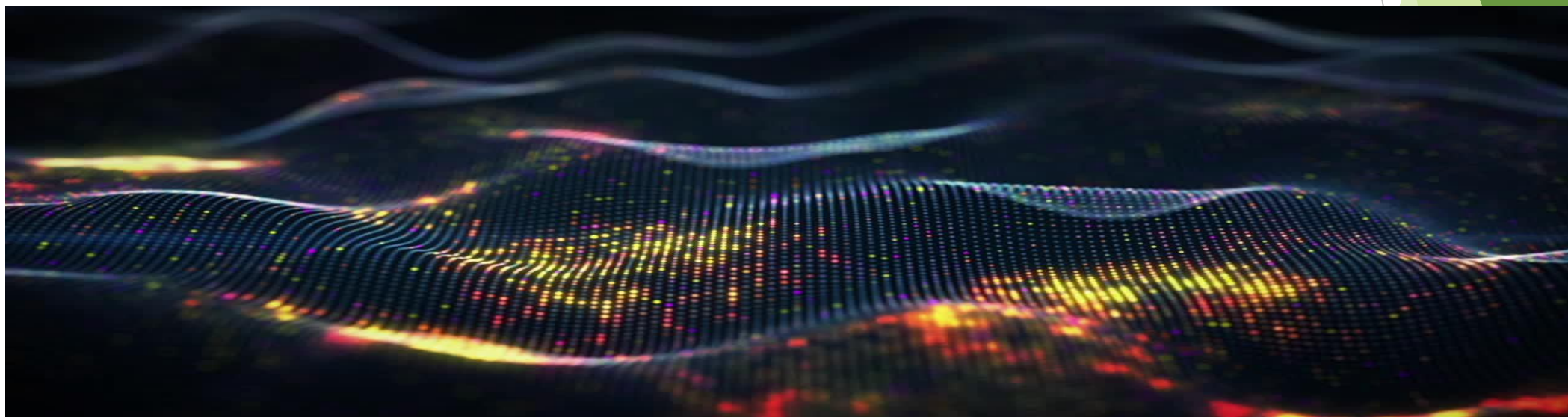


## INTRODUCING OF ENDOSEE ADVANCED

دکتر فرناز منتظری

فلوشیپ ناباروری



پرو



endosee<sup>®</sup>ADVANCE

See now. Know now.<sup>™</sup>

# Effectiveness and appropriateness in the application of office hysteroscopy

- ▶ With the advances in miniature instruments, office hysteroscopy on conscious patients has been the standard to explore the intrauterine pathology, with the ability to perform some minor procedures concomitantly. Patients usually appreciate the efficient “see and treat” procedures with such minimal discomfort that exempt from the inconvenience of going into the operating room and the need for anesthesia. However, controversies exist in the appropriateness of its application in some clinical situations. Concerns include (1) the criteria for hysteroscopy applied in the vast number of patients suffering from abnormal uterine bleeding or subfertility, and (2) the frequency for repeated hysteroscopy on some kinds of patients, such as those of endometrial cancer with fertility-sparing treatment for monitoring the disease, or those of severe intrauterine adhesion who need adhesiolysis for subsequent conception,

## ► Introduction

- Hysteroscopy is a powerful tool to diagnose and treat the pathologies in the uterine cavity. Indications of the diagnostic hysteroscopy include the abnormal uterine bleeding (AUB), suspicious lesions or foreign body involving the endometrial cavity, or post-treatment follow-up, etc., as listed in Table 1. Diagnostic hysteroscopy should be performed in the proliferative phase of the menstrual cycle for reproductive-aged women, and targeted biopsy can be performed whenever needed. However, known pregnancy as well as genital tract infections, such as pelvic inflammatory disease (PID), pyometra, and active herpetic or human papilloma virus infections, are contraindications to hysteroscopy. Although diagnostic hysteroscopy is feasible in patients of endometrial cancer, apparently exophytic-type cervical cancer is contraindicated for the risk of hemorrhage.

