

IMPROVED FERTILITY IN OLIGOSPERMIC MALES TREATED WITH CLOMIPHENE CITRATE

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Significant improvements in oligospermia and asthenospermia can be achieved in men without elevation of base line gonadotropin levels or evidence of anatomical abnormalities by treatment with repeated cycles of clomiphene citrate, 25 mg daily for 25 days, with 5 days' rest.

The efficacy of clomiphene citrate in the treatment of male infertility is still very controversial.¹⁻⁶ Some of the discrepancies may be explained by differences in dosage and duration of treatment. Recently, Paulson and Wacksman⁶ reported an improved count in 31 of 35 men and improved motility in all but 2 men using a dosage schedule for up to 12 months of 25 mg daily for 25 days, then 5 days' rest. However, the fertility rate was only 23%. Although most of the wives in the study by Paulson and Wacksman were considered fertile, it is possible that a gynecologic endocrinologist might have detected some subtle defects.

The present study reports our experience with clomiphene citrate in oligospermic and asthenospermic males using 25 mg for 25 days, with 5 days' rest, for up to 7 months. We report a significantly improved fertility rate when the wives were simultaneously evaluated by a gynecologic endocrinologist.

MATERIALS AND METHODS

The subjects in the study were couples referred for primary infertility. If the husband had a varicocele or if his gonadotropin levels were elevated he was not given clomiphene citrate. No

man was treated with clomiphene for longer than 7 months.

Each man was evaluated by complete history and physical; in most instances, base line serum luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone, and thyroxin (T₄) levels and triiodothyronine (T₃) uptake were determined. In some cases 24-hour urinary 17-ketosteroid and pregnanetriol measurements were obtained.

Each wife had a complete history and physical examination. Ovulation was investigated by basal body temperature charts, vaginal hormonal cytology, urinary pregnanediol determinations, and endometrial biopsy. Cervical mucus was extracted at midcycle and examined for spinnbarkeit, ferning, quantity, cellularity, and sperm viability and motility by postcoital or in vitro testing, using husband's or donor sperm. Tubal patency was established by hysterosalpingography. When there were clinical suspicions for tubal adhesions or endometriosis, a laparoscopy was performed.

RESULTS

A comparison of the spermograms before and after clomiphene therapy is shown in Table 1. Nine of the ten couples achieved a pregnancy within the first 7 months of clomiphene therapy in the husbands. In seven of the nine couples there

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TABLE 2. Associated Fertility Problems in Wives

Patient	Duration of infertility	Infertility problem	Treatment
1	3 ^{yr}	Anovulation	Clomiphene citrate, 150 mg × 5 days
2	4	Inadequate corpus luteum	Low-dose estrogen
3	4	Endometriosis, tubal adhesions, inadequate corpus luteum	Clomiphene citrate, 50 mg × 2 days, 100 mg × 3 days
4	1	Cervical stenosis	Cervical dilatation prior to ovulation
5	3	Anovulation, hostile cervical mucus, only 1 tube patent	Clomiphene citrate, 100 mg × 5 days; human chorionic gonadotropin, 5,000 U 5 days after stopping clomiphene; conjugated estrogens, 3.75 mg beginning day after stopping clomiphene; donor cervical mucus
6	2	Anovulation	Clomiphene citrate, 150 mg × 5 days; conjugated estrogens, 1.25 mg for 1 week after
7	2	Anovulation	Clomiphene citrate, 100 mg × 5 days; conjugated estrogens, 1.25 mg × 8 days
8	1.5	Inadequate corpus luteum	Clomiphene citrate, 50 mg × 5 days
9	2	Inadequate corpus luteum	Clomiphene citrate, 50 mg × 5 days
10	2	Anovulation, hostile cervical mucus	Clomiphene citrate, 150 mg × 5 days, + human chorionic gonadotropin, 10,000 U, + conjugated estrogens, 5 mg × 8 days; mucus still very poor

The disappointing thing about the results of Paulson and Wacksman* was that only 23% of couples achieved a pregnancy. In our experience, even if no therapy at all is used, close to this percentage will achieve a pregnancy over a 9-month period.

Although it is possible that an even better dosage schedule may be found, we confirm that treatment with 25 mg of clomiphene citrate for 25 days, with 5 days' rest, over several subsequent months results in a significant improvement in subfertile specimens in properly selected individuals. Although we do not expect to maintain a

90% pregnancy rate in a larger series, we strongly believe that the low 23% pregnancy rate reported by Paulson and Wacksman* is falsely biased because the female partners were not subjected to the same intensive investigation as the men, and a good percentage may have had associated problems with fertility.

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TABLE 3. LH and FSH Base Line Levels and Response to Clomiphene in Men with Oligospermia and Asthenospermia

Patient	Base line		2 Mo after clomiphene	
	LH	FSH	LH	FSH
			mIU/ml	
1	18.8	15.7	23	22.5
2	6	3	17	14
3				
4	6.5	9.4	16.7	12.9
5	22.5	8.0	17	12.5
6			17	9
7	20	2		
8	1	3		
9	22	5.6	17	9.5
10	20.3	9.0		