Saeed A, Alam MT, Indusyunic Medicine. Research Institute of Indusyunic Medicine, Karachi, Pakistani, 1997. p 601.
2. Kabiruddin M, Kitabul Advia Mukhzanul Muffradata. Dafter Al-Masih, Delhi, India, 1937. p123.
3. Usmanghani K, Abdul Hannan, Farhana Shafique, Aslam MG, Cultivation of Medicinal Plant, MINFAL Research Project Hamdard University, Karachi, Pakistan. 2007. p309.
4. Caretta N, et al. Erectile dysfunction in aging men. Testosterone role in therapeutic protocols. *J Endocrinol Invest.* 2005;28(11 Suppl bis):108-11.
5. Gauthaman K, et al. Sexual effects of puncturevine (*Tribulus terrestris*) extract (protodioscin): an evaluation using a rat model. *J Altern Complement Med.* 2003;9(2):257-65.
6. Subhose V, Narian A. Basic principles of pharmaceutical science in Ayurveda. *Bull Indian Inst Hist Med Hyderabad,* 2005, 35: 83.
7. Adimoelja A. Phytochemicals and the breakthrough of traditional herbs in the management of sexual dysfunctions. *Int J Androl.* 2000;23 Suppl 2:82-84.
8. The Wealth of India, A Dictionary of Indian Raw Materials and Industrial Products, vol 9, Council of Scientific and Industrial Research, New Delhi. 1969.
9. Mazhar M, Saghir AJ, Abdus SS, Sadia A, Farah D, Khurram S, Pak J Med Sci.2007; 23 (6), 840-846.