Clinical Trial/Experimental Study

Medicine

OPEN

Impact of hysterosalpingography on endometrial HOXA-10 and HOXA-11 mRNA expression

A clinical trial

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Abstract

Background: Homeobox genes (HOX) are the basic molecules that regulate endometrial receptivity, decidualization, and progesterone response. This study was designed to investigate the effects of the classical hysterosalpingography (HSG) procedure on endometrial HOXA-10 and 11 mRNA expression.

Methods: Thirty-five primary infertile patients who applied for investigation of infertility etiology and were approved for conventional HSG were included in the study. Ten fertile patients who required biopsy due to an endometrial pathology were accepted as a control group. Women in HSG group were eligible to participate in the study if they were between 22 and 34 years of age, had spontaneous menstrual cycles, and had been trying to conceive for at least 1.5 year and if there was an indication for evaluation of tubal patency with hysterosalpingography. First endometrial sampling was performed with a pipelle before the contrast-medium infusion during the HSG. Endometrial sampling was collected for the second time with a pipelle cannula in the midluteal phase of the next cycle in all cases undergoing HSG. HOXA-10 and 11 mRNA expressions in the endometrial tissues obtained before HSG and respective endometrial tissues after HSG were measured with RT-PCR.

Results: Pre-HSG average ΔCt values of HOXA-10 and HOXA-11 mRNA were found to be significantly lower than fertile controls (4.30 vs 6.74, $P < .001$; 3.93 vs 6.74, $P < .002$). Post-HSG HOXA-10 mRNA levels increased significantly compared to pre-HSG levels (5.66 vs 4.30, $P < .01$). Post-HSG HOXA-10 mRNA levels increased approximately 4.2-fold compared to pre-HSG levels. Post-HSG HOXA-11 mRNA levels increased significantly compared to pre-HSG levels (4.94 vs 3.93, $P < .03$). Post-HSG HOXA-11 mRNA levels increased approximately 3.5-fold compared to pre-HSG levels. When the pre-HSG and post-HSG HOXA-10 and HOXA-11 mRNA levels were compared among themselves, the increase in HOXA-10 average ΔCt was significantly higher than the increase in HOXA-11 average ΔCt (5.66 vs 4.94, $P < .02$.). Similarly, the fold increase in post-HSG mRNA levels was significantly higher in the HOXA-10 group (4.2-fold) than the HOXA-11 group (3.5-fold) ($P < .001$).

Conclusions: Conventional HSG procedure improves fertility by increasing endometrial HOXA-10 and HOXA-11 mRNA levels.

Abbreviations: ACTB = β-actin gene, cDNA = complementary DNA, Ct = cycle threshold, Hcg = human chorionic gonadotropin, HOX = homeobox genes, HSG = hysterosalpingography, SPSS = Statistical Package for Social Sciences software 21.0 for Windows package software.

Keywords: endometrium, HOXA-10 mRNA, HOXA-11 mRNA, HSG, receptivity, RT-PCR

1. Introduction

Oil-based contrast material used in HSG is thought to improve fertility by removing mucus blockages in the fallopian tubes and reordering ciliary activity.[1,2] The positive effects of HSG on fertility begins a month after the procedure and continuing for at least 6 months to a year.[3,4]This is a good evidence

Informed consent was obtained from all individual participants included in the study.

The authors have no funding and conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

This study was performed in line with the principles of the Declaration of Helsinki. The Clinical Research Ethics Committee of Kayseri City Training and Research Hospital provided its approval for the project (April 07, 2022; No: 608).

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How to cite this article: Ozdemir F, Demir MB, Kutuk S, Karaman E, Muderris II, Celik O, Dalkilic S, Dalkilic LK. Impact of hysterosalpingography on endometrial HOXA-10 and HOXA-11 mRNA expression: A clinical trial. Medicine 2025;104:19(e42393).

