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Characteristics Of Hormonal Status After Uterine Embolization In Women With Uterine Myoma

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Abstract: Uterine artery embolization (UAE) is a minimally invasive and effective treatment for uterine fibroids. To assess early postoperative changes in serum and salivary levels of estradiol and progesterone, as well as serum sex hormone-binding globulin (SHBG), in women undergoing UAE. This prospective observational study included 46 women with uterine fibroids who underwent UAE and 46 age- and cycle-matched healthy controls. Serum estradiol, progesterone, and SHBG, along with salivary estradiol and progesterone, were measured before embolization, 6–8 hours after the procedure, 24 hours later, and on days 6–8 postoperatively. Hormone concentrations were determined using immunoassay techniques. Statistical analysis was performed with significance set at $P<0.05$. UAE was associated with a progressive decrease in serum estradiol and progesterone levels, reaching maximal reduction on days 6–8. In contrast, SHBG levels increased significantly at all postoperative time points, with an almost fourfold rise by days 6–8 ($p<0.001$). Salivary analysis revealed a pronounced decline in free estradiol and progesterone, with reductions exceeding those observed in serum hormone levels. UAE induces transient endocrine alterations characterized by reduced ovarian steroidogenesis and decreased hormone bioavailability mediated by increased SHBG. Salivary hormone assessment provides valuable insight into functional endocrine changes after UAE.

Keywords: Uterine artery embolization; uterine fibroids; estradiol; progesterone; salivary hormones; endocrine changes.

Introduction: Uterine fibroids represent the most common benign tumors of the female reproductive system and are a leading cause of abnormal uterine bleeding, pelvic pain, and impaired quality of life in women of reproductive age [1]. The increasing prevalence of uterine fibroids, combined with the tendency toward delayed childbearing, has intensified interest in organ-preserving treatment modalities that effectively control disease progression while minimizing adverse effects on reproductive and endocrine function [2].

Uterine artery embolization (UAE) has emerged as a minimally invasive alternative to surgical management of uterine fibroids [3]. The therapeutic effect of UAE is based on selective ischemic devascularization of myomatous nodes, resulting in their progressive regression while largely preserving the surrounding myometrial tissue [4]. Numerous studies have demonstrated high clinical efficacy of UAE, including significant reduction in fibroid volume, alleviation of symptoms, and improvement in patient-reported outcomes. Nevertheless, despite its widespread use, concerns persist regarding the potential impact of UAE on ovarian function, particularly in women of reproductive age [5].

The anatomical presence of utero-ovarian vascular anastomoses raises the possibility of partial compromise of ovarian blood supply during embolization of the uterine arteries [6]. This mechanism has been proposed as a potential explanation for transient or, in rare cases, persistent disturbances in ovarian endocrine function observed after UAE [7]. Previous investigations have primarily focused on changes in serum gonadotropins and total steroid hormone concentrations; however, the results remain inconsistent, and the functional significance of these alterations is not fully understood [8].

Importantly, circulating sex steroid hormones exist in both bound and free forms, with only the unbound fraction exerting biological activity at the tissue level.

Sex hormone-binding globulin (SHBG) plays a central role in regulating hormone bioavailability, yet its contribution to endocrine changes following UAE has been insufficiently explored [9]. Moreover, serum hormone measurements may not adequately reflect biologically active hormone levels, whereas salivary hormone assessment offers a non-invasive approach to evaluating free steroid fractions and functional endocrine status.

Given these considerations, a comprehensive assessment of both total and free sex hormone fractions, along with SHBG dynamics, is essential for a more accurate understanding of the endocrine consequences of UAE. The present study was therefore designed to evaluate time-dependent changes in serum and salivary concentrations of estradiol and progesterone, as well as serum SHBG levels, in women undergoing uterine artery embolization for uterine fibroids. By elucidating the early postoperative hormonal response to UAE, this study aims to contribute to improved patient selection, counseling, and postoperative management, particularly for women with reproductive intentions.