# Table 1. Indications of diagnostic hysteroscopy.

## Suspicion of intracavitary mass

Endometrial mass: e.g. endometrial polyp

Myometrial mass: e.g. leiomyoma

Retained gestational tissue

Foreign body: e.g. retained IUD remnant or dislocation

Abnormal uterine bleeding (other than the cervical etiology)

Reproductive-aged women<sup>a</sup>

Perimenopausal and/or Postmenopausal bleeding

## Abnormal endometrial thickening

Suspicion of endometrial hyperplasia or malignancy

Suspicion of infertility or implantation problems

Recurrent implantation failure

Recurrent pregnancy loss

Survey for uterine factor<sup>a</sup>

Suspicion of congenital anomaly

Uterine septum: complete or incomplete

Unicornuate/Bicornuate uterus/Uterus didelphys

Suspicion of intrauterine adhesion, or Asherman's syndrome

## Post-treatment (medical or surgical) follow-up

Endometrial cancer with fertility-sparing treatment**b**

Patients of breast cancer with tamoxifen treatment**a**

Second-look for surgeries involving endometrial cavity, as follows**c**

Myomectomy: for FIGO type 0 - type 3 myoma

Septal incision for septate uterus

Adhesiolysis

Miscellaneous

Other abnormal findings suspected within uterine cavity



## ► Hysteroscopy for women with implantation or fertility problems

- In Vitro Fertilization (IVF) becomes increasingly utilized to infertile couples with various indications recently. However, merely hysteroscopic examination does not improve the fertility outcome in women who are undergoing IVF, therefore hysteroscopy should not be routinely offered to infertile women who have normal TVS findings. Some factors, including AUB, [hypomenorrhea](#), and previous D&C, may increase the detection rate of intrauterine lesions on hysteroscopy in infertile women with sonographically normal uterine cavities.

- ▶ Abnormalities in uterine cavity are treatable causes of infertility. Women of submucous uterine fibroids who underwent hysteroscopic myomectomy would achieve a significant improvement of clinical pregnancy rate than those who didn't (39% vs. 21%, odds ratio (OR) 2.44), with a borderline significance of nearly a-half decreased incidence of miscarriage (OR 0.58,  $P = 0.50$ ). Women of endometrial polyps with undergoing hysteroscopic removal of polyps prior to intrauterine insemination (IUI) showed a more significant improvement of clinical pregnancy than without (63% vs. 28%, OR 4.41).

## ► Hysteroscopy for the evaluation of recurrent pregnancy loss

- A clinical pregnancy is defined by the clinical evidence (fetal heartbeat) or ultrasound visualization of an embryonic pole in the gestational sac with heartbeat. Only <5% of women will undergo two consecutive first-trimester pregnancy losses, and only 1% encounter three or more. Various etiologies may result in the recurrent pregnancy loss. Evaluations should be arranged for these patients.
- The uterine abnormality is one of the significant causes of recurrent pregnancy losses besides the factors of age, genetics, antiphospholipid syndrome, or sperm quality. Previous studies demonstrated that congenital uterine abnormalities occurred in 4.3% of the general population of fertile women and in 12.6% of patients with recurrent pregnancy losses. Therefore, hysteroscopic evaluation of uterine cavity is recommended in these patients.

## ► Hysteroscopy in patients with repeated implantation failure

- Repeated implantation failure was defined as the failure for at least 3 consecutive IVF cycles with transferring one to two high-grade quality embryos in each. Uterine factors associated with repeated implantation failure includes endometrial polyp, submucosal myoma, intrauterine adhesion, or uterine septum. Though the good quality of embryo is critical for a successful IVF treatment; however, patients with repeated implantation failure should undergo hysteroscopy to investigate the uterine cavity, and any of these treatable factors should be treated.