Received: 15 January 2025 / Received in final form: 11 April 2025 / Accepted: 18 April 2025

http://dx.doi.org/10.1097/MD.0000000000042393

that the cleansing of the fallopian tubes from debris by the flushing effect of the contrast material.[3,5] Although it has been reported that the use of oil-based contrast agents has a more favorable influence on pregnancy rates than liquid-based contrast agents.[3,5] HSG is believed to have a fertility-enhancing effect regardless of the contrast agent used.[6] It is believed that the contact of the endometrium with the contrast agent does not contribute much to the fertility-enhancing effect due to HSG. The main reason for this belief is that the endometrial tissue is discharged regularly and cyclically with menstruation. Therefore, it does not seem logical that the fertility-enhancing effect seen during a year due to HSG originates from the endometrium.

The considerable rise in the rate of clinical pregnancy observed in follow-up following HSG provides evidence in favor of the flushing action of the contrast agent clearing the fallopian tubes.[3] However, some studies, albeit isolated, have suggested that in addition to the effect in the tubes, some positive immunological changes occur in the endometrium and peritoneal microenvironment due to the use of contrast agents and increase fertility. Immunological changes detected in the endometrium due to the use of contrast agents were mostly evaluated on T cells or dendritic cells. Although these cells play a role in receptivity, they are not the basic receptivity molecules[7,8] The primary receptivity molecules, known as homebox genes, are most expressed in the middle stage of the luteal phase of the menstrual cycle.[9,10] In the implantation window, HOXA expression switches from luminal and glandular epithelium to stromal cells.[11] The main functions of HOX genes are pinopod growth and regulation of the response of endometrial cells to progesterone.[12] In this way, they contribute to the perfect decidualization and successful implantation.[13] HOXA gene expressions decrease in many benign gynecological diseases.[14] The decreased endometrial HOXA expression in endometrioma and hydrosalpinx patients returns to normal after surgical correction of the disease.[9,15] The impact of HSG media on endometrial receptivity genes has not yet been studied and reported. This study was designed to determine whether the key genes responsible for endometrial receptivity, HOXA-10 and -11, are affected by the oil-based contrast medium used in HSG.

2. Materials and methods

2.1. Ethical approval

The Clinical Research Ethics Committee of Kayseri City Training and Research Hospital provided its approval for the project (April 07, 2022; No: 608).

2.2. Study population and participants

While investigating the etiology of infertility, 35 patients whose HSG decision was made were included in the study. Informed consent forms were obtained from all volunteers constituting both the control group and the study group. Patients had to meet all of the following criteria in order to be included in the study. Women in HSG group were eligible to participate in the study if the age is between 22 and 34, had menstrual cycles spontaneously, and had been trying to get pregnant for at least 1.5 year and if they had an indication of hysterosalpingography for evaluation of tubal patency. Exclusion criteria were known endocrine disorders such as endometriosis, endometrioma, polycystic ovary syndrome, and diabetes. Participants high risk for pelvic inflammatory disease, contrast-medium allergy, Asherman syndrome, hydrosalpinx, and out-of date endometrium, endometrial polyp, and submucous were also excluded. Before HSG, pregnancy test was performed on the participants to exclude a possible pregnancy. The positive control group consisted of 10 individuals who needed a biopsy for any endometrial abnormality and had 2 or more children. Because of the difficulty in establishing the phase of the cycle, fertile controls with atypical endometrial bleeding, except those with heavy menstrual bleeding (regular but heavy bleeding), were excluded from the study. The control group of our study consisted of patients who applied with complaints of regular but heavy menstrual bleeding and who were found to have thick and heterogeneous endometrium in ultrasonographic examination. Patients with abnormal endometrial pathology (endometrial hyperplasia, endometrial polyp, endometrial cancer) detected as a result of biopsy were excluded from the study. Ten patients whose biopsy result was reported as "secretory endometrium" were included in the study as a control group.

The stages of creating the control group are given as a flowchart in Figure 1.

2.3. Determination of menstrual cycle phase

Serum Hcg values of the patients were measured in the midluteal phase. In order to detect the midluteal phase in the patients, first of all, ovulation was confirmed ultrasonographically. Serum progesterone levels of all patients were measured 7 to 9 days after the ovulation. Additionally histological dating was performed for confirming the midluteal phase. Midluteal serum progesterone measurement was made in all patients participating in the study, and the progesterone value was > 10 ng/mL, confirming that the cycles were ovulatory. Cases whose endometrium was out of phase according to Noyes criteria were not included in the study. Endometrial samples with a delay of more than 3 days between chronological and histological days were defined as out-of-date biopsy.

