

SERUM PROLACTIN LEVELS IN INFERTILE PATIENTS WITH ENDOMETRIOSIS

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Summary

Raised prolactin levels have been implicated as a cause for infertility in patients with endometriosis. This study was done to investigate if serum prolactin levels were significantly raised in infertile patients with endometriosis. Serum prolactin levels were studied in 43 infertile patients with endometriosis. For controls, 36 infertile patients with normal pelvic findings were used. For standardization, blood samples were drawn on day 21 of the menstrual cycle. Analysis was done by radioimmunoassay using reagent kits. The mean prolactin level in the endometriotic group was 372 mIU/l (range 187–752) while that in the controls was 333 mIU/l (range 124–767). There was no statistical difference ($t=1.12$). Furthermore the accepted normal level for serum prolactin in our population is <540 mIU/l. These results show that there is no evidence to implicate raised prolactin levels as a cause for infertility in patients with endometriosis.

Key words: Endometriosis, infertility, serum prolactin.

INTRODUCTION

Hirchowitz *et al*¹ first reported the relationship between endometriosis and hyperprolactinemia when they incidentally found endometriosis in 9 patients with galactorrhea; of these 3 had raised prolactin levels. However, they could not offer an explanation for the association. Hargrave and Abraham² confirmed the findings of Hirchowitz *et al* when they found galactorrhea in 7 out of 14 patients with endometriosis; of these 3 had raised prolactin levels.

Because both endometriosis and hyperprolactinemia are associated with infertility it became an attractive theory to implicate raised prolactin levels as the cause for infertility in patients with endometriosis, especially in minimal or mild disease. Since the normal luteal phase endometrium secretes prolactin, it may be argued that endometriotic implants may also secrete prolactin and possibly cause ovarian dysfunction. Workers have since tried to establish this relationship.^{4,5}

This study was done to see if prolactin levels are significantly raised in the serum of patients with endometriosis.

PATIENTS AND METHODS

Patients were recruited from women undergoing infertility investigation at the University Hospital, Kuala Lumpur. The ages ranged from 23 to 35 years and the patients had been infertile for at least two years. All

patients had regular ovulatory cycles as shown by basal body temperature charting and raised mid-luteal phase serum progesterone levels.

Blood sampling

The two groups were studied based on laparoscopic findings. The first included 43 patients diagnosed to have endometriosis. Based on the Revised American Fertility Society Classification 1985,⁶ there were 25 patients with minimal or mild endometriosis and 18 patients with moderate or severe endometriosis.

The second group, which served as controls, included 36 patients with normal pelvic findings at laparoscopy.

For standardization, all blood samples were drawn by venipuncture on the morning of day 21 of the menstrual cycle. The samples were transported to the laboratory, centrifuged, and frozen at -28°C for assay later.

Prolactin assay

Prolactin levels were determined by double antibody radioimmunoassay (RIA) using reagent kits purchased from Pharmacia AB, Uppsala, Sweden. Intra-assay coefficient of variation was 7.2%; normal values for serum prolactin for our laboratory were <540 mIU/l.

Statistical analysis was done using the Student t-test.

RESULTS

The results are summarized in Table 1. There was no significant difference in prolactin levels between patients with and without

Muse *et al*³ showed that baseline levels of serum prolactin were higher in patients with endometriosis when compared to suitable

TABLE 1
MEAN SERUM PROLACTIN LEVELS (\pm SEM) IN PATIENTS WITH
ENDOMETRIOSIS AND IN CONTROLS

	Endometriosis (n = 43)			Controls (n = 36)
	Minimal or mild (n = 25)	Moderate or severe (n = 18)	All cases	
Prolactin (mIU/l)	365 (\pm 25.5)	170 (225.9)	372 (222.2)	333 (\pm 27.1)
(Range)	(198 - 613)	(187 - 752)		(124 - 767)

(SEM) = standard error of the mean.

endometriosis (t = 1.12; p = NS). Furthermore, there was no increase in the prolactin levels with the severity of the disease.

DISCUSSION

The reasons for infertility in patients with endometriosis, especially in minimal or mild disease is obscure. These patients have as their only abnormality small deposits with little or no distortion of anatomy. This has led workers to believe that there are subtle causes not being detected by conventional means. A variety of causes have been proposed: altered prostaglandin secretion," a hostile peritoneal fluid environment,⁸ autoimmune phenomena,⁹ the luteinized unruptured follicle syndrome¹⁰ and an increased abortion rate.¹

Since Hirschowitz *et al*¹ in 1978 reported an incidental finding of galactorrhea and raised prolactin levels in patients with endometriosis, workers have tried to implicate hyperprolactinemia as a cause for infertility in these patients, especially in minimal or mild disease.

Hargrave and Abraham² evaluated 14 patients with endometriosis and found that 7 patients had galactorrhea; of these, 3 had raised prolactin levels. In addition these patients had low serum progesterone levels in the luteal phase. This indicated a luteal phase defect in them. However, there were no control patients in their report

controls. Furthermore these patients were shown to hypersecrete prolactin in response to thyrotropin-releasing hormone. The response was directly related to the severity of the disease.

A similar exaggerated response to thyrotropin-releasing hormone was seen in patients with histological evidence of luteal phase defect.⁴ It was postulated therefore that raised prolactin levels in the peritoneal fluid surrounding the ovary affected corpus luteal function. Ronnberg *et al*¹² studied the luteinizing hormone (LH) receptor concentrations in ovarian follicles and corpora lutea in patients with endometriosis and found them to be significantly lower than in controls. To explain this finding, the authors suggested that the low numbers of LH binding sites in the granulosa and luteal cells might be caused by a relative hyperprolactinemia in the surrounding peritoneal fluid.

The ability of ectopic endometrium to secrete prolactin is controversial. While the normal endometrium retains the ability to secrete prolactin in the late luteal phase,¹³ studies on prolactin levels in the peritoneal fluid show no evidence that the implants secrete prolactin.¹⁴

In our study, infertile patients with endometriosis were compared to infertile patients without endometriosis. Furthermore the patients were matched for the time of

cycle. There was no significant difference seen in the prolactin concentration in the serum.

In conclusion, the results of this study show no evidence to implicate raised prolactin levels in the serum as a cause of infertility in patients with endometriosis.

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