## ► Hysteroscopic endometrial scratching and its effects in IVF treatment

- To deal with the repeated IVF treatment failure, many efforts have been tried to improve the embryo quality or endometrial receptivity. For example, hysteroscopic endometrial scratch - intentional injury to the endometrium - in women undergoing ART is one of the procedures proposed to improve the endometrial receptivity. A Cochrane review found that endometrial scratch performed between day 7 of the previous cycle and day 7 of the embryo transfer (ET) cycle is associated with an improved live birth and clinical pregnancy rates (RR 1.34, 95% CI 1.21 to 1.61) versus those without scratch in women with >2 previous embryo transfers. The procedure did not increase the adverse events of miscarriage, multiple pregnancy or bleeding. However, a randomized controlled trial (RCT) of endometrial scratch on the day of oocyte retrieval found a marked reduction of live birth (RR 0.31, 95% CI 0.14 to 0.69) and clinical pregnancy (RR 0.36, 95% CI 0.18 to 0.71) rates versus those without scratch.

## ► Hysteroscopy for intrauterine adhesions or synechiae

- In situations causing trauma to the endometrial basalis, the inflammatory reaction of wound healing could result in a fibrotic change and adhesion formation within uterine cavity. This disorder became well-known because Dr. Joseph Asherman reported the formation of IUA after miscarriage, curettage, and/or endometritis of the gravid uterus. Nowadays the term “Asherman syndrome” is accepted as a synonym of IUA or synechia, but some authors still prefer to restrict it for the sequela of gravid uterus.
- IUAs in the non-gravid uterus are often produced following intrauterine surgery and/or infections which causes significant endometritis. Principally, procedures creating opposing wound and breaking through the endometrial basalis (ex., septal incision or adhesiolysis) or entering the myometrium (ex., myomectomy) yielded higher incidence of IUA formation;

- ▶ however, those wounding superficially and above the endometrial basalis (ex., polypectomy) had the lowest risk. Spatially, the adhesion and/or fibrotic change could happen along the surface of endometrium, or extend deep into the myometrium, and/or produce fibrotic adhesion bands between two opposing surfaces. Office hysteroscopy serves good in postoperative follow-up to check the *de novo* intrauterine adhesions (IUAs) formation. A study found that the *de novo* IUAs formation after septal incision, adhesiolysis, and myomectomy were 88%, 76%, and 40%, respectively; in contrast to none of the polypectomy

## ► Concluding remarks

- It seems the controversies were raised not for the efficacy of hysteroscopy *per se.*, but from its relatively invasive and costly nature in comparison with other imaging examinations, such as the TVS. Therefore, hysteroscopy was currently suggested as a confirmative tool for patients of AUB when the intracavitary lesion has already been suspected and to avoid blind D&C.
- Given that the menstrual regurgitation is a physiologic phenomenon and the finding that the hysteroscopy did not negatively impact the outcomes of endometrial carcinoma, hysteroscopy is now accepted as a powerful tool for early detection of endometrial cancer and monitoring for FST patients. The remaining controversy of this issue could be on the consensus of establishing standard protocol about the frequency of hysteroscopic evaluation on these patients.



- Currently, the treatment of IUA relies on the mechanical methods of surgical lysis and barrier applied between to prevent the adhesion reformation. Controversies raised in the treatment of severe IUA is the frequency of repeated hysteroscopic adhesiolysis. However, before any promising results could be obtained from the trials of other modalities, such as the stem cell therapies mentioned above, repeated hysteroscopy with adhesion prevention is still the gold standard and a known way to reach the success of IUA treatment. As IUA has been questioned not merely a surgical disease, sound knowledge of endometrial regeneration and adhesion prevention are needed to find better strategies of treatment.

- ▶ Conclusively, the application of office hysteroscopy in conscious patient has been a great advance. Patients were amazed at its directly “see and treat” process with such minimal invasiveness and without the inconvenience of going into the OR. To resolve the current controversies, well-designed prospective, comparative studies to reveal the best efficacy of treatment strategies and the cost-effectiveness between medical quality and health-care expense are needed. Nevertheless, a deeper insight into the biological nature and disease mechanisms are pending to facilitate the progress of women health care.