METHODS

Study design and patients. A prospective observational study was conducted involving women diagnosed with uterine fibroids who underwent uterine artery embolization (UAE) as an organ-preserving treatment. The study included 46 patients, constituting the main study group. A control group consisted of 46 apparently healthy women without uterine fibroids or known endocrine disorders, matched by age and menstrual cycle phase.

Inclusion and exclusion criteria.

Inclusion criteria were:

-reproductive age;

-confirmed diagnosis of uterine fibroids based on ultrasound examination;

-indication for uterine artery embolization;

-preserved menstrual function prior to intervention.

Exclusion criteria included:

-pregnancy or lactation;

-history of ovarian surgery;

-endocrine disorders affecting gonadal or hepatic function;

-use of hormonal therapy within three months prior to the study;

-inflammatory diseases of the pelvic organs at the time of examination.

Uterine artery embolization procedure. Uterine artery embolization was performed using a standard transcatheter technique under fluoroscopic control. Selective catheterization of both uterine arteries was achieved, followed by embolization with calibrated embolic particles until complete stasis of blood flow in the target vessels was confirmed angiographically. All procedures were carried out by experienced interventional radiologists according to accepted clinical protocols.

Hormonal assessment. Hormonal evaluation included the determination of serum and salivary concentrations of estradiol and progesterone, as well as serum levels of sex hormone-binding globulin (SHBG).

Blood and saliva samples were collected at the following time points:

-before uterine artery embolization (baseline);

-6–8 hours after the procedure;

-24 hours after the procedure;

-on days 6–8 after embolization (prior to hospital discharge).

Serum estradiol and progesterone concentrations were measured using immunoassay methods with certified commercial kits, according to the manufacturer's instructions. SHBG levels were determined by enzyme-linked immunosorbent assay. Salivary hormone concentrations were assessed to estimate the biologically active (free) fraction of steroid hormones, as saliva reflects the unbound component of circulating hormones.

Ultrasound examination. Pelvic ultrasound examination was performed before embolization and during the postoperative period to assess the size and localization of myomatous nodes, as well as to monitor structural changes in the uterus. Ultrasound evaluation was carried out using a high-resolution transvaginal probe by experienced specialists.

Post-embolization syndrome assessment. Clinical manifestations of post-embolization syndrome, including pain intensity, fever, nausea, vomiting, and general weakness, were recorded during hospitalization. The duration and severity of symptoms were assessed using standard clinical criteria.

Statistical analysis. Statistical analysis was performed using standard statistical software. Quantitative data are presented as mean ± standard error of the mean (SEM). Comparisons between pre- and post-embolization values were carried out using paired statistical tests. Differences were considered statistically significant at $P<0.05$.

RESULTS

As is known, uterine artery embolization is based on reducing the blood supply to the entire myometrium (short-term) and to the myomatous nodes (long-term) by occlusion of the branches of the uterine artery. This surgical therapy allows for selective action on uterine fibroids relative to surrounding tissues.

Post-embolization syndrome of varying severity: fever, nausea, vomiting, weakness, "diffuse" pain in the abdominal area with the addition of leukocytosis occurred in 30-40% of patients and usually resolved independently within the first 48 hours.

The post-embolization syndrome lasted an average of 7.3±2.2 days. In 70% of cases, in patients with a node diameter of up to 5 cm, the fibroids completely disappeared and were not detected on ultrasound. However, uterine artery embolism, according to some authors, can lead to ovarian failure. Given the possibility of such a complication, we decided to study the hormonal status of women examined after uterine artery embolism.

The results obtained, as shown in Table 1, show that 6-8 hours after uterine artery embolization, serum estradiol levels tended to decrease by 11%. One day later, this trend was maintained and averaged 88.4±7.63 pg/ml (compared to 109.6±8.32 pg/ml in the control group). The lowest serum estradiol levels were detected on days 6-8 after surgery, when the measured value averaged 56.4±6.01 pg/ml, which is 49% lower than the initial values (P<0.05).

Analysis of serum progesterone levels in women who underwent uterine artery embolization showed a similar trend. For example, 6-8 hours after surgical therapy, serum progesterone level decreased by 5% and was 6.84±0.83 mg/ml.

