Pre-transfer progesterone evaluation in women with endometriosis or adenomyosis undergoing assisted reproductive technology

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Introduction

Endometriosis and adenomyosis, once considered incidental findings in ART patients, are now recognized as distinct conditions requiring individualized treatment strategies [1]. Progesterone is pivotal for embryo transfer success, particularly in HRT-FET cycles, where emerging evidence suggests that higher levels may improve live birth rates [2]. Recent studies demonstrate that progesterone plays a key role in regulating endometrial structure and function, particularly in the inflammatory uterine environment characteristic of these conditions. Notably, progesterone resistance may impair absorption in affected women, further compromising implantation rates [3].

Objectives

This study aims to evaluate progesterone levels in patients with endometriosis or adenomyosis versus unaffected controls to determine the need for adjustments in progesterone supplementation. Additionally, a meta-analysis incorporating recent findings by Bourdon *et al*. [1] provides a broader perspective on its clinical implications.

Results

A total of 1,927 patients were included: 327 with endometriosis, 359 with adenomyosis and 1,344 controls. Progesterone levels on the day of FET were analyzed in both medicated (MCT) and spontaneous modified (SMC) cycle protocols. A meta-analysis incorporating data from Bourdon et al. was performed. No significant differences in progesterone levels were observed between women with endometriosis or adenomyosis and controls, regardless of live birth or non-pregnancy outcomes, in both MCT and SMC protocols. However, among non-conceiving women, meta-analysis revealed significantly lower progesterone levels in those with adenomyosis compared to controls (p=0.03), with the difference being more pronounced in the diffuse adenomyosis subgroup (p=0.02). Additionally, within the adenomyosis group, women who achieved live births had significantly higher progesterone levels than their non-pregnant counterparts (p=0.022). This difference was not observed in the endometriosis group nor in the control group. Notably, in SMC subgroup, progesterone levels difference between non-conceiving women with adenomyosis and controls approached statistical significance, despite substantial progesterone production by the corpus luteum in these patients.

Conclusions

Our study demonstrates that while overall serum progesterone levels at FET do not differ significantly between women with endometriosis or adenomyosis and controls, a meta-analysis revealed that non-conceiving women with adenomyosis, especially those with diffuse adenomyosis, exhibit significantly lower levels. Moreover, among adenomyosis patients, those achieving live births had higher progesterone levels than non-pregnant counterparts, suggesting that inadequate luteal phase support may contribute to reduced reproductive success. These findings, coupled with the influence of BMI on serum progesterone, underscore the potential benefit of individualized progesterone supplementation strategies in adenomyosis patients.

Bibliography

1 *Bourdon M, Sorel M, Maignien C, et al. Progesterone levels do not differ between patients with or without endometriosis/adenomyosis both in those who conceive after hormone replacement therapy-frozen embryo transfer cycles and those who do not. Hum Reprod. 2024;39(8):1692-700.*

2 *Melo P, Chung Y, Pickering O, et al. Serum luteal phase progesterone in women undergoing frozen embryo transfer in assisted conception: a systematic review and meta-analysis. Fertil Steril. 2021;116(6):1534-56.*

3 *Alsbjerg B, Kesmodel US, Humaidan P. Endometriosis patients benefit from high serum progesterone in hormone replacement therapy-frozen embryo transfer cycles: a cohort study. Reprod Biomed Online. 2023;46(1):92-98.*