# Office hysteroscopy before first in vitro fertilization. A randomized controlled trial

## Background

Implantation failure remains a mystery since decades. This procedure needs a “top quality embryo” and a “normal” uterine cavity. To assess uterine cavity before first in vitro fertilization (IVF), many diagnostic tools could be used. Hysteroscopy remains the gold standard to diagnose and treat intra-uterine anomalies. However, it is not clearly recommended to offer an office hysteroscopy before first IVF when transvaginal ultrasound (TVUS) and hysterosalpingography (HSG) were normal.

## Purpose

This study aimed to assess the role of office hysteroscopy before first IVF when no intra-uterine anomalies are suspected

## Basic procedures

We conducted a randomized controlled trial including 171 women scheduled for their first IVF. Women were assigned to either Group I: office hysteroscopy before IVF or Group II: immediate IVF.

We included women aged less than 40 years, having regular cycles, FSH levels less than 10 UI/l, antral follicular count  $\geq 12$ , normal TVUS and HSG. Their body mass index (BMI) ranged from 19 to 30 kg/m<sup>2</sup>.

We excluded patients known having severe endometriosis, polycystic ovarian syndrome (PCOS) and oocyte receivers. The primary outcome were livebirth rate and clinical pregnancy rate.

## Main fundings

Between january 2016 and september 2017, we randomly assigned 171 women to either Group I (n = 84) or Group II (n = 87). Hysteroscopy was done in the mid-follicular phase immediately before IVF. Baseline characteristics and IVF features were comparable between groups except for the IVF protocol. Live birth rate was 23,9% in Group I versus 19,3% in Group II. ( $p = 0,607$ ). Clinical Pregnancy rate was 32,4% in Group I versus 21,7% in Group II. ( $p = 0,326$ ). No statistical significance was observed for neither miscarriage rate nor multiple pregnancy rate. Hysteroscopy showed 30% unsuspected intra-uterine anomalies: 11 intra-uterine adhesions, 7 polyps, 7 clinical endometritis and one fibroid print. Therapeutic hysteroscopy was done only for 6 intra-uterine adhesions and 3 polyps. Other anomalies did not require operative hysteroscopy. Visual analog score during hysteroscopy was  $4,69 \pm 2,892$ . 5 women (6%) of Group I experienced discomfort during diagnostic hysteroscopy. Only one patient had vagal syncope. No further complications were observed.

## Principal conclusions

Office hysteroscopy before first IVF seems not improve IVF results. Minimal intra-uterine anomalies not diagnosed by transvaginal ultrasound and hysterosalpingography do not seem to reduce IVF results.

## The effect of performing hysteroscopy prior to the first in vitro fertilization (IVF) cycle on live birth rate

In this retrospective cohort study, a total of 707 couples underwent in vitro fertilization (IVF) at Hacettepe University Hospital between 01 January 2010 and 01 November 2014 with their chronologically first cycle were evaluated. Patients who have diagnostic hysteroscopy prior to first IVF cycle served as a study group (n = 42) and patients without diagnostic hysteroscopy served as control group (n = 282). In study group in all patients, diagnostic hysteroscopy was performed at the follicular phase of previous menstrual cycle, namely immediately before ovarian stimulation (OS) cycle. Demographic features, clinical characteristics and treatment outcomes were compared between the groups. The logistic regression analysis was performed in order to assess independent predictors of live birth rates (LBRs). There was no statistically significant difference between the groups for demographic features and OS cycle characteristics. Implantation rate (22.2% vs. 21.5%,  $p=.840$ ), clinical pregnancy rate (33.3% vs. 28.7%,  $p=.541$ ), and LBRs (23.8% vs. 18.5%,  $p=.420$ ) were comparable. In logistic regression analysis, performing hysteroscopy prior to first IVF cycles per se without correcting anatomic abnormalities was not an independent predictor of LBRs (OR: 0.72, 95% CI: 0.310-1.68,  $p=.45$ ). In conclusion, performing diagnostic hysteroscopy prior to first IVF treatment cycle without correcting any anatomic abnormalities did not improve LBRs.

