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IS THERE ANY RELATION BETWEEN ESTROGEN LEVEL AND POOR CERVICAL MUCUS IN PATIENTS RECEIVING CLOMIPHENE CITRATE?

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ABSTRACT

Clomiphene citrate (CC) has an adverse effect on the quality and quantity of cervical mucus (CM). Poor cervical mucus has been reported in 15% of CC-treated women. CC exhibits estrogen agonist and antagonist activities. Antiestrogenic activity affecting the endocervical glands is theorized to cause a decrease in cervical mucus quality and quantity. An experimental study was performed to assess if there is any relation between poor CM and the level of estrogen in those to whom the drug is administered. We used CC on 50 subjects and evaluated CM and measured serum E2 levels simultaneously. We concluded that there is no relation between the level of estrogen and the quality or quantity of CM in these patients.

Key Words: Clomiphene citrate, cervical mucus, fern test.

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INTRODUCTION

The pharmacology of clomiphene citrate (CC) is confusing and not easily summarized. Clomiphene citrate is a mixed estrogen agonist-antagonist.[3] Available data suggest that CC is primarily an antiestrogen in humans. CC has the capacity to interfere with CM production. The exact mechanism of the action of CC at the cellular level is not fully characterized, but it is known to bind to the nuclear receptor for estrogen (E) for several weeks, and this effects a reduction in receptor replenishment.

Antiestrogenic activity affecting the endocervical glands may cause poor CM. This study was undertaken to investigate the etiology of this phenomenon.

MATERIALS AND METHODS

50 subjects were selected from the author's infertility practice. They were treated with CC for anovulation and were enrolled after a consistent ovulation response was established. The response was evaluated by folliculography through a vaginal probe after the dominant follicle was about 14 mm in diameter and continued to grow. The CM was evaluated and serum E2 level was measured simultaneously.

The dose of CC was 100 to 200 mg for 5 days. The CM was evaluated before treatment to rule out any intervening factors. For this reason, all patients who had mucopurulent discharge were treated with antibacterial therapy. A single technician evaluated all CM samples. The subjects who had any atypical fern formation were considered negative and those who had tertiary and quarternary stems in their fern patterns, positive fern (Table I). The serum E2 levels were classified into five

Table I. Fern test criteria.

	Cervical mucus pattern
Negative fern	Atypical fern formation, primary and secondary stems.
Positive fern	Tertiary and quarternary stems.

groups as seen in Table II.

Table II. Comparison between the number of subjects in each E2 level.

Serum E2 level (pg/ml)	Negative fern		Positive fern	
	n	%	n	%
25-330	7	64	18	46
331-636	1	9	10	25
637-942	2	18	7	18
943-1248	--	--	2	5
1249-1554	1	9	2	5

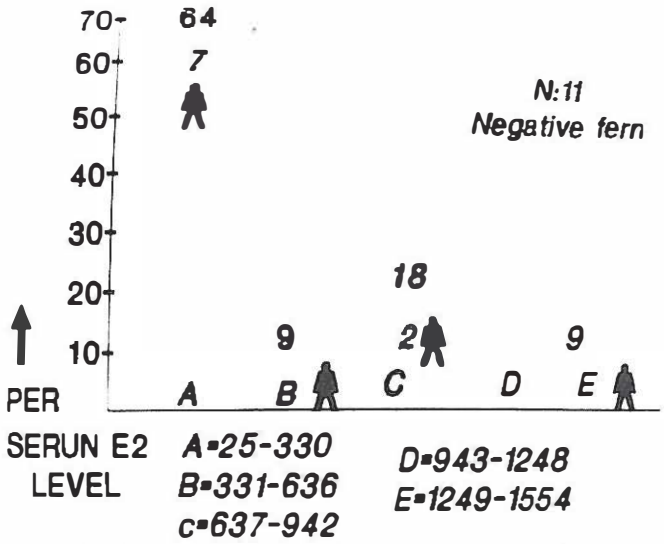

Fig. 1. The relationship between the serum E2 level and the percent of patients with negative fern test.

RESULTS

50 subjects were observed. The mean serum E2 level for each fern group was: positive fern test, 470.7 pg/ml; and negative fern test, 441.7 pg/ml; the means of the two treatment groups were not significantly different (Student's t test), and in the analyses of variance between the two groups, the variances were similar.

DISCUSSION

Since clomiphene has been in widespread clinical

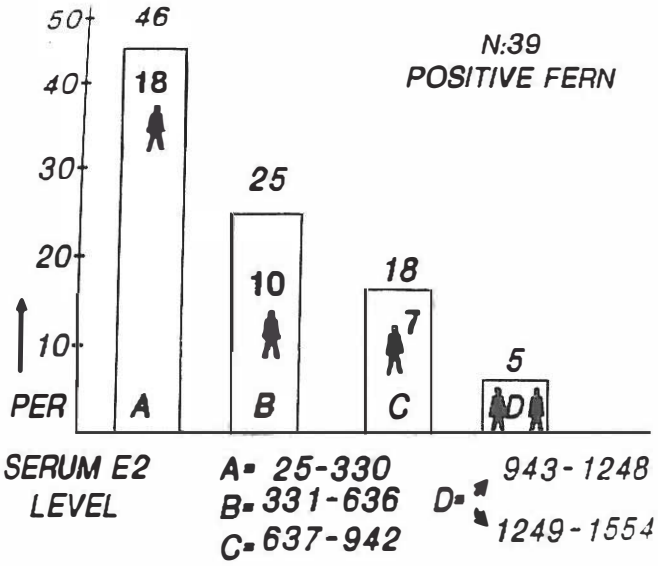

Fig. 2. The relationship between the serum E2 level and the precent of patients with positive fern test.

use for almost 20 years, many studies were done in the literature concerning this drug. In general, most results are comparable. The majority of investigators report a success rate of ovulation induction of approximately 70 to 80 percent, and in most studies, approximately 50 percent of those who ovulated conceived.[7,10,12,13]

The apparent ovulation-conception disparity has been the focus of much attention. There are factors that do relate to possible disparity in the ovulation versus conception rates with CC. Some apparent ovulatory cycles may represent luteinization of follicles without ovum release.[6]

Moreover, Graff[1] and others[2,9] have reported that clomiphene has an adverse estrogen antagonistic effect on cervical mucus. Thus, there are recognized effects suggesting that the conception-ovulation ratio of clomiphene cycles is less than that of normal ovulatory cycles, and the disparity may not be as great as previously thought.

Changes of cervical mucus attributed to clomiphene have been described by numerous investigators. The significance of this cervical mucus effect however is not clearly established.

We found an incidence of poor cervical mucus in nearly 22% of our subjects, an incidence greater than that of other infertility patients attending our clinic who did not have an ovulatory disorder. We concluded that there is no relation between the serum E2 level and poor CM and in view of this evidence, the recommendation of supplemental estrogens appears questionable.[8]

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