Table 1

Dynamics of indicators of hormonal status before and after uterine artery embolism

Index	Control group, n=46	Before uterine artery embolism	After uterine artery embolism		
			Within 6-8 hours	After 1 day	On the 6th-8th day
Serum estradiol, pg/ml	62,1±2,71	109,6±8,32	98,1±7,21	88,4±7,63	56,4±4,72*
Serum progesterone, mg/ml	0,92±0,11	7,21±0,59	6,84±0,56	6,01±0,52	3,05±0,24*
Sex hormone binding globulin, nmol/l	64,6±4,27	18,4±1,64	38,1±4,01*	62,6±5,14*	72,4±6,28*
Estradiol in saliva, pg/ml	5,24±0,44	223,7±9,86	112,4±8,12*	51,2±4,43*	7,41±0,57*
Progesterone in saliva, mg/ml	0,11±0,01	0,5±0,03	0,31±0,02*	0,24±0,02*	0,28±0,02*

Note: * – differences compared to pre-operative indicators are reliable (*-p<0.05; **-p<0.01; ***-p<0.001).

After a day, the measured value was 6.01±0.76 mg/ml, which was 17% lower than the initial values. Before discharge from the clinic, that is, on the 6th-8th day after uterine artery embolism, the level of progesterone in the blood serum decreased by 2.4 times compared to the initial values (P<0.001).

An interesting dynamic was noted in sex hormone binding globulin. For example, the measured protein values had an increasing dynamic at all times after uterine artery embolism. In the early period (6-8 hours) after uterine artery embolism, the level of globulin increased 2 times and amounted to 38.1±4.01 nmol/l (P<0.001). After 1 day, the studied indicator increased 3.4 times from the initial indicator, and by the end of the study (6-8 days) it was on average 3.9 times higher than the indicator before uterine artery embolism (R<0.001).

To determine the characteristics of changes in free estradiol not bound to globulin, we examined saliva for sex hormones.

After uterine artery embolization, the amount of free estradiol in the saliva of women tended to decrease, i.e. after 6-8 hours its level was 112.4±8.12 pg/ml, which was 2 times lower than the initial values.

This dynamics of estradiol in saliva was maintained in the later periods of the study, i.e. on the 1st day after

uterine artery embolization it decreased by an average of 4 times, and by the end of the study (6-8 days) the estradiol levels in saliva were 7.41±5.71 pg/ml, which is 30 times lower than the initial values (P<0.05).

The study of progesterone levels in saliva of women after uterine artery embolism showed a specific dynamic, i.e. in the first hours after the procedure, the level of progesterone significantly decreased and amounted to 0.31±0.02 mg/ml versus 0.51±0.03 mg/ml (P<0.05). By the 1st day after uterine artery embolism, the level of progesterone decreased by 53% compared to the control group (P<0.05). After 6-8 days, i.e. at the time of discharge from the hospital, the level of progesterone in saliva became specific, i.e. a slight increase was noted compared to the previous examination period, but this indicator remained low compared to the preoperative group.

Thus, uterine artery embolism in women with uterine fibroids is accompanied by changes in serum and salivary hormonal status indicators at different times after surgery, with an increase in the level of sex hormone-binding globulin, which indicates the activation of the protein-synthesizing function of the liver.

DISCUSSION

Uterine artery embolization (UAE) is widely recognized as an effective organ-preserving treatment for uterine fibroids, based on selective ischemic devascularization of myomatous tissue. However, the systemic endocrine consequences of this intervention remain insufficiently elucidated, particularly in women of reproductive age. The present study demonstrates that UAE is accompanied by distinct, time-dependent alterations in both total and free fractions of sex steroid hormones, indicating a complex endocrine response extending beyond local uterine ischemia.

The observed progressive decline in serum estradiol and progesterone levels during the early post-embolization period suggests transient suppression of ovarian steroidogenesis. This effect was most pronounced on days 6–8 after the procedure, when estradiol and progesterone concentrations decreased by 49% and 2.4-fold, respectively, compared with baseline values. These findings are consistent with the hypothesis that partial compromise of ovarian perfusion may occur following UAE due to utero-ovarian anastomoses, leading to temporary ischemia of ovarian tissue. Similar mechanisms have been proposed by other authors, who reported short-term disturbances in ovarian hormonal function after UAE, particularly in women approaching late reproductive age.