# Hysteroscopy prior to the first IVF cycle: A systematic review and meta-analysis

- This systematic review and [meta-analysis](#) investigated the use of routine [hysteroscopy](#) prior to starting the first IVF cycle on treatment outcome in asymptomatic women. Searches were conducted on MEDLINE, EMBASE, Cochrane Library, National Research Register and ISI Conference Proceedings. The main outcome measures were clinical pregnancy and live birth rates achieved in the index IVF cycle. One randomized and five non-randomized controlled studies including a total of 3179 participants were included comparing hysteroscopy with no intervention in the cycle preceding the first IVF cycle. There was a significantly higher clinical pregnancy rate (relative risk, RR, 1.44, 95% CI 1.08-1.92,  $P = 0.01$ ) and LBR (RR 1.30, 95% CI 1.00-1.67,  $P = 0.05$ ) in the subsequent IVF cycle in the hysteroscopy group. The [number needed to treat](#) after hysteroscopy to achieve one additional clinical pregnancy was 10 (95% CI 7-14) and live birth was 11 (95% CI 7-16). Hysteroscopy in asymptomatic woman prior to their first IVF cycle could improve treatment outcome when performed just before commencing the IVF cycle. Robust and high-quality randomized trials to confirm this finding are warranted.



Currently, there is evidence that performing hysteroscopy (camera examination of the womb cavity) before starting IVF treatment could increase the chance of pregnancy in the subsequent IVF cycle in women who had one or more failed IVF cycles. However, recommendations regarding the efficacy of routine use of hysteroscopy prior to starting the first IVF treatment cycle are lacking. We reviewed systematically the trials related to the impact of hysteroscopy prior to starting the first IVF cycle on treatment outcomes of pregnancy rate and live birth rate in asymptomatic women. Literature searches were conducted in all major database and all randomized and non-randomized controlled trials were included in our study (up to March 2013). The main outcome measures were the clinical pregnancy rate and live birth rate. The secondary outcome measure was the procedure related complication rate. A total of 3179 women, of which 1277 had hysteroscopy and 1902 did not have a hysteroscopy prior to first IVF treatment, were included in six controlled studies. Hysteroscopy in asymptomatic woman prior to their first IVF cycle was found to be associated with improved chance of achieving a pregnancy and live birth when performed just before commencing the IVF cycle. The procedure was safe. Larger studies are still required to confirm our findings.



# Patient and provider satisfaction with saline ultrasound versus office hysteroscopy for uterine cavity evaluation prior to in vitro fertilization: a randomized controlled trial

- ▶ Purpose
- ▶ To compare patient and provider satisfaction with saline ultrasound (SIS) versus office hysteroscopy for cavity evaluation prior to in vitro fertilization (IVF) and to assess the capability of hysteroscopy to manage pathology at time of diagnosis to reduce delays and supernumerary procedures.
- ▶ Methods
- ▶ This was a randomized, controlled trial in a university fertility clinic. One hundred enrolled subjects undergoing routine uterine cavity evaluation prior to planned embryo transfer were randomized to SIS or office hysteroscopy without anesthesia. Subjects and providers completed surveys about their experience. Subjects with findings on SIS had a hysteroscopy performed or scheduled for further evaluation. Those with hysteroscopy findings had management attempted within the same procedure.

## Results

Overall patient satisfaction was high and did not differ between groups, while providers indicated that hysteroscopy provided a better cavity evaluation. There was no difference in time to complete procedures between groups. Pain score on a ten-scale was slightly higher in the hysteroscopy group compared to the SIS group ( $3.38 \pm 1.85$  vs.  $2.44 \pm 1.64$ ,  $p < 0.01$ ), but this did not impact satisfaction scores. Although pathology was found in a similar rate (22% vs. 36% for SIS and HSC groups, respectively), those in the SIS group all required secondary procedures, while only 1/17 did in the HSC group ( $p < 0.01$ ).