2.4. HSG procedure

All HSGs were performed by FO and EK according to the local protocols of Erciyes University Faculty of Medicine Department of Obstetrics and Gynecology. While performing HSG, a radiopaque contrast agent (Omnipaque^{R} 350 mg/100 mL) was administered into the uterus and Fallopian tubes through the cervix. A metal cannula was used for infusing 5 to 10 ml of contrast material into the uterus during the HSG. 4 to 6 radiographs were taken concurrently to assess the contrast-medium's passage throughout the endometrial cavity, fallopian tubes, and lastly into the peritoneal cavity. Radiographs were examined by a gynecologist or radiologist. A pipelle cannula was used for performing endometrial sampling during the HSG procedure just before the contrast-medium infusion. In all patients undergoing HSG, second endometrial sampling was performed in the midluteal phase of the next cycle by using pipelle cannula. In the HSG group where the second endometrial sampling was performed; patients who were histologically out of date were excluded from the study and HOXA expression levels were studied from the endometrial samples of patients with histological compatibility. The HOXA-10 and HOXA-11 mRNA expressions were evaluated in the endometrial tissues which obtained before and after HSG procedure.

2.5. RT-PCR

We transferred the endometrial samples obtained from participants in HSG and control groups into RNA stabilization buffer (RNA Later; Qiagen, Germantown) and then we stored them at –20 °C until used. Rneasy Mini Kits (Qiagen) were used for extracting total RNA from decidua. By using Maestronano, the purity and quantity of RNA was measured spectrophotometrically. Quantitect Reverse Transcription Kit (Qiagen) was used for obtaining Complementary DNA (cDNA). We used β-Actin gene (ACTB) as housekeeping gene. The RotorgeneQ realtime

