

Indian Clinical Experience on Innovative Product in Treatment of Male Infertility

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ABSTRACT

Rising number of infertile males in India provokes the need of evidence-based comprehensive formula addressing unattended causes of male infertility. There is an innovative product*, a combikit available in Indian market, containing 30 tablets of antioxidant, multivitamin, amino acid and mineral tablets, with documented evidence on ingredients in treatment of male infertility, and 25 tablets of clomiphene citrate which is a time-tested drug in treatment of male infertility (in particular oligospermia and/or asthenospermia). In order to assess efficacy of the product in Indian infertile male patients, we undertook phase IV multicentric clinical study, at 18 centers across India in 100 patients.

Very high couple pregnancy rate of 53% was reported. As first line treatment of male infertility (in particular oligospermia and/or asthenospermia), the use of this innovative product therefore holds a strong promise.

Keywords: Male infertility, Combikit, Couple pregnancy rate.

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INTRODUCTION

Male infertility is rising phenomenally in India. Although products are available, it is observed that hyperhomocysteinemia, oxidative stress, amino acid and mineral deficiency which are the independent causative factors for male infertility^{1-3,13} are not being addressed by one comprehensive product in the routine management of male infertility.

There is an innovative product available in Indian market, launched for the first time in the year 2009. The product is a combikit containing 30 tablets of fixed dose combination of antioxidants, multivitamin, amino acid and mineral (each tablet containing zinc sulphate—66 mg, folic acid—5 mg, methylcobalamin—1500 µg, pyridoxine—1.5 mg, coenzyme Q₁₀—60 mg, Lycopene—4 mg, selenium—200 µg, L-carnitine tartarate—50 mg, L-arginine—20 mg), with documented evidence on ingredients in treatment of male infertility and 25 tablets of clomiphene citrate (25 mg) which is a time tested drug in treatment of male infertility (in particular oligospermia and/or asthenospermia). To assess efficacy of this

product in Indian male infertile patients, a multicentric study was planned.

MATERIALS AND METHODS

This was a phase IV, multicentric clinical study carried out at 18 centers across India. The cities included in the study were Mumbai, Pune, Nagpur, Kolkata, Ahmedabad, Midnapur (West Bengal), Gangtok, Indore, Ankleshwar (Gujarat), Allahabad, Kondagaon (Chhattisgarh), Jaunpur (UP), Dombivali (Maharashtra).

One hundred married men with oligospermia (sperm count less than 20 million/ml of semen but above 1 million/ml after Percoll centrifugation; gradient 40/90) and/or asthenospermia with sperm motility less than 50% progressive or less than 25% rapidly progressive were enrolled in the study and all of them completed the study.

The exclusion criteria were as follows:

- Greater than 20% antibodies present on the spermatozoa after processing with Percoll centrifugation.
- Greater than 50% of spermatozoa without an acrosome.
- Patients with sertoli cell-only syndrome, testicular malignancy or varicocele and those receiving chemotherapy or radiotherapy.
- Teratospermia—normal morphology found in less than 30% of spermatozoa.
- Subjects who, within 3 months before enrollment, were treated with any drugs indicated to increase sperm count or motility.

After enrollment, the baseline characteristics, like age, weight, history of infertility, were documented. Mean age of all the married men enrolled in the study was 31 years of age. 51.8% men suffered from 1 to 5 years of infertility. 48.2% men suffered from more than 5 years of infertility. The baseline characteristics of the patients are given in Table 1.

All the infertile married men enrolled in the study received study medication. Each patient had to consume two tablets, one brown colored antioxidant, multivitamin, amino acid and mineral tablet to be taken once daily and second white colored tablet of clomiphene citrate 25 mg to be taken once daily for

Table 1: Baseline characteristics of married men suffering from infertility

Mean age (years)	31
Weight (kg)	64.8
1-5 years of infertility	51.8%
More than 5 years of infertility	48.2%

* Productiv M

25 days followed by 5 days abstinence. The therapy was to be continued for 6 months. After baseline, the patient had to visit the clinic after completing 3 months treatment as well as 6 months treatment. During this visit, sperm count and sperm motility were documented in the case report form. The overall study design is given in Figure 1.