## Conclusion

Although the hysteroscopy group exhibited slightly higher pain scores, overall patient and provider satisfaction was high and similar between groups. There were significantly fewer secondary procedures and delays in the hysteroscopy group. Hysteroscopy is a reasonable first line screening tool for patients requiring cavity evaluation.

# Endometrial scratch injury with office hysteroscopy before IVF/ICSI: A randomised controlled trial

- ▶ Objective
- ▶ Endometrial scratch injury (ESI) has been proposed to improve endometrial receptivity and thereby increase implantation rates in assisted reproductive technology (ART) treatment. ESI has been widely incorporated into clinical practice despite inconclusive evidence of its effect on reproductive outcomes. We aimed to assess pregnancy and live birth rates in subfertile women receiving ESI before IVF treatment in comparison to controls.
- ▶ Study design
- ▶ This was a randomised controlled trial (RCT) with no blinding of participants, investigators or health care personnel. Women in ART treatment were allocated to either office hysteroscopy with ESI (ESI group) or no intervention (control group). In total 184 women in IVF/ICSI treatment with minimum one previous failed IVF/ICSI cycle, were included in the final analysis. The primary outcome was positive serum hCG (s-hCG). Secondary outcomes were ongoing pregnancy and live birth rate. Only per-protocol analyses were performed as all patients included at one centre had to be excluded. The trial is registered at ClinicalTrials.gov, NCT01743391.

## Results

Our results showed a non-significant increase in positive s-hCG (OR 1.23, 95 % CI (0.65-2.33)), ongoing pregnancy (OR 1.52, 95 % CI (0.73-3.17)), and live birth rates (OR 1.69, 95 % CI (0.78-3.64)) per randomised woman between the ESI and the control group.

## Conclusion

We observed no significant differences in positive s-hCG or other reproductive outcomes in the ESI vs. the control group. While the crude estimates of positive reproductive outcomes were higher in the ESI group, statistical significance was not reached, and the study was not powered to show smaller differences. However, data from this study will be re-evaluated in the context of an individual participant data meta-analysis (IPD-MA) of RCTs on ESI.

# Hysteroscopy Prior In To Vitro Fertilization

- ▶ This manuscript stresses the role and importance of hysteroscopy in patients prior to IVF treatment. Office hysteroscopy, technically feasible and with high levels of patient compliance, is today's gold standard for the study of uterine cavity. Published trials have demonstrated a relatively high incidence of intracavitary abnormalities diagnosed at outpatient hysteroscopy and in patients with prior IVF treatment and previous IVF cycle failure, the correction of which markedly improves outcomes.
- ▶ Although observational studies indicate higher pregnancy rates following hysteroscopic removal of endometrial polyps, submucous fibroids, uterine septum, and intrauterine adhesions, more randomized studies are needed to substantiate the effectiveness of hysteroscopic removal of polyps, submucous fibroids, uterine septum, or intrauterine adhesions in women prior to IVF.
- ▶ Endometritis and such recent hysteroscopic technology as endometrial scratching, are discussed in the case of RIF (Recurrent Implantation Failure), but more studies are needed to confirm their effective role in infertility

# Analgesia for Office Hysteroscopy: A Systematic Review and Meta-analysis

## ► Objective

- To identify the most effective analgesia for women undergoing office hysteroscopy.

## ► Data Sources

- We searched Medline, Embase, the Cumulative Index to Nursing and Allied Health Literature, and the Cochrane Library from inception until August 2019 for studies that investigated the effect of different analgesics on pain control in office hysteroscopy.

## ► Methods of Study Selection

- We included randomized controlled trials that investigated the effect of analgesics on pain experienced by women undergoing diagnostic or operative hysteroscopy in an office setting compared with the control group.