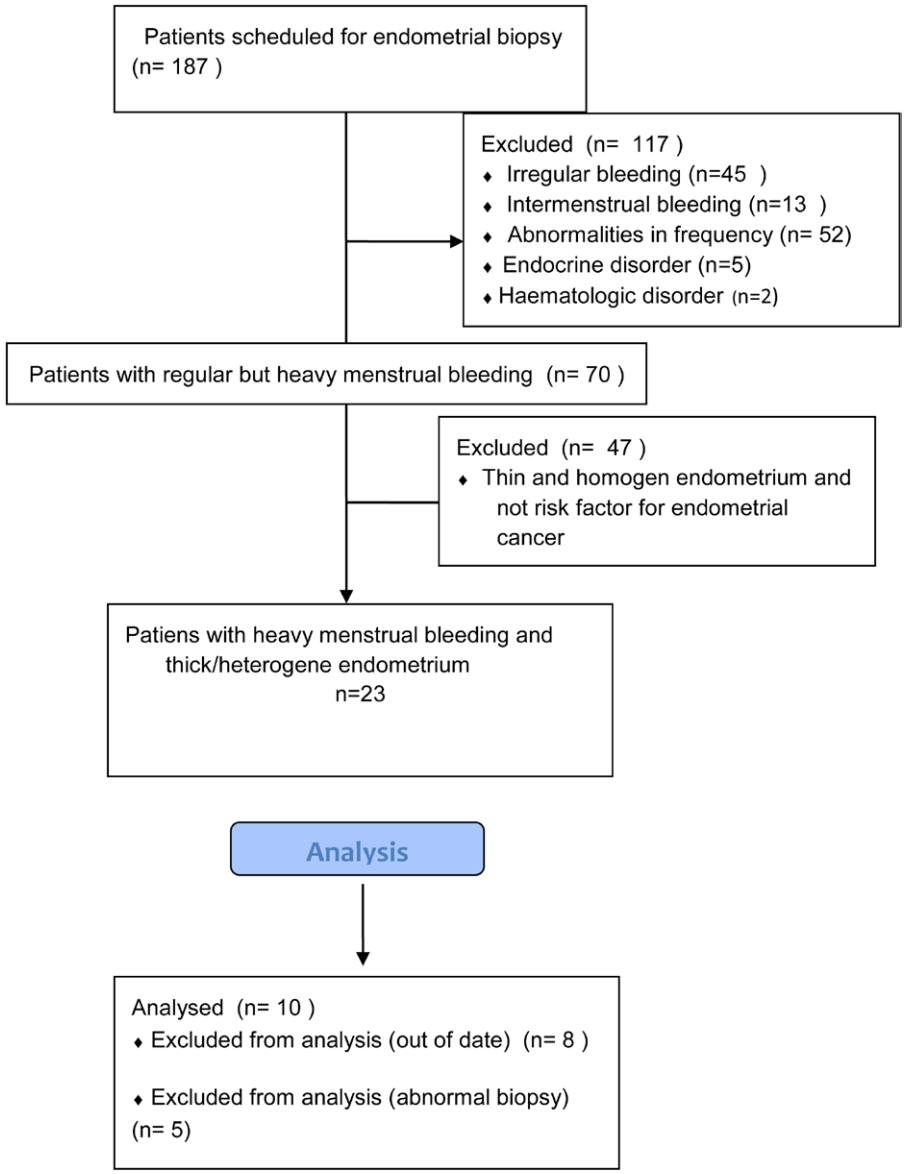

Figure 1. Stages of creating the control group.

PCR device and Quantitect Probe PCR Kit were used for performing Realtime PCR reaction. Sequences and accession numbers of all primers designed tobe used as forward and reverse primers for RT-PCR were: HOXA-10": F 5'-GGT TTG TTC TGA CTT TTTGTT TCT-3', R 5'-TGA CAC TTA GGA CAA TAT CTA TCTCTA-3'"; HOXA-11": F 5'-AGT TCT TTC TTCAGC GTC TAC ATT-3', R 5'-TTT TTC CTT CAT TCT CCT GTTCTG-3'";ACTB forward": F 5'-GCA AGC AGG AGT ATG ACG AGT-3', *R* -5'-CAA GAA AGG GTG TAA CGC AAC TAA-3'." ΔCt, ΔΔCt and Cycle threshold (Ct) is used to represent the results of gene expression. Each endometrial sample was examined 3 times in order to determine the average CT results. We used the 2-Ct comparative approach to determine the relative gene expression using RT2 Profiler PCR Array Data Analysis version 5.5 (SA Biosciences, Hilden, North Rhine-Westphalia, Germany). According to the mRNA of β-actin, all results were normalized. By dividing the normalized gene expression ($2^{-\Delta\Delta Ct}$) of patient group to the normalized gene expression($2^{-\Delta\Delta Ct}$) of fertile control group, fold change ($2^{-\Delta\Delta Ct}$) is calculated. If the fold change is found to be > 2, it indicates upregulation. If the fold change is found to be < 2, it indicates downregulation.

2.6. Statistical analysis

"Statistical Package for Social Sciences software 21.0 for Windows package software (SPSS)" was used for statistical analysis of data. Kolmogorov–Smirnoff test was used for testing the normality distribution of data, and all variables were distributed normally. For analyzing the continuous variables, Mann–Whitney *U* test and Variance test with post hoc Tukey procedure were used. Pearson chi-square test was used for analyzing the categoric data. We considered significant the *P* value of <.05. And we expressed the results as mean ± SD. When the associated mRNA level exceeded the initial transcript expression level by more than 2-fold, it was deemed positive; if it fell below that level by 2-fold, it was deemed negative.

3. Results

The mean age of infertile patients who underwent HSG (25.3 ± 0.32) was found to be significantly lower than fertile controls (31.4 ± 0.93). Similarly, body mass indexes of the cases in the fertile group were found to be significantly higher than the HSG group. Hysterosalpingography showed bilateral

tubal patency in 29 of 35 women. Bilateral tubal occlusion was detected in 2 women and unilateral tubal occlusion occurred in 4 women.