An important and novel aspect of the present study is the dynamic increase in sex hormone-binding globulin (SHBG) observed at all evaluated time points after embolization. The rapid elevation of SHBG levels as early as 6–8 hours post-procedure, followed by a sustained increase throughout the observation period, indicates activation of hepatic protein synthesis, likely mediated by stress-related metabolic and inflammatory responses. Since SHBG plays a central role in regulating the bioavailability of circulating sex steroids, its marked increase substantially alters the balance between total and free hormone fractions.

This mechanism is clearly reflected in the salivary hormone measurements. Saliva analysis, which reflects the biologically active, unbound fraction of steroid hormones, revealed a dramatic reduction in free estradiol and progesterone levels. Notably, salivary estradiol decreased up to 30-fold by days 6–8 after UAE, a change far exceeding the decline observed in serum estradiol. This discrepancy underscores that total serum hormone concentrations may underestimate the true degree of functional hypoestrogenism occurring after UAE. The reduction in free progesterone followed a similar pattern, with a pronounced early decrease and only partial recovery by the time of hospital discharge.

The combined decrease in ovarian hormone production and simultaneous increase in SHBG suggests that post-embolization endocrine changes are mediated by both ovarian and extra-ovarian mechanisms. This dual effect may explain the variability in clinical manifestations reported after UAE, ranging from transient menstrual irregularities to, in rare cases, signs of premature ovarian insufficiency. Importantly, the gradual stabilization of salivary progesterone levels toward the end of the observation period may indicate the initiation of compensatory endocrine adaptation.

From a clinical perspective, the findings of this study have significant implications for patient selection and counseling. While UAE remains a highly effective method for fibroid control, the demonstrated transient hypoestrogenic state may be clinically relevant for women with low baseline ovarian reserve or those planning future fertility. In such patients, short-term endocrine monitoring, including assessment of SHBG and free hormone fractions, may provide valuable information beyond conventional serum hormone measurements.

Several limitations of the present study should be acknowledged. The observation period was limited to the early postoperative phase, and long-term hormonal recovery could not be assessed. Additionally, ovarian reserve markers such as anti-Müllerian hormone were not evaluated, which would have allowed a more

comprehensive assessment of ovarian functional capacity. Future studies incorporating extended follow-up and additional biomarkers are warranted to clarify the long-term reproductive endocrine consequences of UAE.

In summary, the present data indicate that uterine artery embolization induces a transient but multifactorial endocrine response characterized by reduced ovarian steroidogenesis and decreased bioavailability of sex hormones due to increased SHBG levels. These findings support the concept that the endocrine impact of UAE is dynamic and potentially reversible, emphasizing the need for individualized risk assessment and hormonal monitoring, particularly in women of reproductive age.

CONCLUSIONS

The dissociation between total serum hormone levels and their free fractions indicates that post-embolization endocrine changes are mediated not only by decreased ovarian hormone production but also by altered hormone transport and bioavailability. The pronounced reduction in salivary estradiol and progesterone underscores the functional hypoestrogenic and hypoprogestogenic state that may develop in the early postoperative period after UAE.

Clinically, these findings are of particular importance in the context of reproductive-aged women, as transient ovarian dysfunction and reduced steroid hormone bioactivity may contribute to menstrual disturbances and, in susceptible patients, potentially impair ovarian reserve. At the same time, the observed hormonal changes appear to be dynamic rather than static, suggesting a reversible adaptive response to uterine ischemia rather than irreversible ovarian failure in the majority of cases.

In conclusion, uterine artery embolization should be regarded as an intervention with complex systemic endocrine effects extending beyond local uterine ischemia. Comprehensive hormonal monitoring, including assessment of SHBG and free hormone fractions, may provide a more accurate evaluation of ovarian function after UAE and help to optimize patient selection, counseling, and postoperative management, particularly in women with reproductive intentions.

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