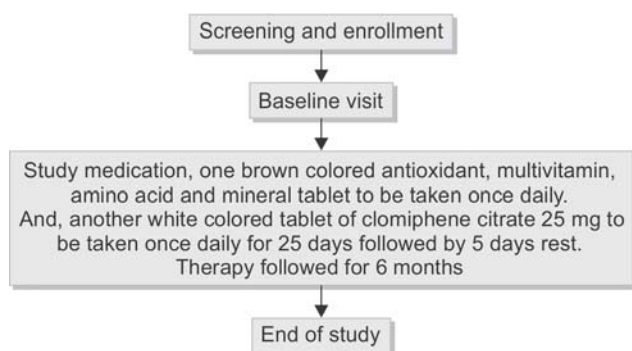


Fig. 1: Overall study design

Whether the female partner of the male subject enrolled in study conceived during treatment and at which month was recorded.

Any adverse effects if observed were recorded and whether the adverse effect was causally related to the treatment was reported. Any concomitant medications, if taken, were also recorded mentioning its name, dose, duration and the condition for which it was prescribed.

RESULTS

After 6 months of therapy, very high couple pregnancy rate of 53% was reported. The month of conception details are as mentioned below.

Out of 53 couples, who conceived during the treatment, 18 conceived at the end of 1st month, five conceived at the end of 2nd month, 10 conceived at the end of 3rd month, seven conceived at the end of 4th month, two conceived at the end of 5th month and 11 conceived at the end of 6th month.

DISCUSSION

Even with newer and newer technological advances in the male infertility, evidence-based oral product which proves to be a first line treatment for management of male infertility is still the need of time. Also, it is observed that hyperhomocysteinemia, oxidative stress, amino acid and mineral deficiency which are the independent causative factors for male infertility are not being addressed by one comprehensive product in the routine management of male infertility. There is an innovative product* which is available in Indian market since 2009. This is combikit containing 30 – antioxidants, multivitamin, amino acid and mineral tablets, with documented evidence³⁻¹² on ingredients in treatment of male infertility and 25 tablets of clomiphene citrate which is a time tested drug in treatment of male infertility (in particular oligospermia and/or asthenospermia). For a product, for treatment of male infertility, the best way to assess the efficacy is to assess the couple pregnancy rate.

In this phase, IV multicentric study carried in 100 infertile males at 18 centers across India, the reported couple pregnancy rate is 53%. This is a very high couple pregnancy rate reported during just 6 months of treatment. Data on sperm count and sperm motility on treatment were available only for eight patients. Yet, there was a good rise reported in these parameters too. Percent increase in sperm count over baseline was 125.8% and percent increase in sperm motility over baseline was reported to be 19.27%.

CONCLUSION

Success of male infertility treatment is best judged by the couple pregnancy rate. This phase IV multicentric study evaluated 6 months therapy of innovative product in treatment of 100 infertile males (suffering from oligospermia and/or asthenospermia). This product* is a combikit containing 30 – antioxidants, multivitamin, amino acid and mineral tablets, (each tablet containing zinc sulphate—66 mg, folic acid—5 mg, methylcobalamin—1500 µg, pyridoxine—1.5 mg, coenzyme Q₁₀—60 mg, lycopene—4 mg, selenium—200 µg,

	Males		Study group
	Males (N)		100
Did the couple conceive?	Yes N (%)		53 (53)
	No N (%)		47 (47)
What duration did couple conceive after starting treatment?	N (%)		18 (34.0)
After 1 month	N (%)		5 (9.4)
After 2 months	N (%)		10 (18.9)
After 3 months	N (%)		7 (13.2)
After 4 months	N (%)		2 (3.8)
After 5 months	N (%)		11 (20.7)
After 6 months	N (%)		
Increase in sperm count over baseline (%) [#]		Increase in sperm motility over baseline (%) [#]	
125.8%		19.27%	

[#]N—represents number of cases; (%)—represents percent of those cases out of total population; [#]Data on 8 patients; No adverse events were reported during the treatment period

* Productiv M

L-carnitine tartarate—50 mg, L-arginine—20 mg) with documented evidence¹⁴⁻²⁸ on ingredients in treatment of male infertility and 25 tablets of clomiphene citrate 25 mg which is a time tested drug in treatment of male infertility. 53% couple pregnancy rate was reported with the study treatment. Data on eight patients also reported 125.8% increase in sperm count over baseline and 19.27% increase in sperm motility over baseline.

With a phenomenally high couple pregnancy rate in this study, this innovative product* available in Indian market containing 30 – antioxidants, multivitamin, amino acid and mineral tablets and 25 tablets of clomiphene citrate as a monthly therapy, holds a strong promise for being first line treatment of male infertility (in particular oligospermia and/or asthenospermia).

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