Pre-HSG average ΔCt values of HOXA-10 mRNA were found to be significantly lower than fertile controls (4.30 vs 6.74, $P < .001$). Similarly, pre-HSG average ΔCt values of HOXA-11 mRNA were found to be significantly lower than fertile controls (3.93 vs 6.74, $P < .002$). After HSG, HOXA-10 mRNA expression levels increased close to fertile controls (5.66 vs 6.74). Post-HSG HOXA-10 mRNA levels increased significantly compared to pre-HSG levels (5.66 vs 4.30, $P < .01$). When compared to pre-HSG levels, post-HSG HOXA-10 mRNA levels increased approximately 4.2-fold (Table 1). Following HSG, HOXA-11 mRNA expression levels increased close to fertile controls (4.94 vs 6.74). Post-HSG HOXA-11 mRNA levels increased significantly compared to pre-HSG levels (4.94 vs 3.93, $P < .03$). HOXA-11 mRNA levels increased almost 3.5-fold from pre-HSG levels to post-HSG values. When the pre-HSG and post-HSG HOXA-10 and HOXA-11 mRNA levels were compared among themselves, the increase in HOXA-10 average ΔCt was significantly higher than the increase in HOXA-11 average ΔCt (5.66 vs 4.94, $P < .02$.). Similarly, the fold increase in post-HSG mRNA levels was significantly higher in the HOXA-10 group (4.2-fold) than the HOXA-11 group (3.5-fold) ($P < .001$).

4. Discussion

The endometrium was the least examined area among the tissues that had a role in the fertility-enhancing effect of HSG. The main reason for this handicap is the belief that the contrast substance cannot have a long-term positive effect due to the rapid passage of the endometrial cavity to the fallopian tubes and the abdominal cavity.[3,4] However, if it is accepted that there is an increase in fertility after hysteroscopy, cesarean delivery and controlled local endometrial injury, it is reasonable to see positive effects after HSG. Our study has importance clinically since it is the first to address the potential effects of HSG on the primary endometrial receptivity genes, HOXA-10 and HOXA-11 mRNA expression.

The objective of this study was to evaluate whether endometrial implantation plays a role in the fertility-enhancing effect of HSG. To evaluate this, 2 genes that play an important role in the implantation process, HOXA-10 and HOXA-11, were chosen. Pre-HSG average Ct values of HOXA-10 and HOXA-11 mRNA were determined to be considerably lower in the current study compared to fertile controls. After HSG, both HOXA-10 and HOXA-11 mRNA expressions increased close to fertile controls. Comparing pre-HSG and post-HSG levels, the amount of HOXA-10 mRNA increased almost 4.2-fold. Likewise, post-HSG HOXA-11 mRNA levels increased significantly compared to pre-HSG levels HOXA-11 mRNA levels increased almost 3.5-fold from pre-HSG levels to post-HSG values. The HOXA-10 (4.2-fold) increased its post-HSG mRNA levels much more than the HOXA-11 (3.5-fold). In summary, when compared with fertile patients, pre-HSG endometrial HOXA-10 and 11 mRNA levels were significantly lower in infertile patients. In the measurements made after HSG, both HOXA-10 and HOXA-11 mRNA levels increased significantly. The increase in HOXA-10 mRNA was greater than that of HOXA-11 mRNA.

We do not know by what mechanism HSG increases homeobox gene expression. However, we can uncover hints concerning this growth in light of earlier, comparable investigations. In a study by Celik et al,[9] the decrease in HOXA-10 mRNA levels in the endometrium of endometrioma patients returned to normal after endometrioma surgery. Similar to this, Daftary et al[15] observed that after surgical excision of cases of hydrosalpinx, HOXA-10 expression levels increased. However, it is unclear whether this rise in endometrial HOXA-10 and HOXA-11 mRNA following HSG is a result of the HSG operation per se or a result of other infertility-related variables. Since those with other benign gynecological diseases that may lead to endometrioma, hydrosalpinx and subfertility were not included in the study, we cannot attribute the upregulation occurring after HSG in homeobox genes to another reason. Upregulation of HOXA-10 and HOXA-11 mRNA may be a direct result of HSG procedure itself or may be the result of oil-based contrast-medium use.