## Tabulation, Integration, and Results

The literature search returned 561 records. Twenty-two studies were selected for a systematic review, of which 16 were suitable for meta-analysis. There was a statistically significant reduction in pain during office hysteroscopy associated with preprocedural administration of nonsteroidal anti-inflammatory drugs (NSAIDs) (standardized mean difference [SMD] -0.72; 95% confidence interval [CI] -1.27 to -0.16), opioids (SMD -0.50; 95% CI -0.97 to -0.03), and antispasmodics (SMD -1.48; 95% CI -1.82 to -1.13), as well as with the use of transcutaneous electrical nerve stimulation (TENS) (SMD -0.99; 95% CI -1.67 to -0.31), compared with the control group. Moreover, similar reduction in pain was observed after office hysteroscopy: NSAIDs (SMD -0.55; 95% CI -0.97 to -0.13), opioids (SMD -0.73; 95% CI -1.07 to -0.39), antispasmodics (SMD -1.02; 95% CI -1.34 to -0.69), and TENS (SMD -0.54; 95% CI -0.95 to -0.12).

Significantly reduced pain scores with oral NSAID administration during (SMD -0.87; 95% CI -1.59 to -0.15) and after (SMD -0.56; 95% CI -1.02 to -0.10) office hysteroscopy were seen in contrast to other routes. Significantly more adverse effects were reported with the use of opioids ( $p < .001$ ) and antispasmodics ( $p < .001$ ) when compared with the control group, in contrast to NSAIDs ( $p = .97$ ) and TENS ( $p = .63$ ).

### Conclusion

Women without contraindications should be advised to take oral NSAIDs before undergoing office hysteroscopy to reduce pain during and after the procedure. TENS should be considered as an alternative analgesic in women with contraindications to NSAIDs.



# Waiting Time and Pain During Office Hysteroscopy

- ▶ Study Objective
  - ▶ To find a correlation between the waiting time between counseling about and performance of office hysteroscopy and the perception of pain.
- ▶ Design
  - ▶ Observational study (Canadian Task Force classification II-2).
- ▶ Setting
  - ▶ Academic environment.
- ▶ Patients
  - ▶ Two hundred eighty-four women undergoing hysteroscopy.
- ▶ Interventions
  - ▶ Diagnostic hysteroscopy with endometrial biopsy

- ▶ Measurements and Main Results
- ▶ Before examination, patients were asked to complete 2 forms, the STAI-S (State-Trait Anxiety Inventory, State) and STAI-T (State-Trait Anxiety Inventory, Trait) anxiety scales, for evaluation of their usual anxiety state and their state of anxiety during the examination. Patients were asked to quantify on a visual analog scale the pain felt during the examination. A statistically significant positive correlation, even if weak, was demonstrated between pain and waiting time ( $r = 0.45$ ;  $p < .01$ ) but not with the values for the anxiety state ( $r = 0.06$ ;  $p = .56$ ) and anxiety trait ( $r = -0.05$ ;  $p = .66$ ). Pain ( $\geq 4$ ) was significantly associated with waiting time ( $\geq 60$  minutes) (odds ratio [OR], 5.21; 95% confidence interval [CI], 1.29–35.50), age (OR, 1.57; 95% CI, 0.40–5.87) and menopause (OR, 2.81; 95% CI, 1.10–7.40) but not with STAI-S level ( $\geq 34$ ) (OR, 0.87; 95% CI, 0.26–3.12) or STAI-T level ( $\geq 34$ ) (OR, 0.65; 95% CI, 0.19–2.32).

## Conclusion

Office hysteroscopy is associated with a level of anxiety that can affect patient tolerability of the procedure. However, factors such as reducing waiting time may have a positive effect on patient compliance, making hysteroscopy easier and thereby increasing its diagnostic and therapeutic potential.

THANK YOU  
FOR YOUR  
ATTENTION