The conventional HSG procedure itself and the cumulative effect of the contrast agents used show fertility-enhancing effects. Since the fertility-enhancing effect of HSG is long-term, it is a widely accepted belief that this effect is mostly related to the removal of physiological plugs in the fallopian tubes.[3,5] In addition, the mechanical effects that occur in endometrial and tubal cells due to the washing effect of the contrast agent may stimulate a healthier receptivity and ciliary activity. Changes in the endometrial dendritic cell population due to the use of contrast agents may contribute positively to fertility. All these theories focus on the mechanical effects of HSG. However, the increase in the expression levels of implantation genes observed in the results of our study opened a new window into the effects of HSG on fertility. In the study conducted by Celik et al in 2023, which investigated the effects of endometrial injury on HOXA-10 and HOXA-11 expression, it was shown that endometrial injury leads to an increase in gene expression levels. Based on this, it can be speculated that the increase in gene expression levels caused by HSG may have occurred through a similar mechanism.[16]

Contrary to all these findings and positive expectations on fertility; there are also studies in the literature reporting results that HSG may have negative effects on fertility. In an experimental study conducted by Can B et al in 2018; significant damage was observed in the ovarian tissue in rats exposed to low-dose ionizing radiation during the HSG procedure. This damage was found to be associated with oxidative stress, especially caused by the effect of radiation. In addition; it was observed that HSG created degenerative effects on the epithelial cells in the ovarian tissue and was associated with increased apoptosis.[17]

Table 1

Expression levels of HOXA-10 and HOXA-11 mRNA in pre-HSG and post-HSG endometrial samples.

	Groups	Average ΔCt	Average $2^{-\Delta Ct}$	Fold change	*P* value	Regulation
HOXA-10 mRNA	Fertile control	6.74	0.0012	0.63	.22	Down
	Pre-HSG	4.30	0.0033	0.37	.64	Down
	Post-HSG	5.66	0.0055	4.20	.01	Up
HOXA-11 mRNA	Fertile control	6.74	0.0012	0.63	.22	Down
	Pre-HSG	3.93	0.0022	0.76	.58	Down
	Post-HSG	4.94	0.0057	3.56	.03	Up

In another experimental study investigating the effects of HSG on endometrial tissue, significant degeneration of the endometrial epithelium and an increase in MDA (malondialdehyde) and Ki-67 immunoreactivity were observed after the HSG procedure. These changes indicate that HSG causes damage to the endometrial tissue. Again, in the same study, it was found that oxidative stress caused by radiation during the HSG procedure caused damage to the endometrial cells.[18]

We do not know if manipulations such as holding the cervix with the teneculum and pulling it forward during HSG affect the endometrium. However, the receptivity genes due to the mechanical and immunological stimulation created by the oil-based contrast medium used in endometrial cells may be activated. We do not know how long the intensity and duration of this activation due to the use of contrast agent will continue, but we can say that it significantly increases the receptivity for the following cycle. In order to say something clear about the positive effect of using oil-based contrast media on homeobox genes, it is necessary to compare the results of HSG using liquid-based contrast.

The small number of cases and single endometrial sampling from the control groups are the main limitations of our study. Further, it is another handicap that we do not analyze the effects of the increase in HOXA-10 and 11 mRNA on protein synthesis. Despite all limitations, our findings are clinically important, since it is the first study to show a significant increase in endometrial HOXA-10 and 11 mRNA levels in infertile patients after HSG using oil-based contrast. It is clear from our study and earlier research.[3,4] that HSG has a positive effect on fertility in both the endometrial and tubal regions. Removal of fallopian tubes mucus plaque and debris are the main mechanisms for the continuation of long-term fertility-enhancing effects of HSG. On the other hand, upregulation in endometrial homeobox genes after contrast agent use may contribute to fertility-enhancing effect of HSG. Although the mechanism of the positive effects of hysterosalpingography on fertility is not fully understood, a positive effect of oil-based contrast infusion on reproductive outcome has been speculated.[3,5] The exact underlying HOXA-10 and 11 mRNA-enhancing mechanism of HSG is unclear, but we proposed that use of oil-based contrast medium during HSG may improve synthesis and release of homeobox genes from otherwise normal endometrium.

Acknowledgments

No financial support was received from any institution or individual for this study.

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References

[1] Lu J, Qi D, Xu W. Fertility-enhancing effect of oil-based contrast agents during hysterosalpingography and the variation of this effect within a 3-year follow-up period in infertile patients. Front Med. 2022;9:948945.
[2] Zhang J, Lan W, Wang Y, et al. Ethiodized poppyseed oil-based contrast medium is superior to water-based contrast medium during hysterosalpingography regarding image quality improvement and fertility enhancement: a multicentric, randomized and controlled trial. EClinicalMedicine. 2022;46:101363.
[3] Chen J, Liu S, Lu J. Comparison of fertility outcomes between oil-based and water-based contrast media during hysterosalpingography: a meta-analysis. Exp Ther Med. 2023;26:1–11.
[4] Van Welie N, Ludwin A, Martins WP, Mijatovic V, Dreyer K. Tubal flushing treatment for unexplained infertility. Semin Reprod Med. 2020;38:74–86.
[5] Weir WC, Weir DR. Therapeutic value of salpingograms in infertility. Fertil Steril. 1951;2:514–22.
[6] Dreyer K, van Eekelen R, Tjon-Kon-Fat R, et al. The therapeutic effect of hysterosalpingography in couples with unexplained subfertility: a post-hoc analysis of a prospective multi-centre cohort study. Reprod Biomed Online. 2019;38:233–9.
[7] Izumi G, Koga K, Takamura M, et al. Oil-soluble contrast medium (OSCM) for hysterosalpingography modulates dendritic cell and regulatory T cell profiles in the peritoneal cavity: a possible mechanism by which OSCM enhances fertility. J Immunol. 2017;198:4277–84.
[8] Roest I, Hajiyavand A, Bongers M, et al. What is the fertility-enhancing effect of tubal flushing with ethiodized oil? J Obstet Gynaecol. 2022;42:1619–25.
[9] Celik O, Unlu C, Otlu B, Celik N, Caliskan E. Laparoscopic endometrioma resection increases peri-implantation endometrial HOXA-10 and HOXA-11 mRNA expression. Fertil Steril. 2015;104:356–65.
[10] Governini L, Luongo FP, Haxhiu A, Piomboni P, Luddi A. Main actors behind the endometrial receptivity and successful implantation. Tissue Cell. 2021;73:101656.
[11] Ekanayake DL, Małopolska MM, Schwarz T, Tuz R, Bartlewski PM. The roles and expression of HOXA/Hoxa10 gene: a prospective marker of mammalian female fertility? Reprod Biol. 2022;22:100647.
[12] Daftary GS, Troy PJ, Bagot CN, Young SL, Taylor HS. Direct regulation of β3-integrin subunit gene expression by HOXA10 in endometrial cells. Mol Endocrinol. 2002;16:571–9.
[13] Lim H, Ma L, W-g M, Maas RL, Dey SK. Hoxa-10 regulates uterine stromal cell responsiveness to progesterone during implantation and decidualization in the mouse. Mol Endocrinol. 1999;13:1005–17.
[14] Celik O, Acet M, Kucuk T, et al. Surgery for benign gynecological disorders improve endometrium receptivity: a systematic review of the literature. Reprod Sci. 2017;24:174–92.
[15] Daftary GS, Kayisli U, Seli E, Bukulmez O, Arici A, Taylor HS. Salpingectomy increases peri-implantation endometrial HOXA10 expression in women with hydrosalpinx. Fertil Steril. 2007;87:367–72.
[16] Celik O, Yurci A, Ersahin A, et al. Endometrial injury upregulates expression of receptivity genes in women with implantation failure. Int J Environ Res Public Health. 2023;20:3942.
[17] Can B, Atilgan R, Pala S, Kuloğlu T, Kiray S, Ilhan N. Examination of the effect of ovarian radiation injury induced by hysterosalpingography on ovarian proliferating cell nuclear antigen and the radioprotective effect of amifostine: an experimental study. Drug Des Devel Ther. 2018;Volume 12:1491–500.
[18] Pala S, Atilgan R, Kuloğlu T, et al. Protective effects of vitamin C and vitamin E against hysterosalpingography-induced epithelial degeneration and proliferation in rat endometrium. Drug Des Devel Ther. 2016;Volume 10:4079–89.