Title

Pre-removal plasma levonorgestrel level and return ot fertility after levonorgestrel 52 mg intrauterine system discontinuation

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baseline tubal patency and pelvic adhesions, followed by transcervical infusion of either 20 mL of 5% PDF (each 5 mL of foam contains 25 mg doxycycline; n=12, 8 nulliparous, 4 parous), 20 mL of 1% control methylcellulose foam (MC; n = 6, 5 nulliparous, 1 parous), or no additional treatment (Control; n=6, all nulliparous). All of the females received an intramuscular injection of depomedroxyprogesterone acetate (DMPA, 2 mg/kg) after the treatment. After recovery, females were socially-housed with males (n=4) of proven fertility, and observed for resumption of menstrual cyclicity and evidence of mating. The primary outcomes was pregnancy within 6 months of resumption of menses. We plan to follow pregnancy and safety outcomes thorough 18 months in the PDF-treated animals, and evaluate histologic features of tubal occlusion.

RESULTS: The baseline laparoscopy demonstrated bilateral tubal patency in all of animals selected for the study. All females resumed normal menstrual cycles and mating activity within 3 months of treatment. After 6 months of regular cycles, 11/12 (92%) of control females became pregnant (6/6 MC control, 5/6 untreated control). Significantly fewer (2/12, 16%) pregnancies occurred in PDF-treated females ($p < .001$, Fisher's exact test). All of the pregnancies were intrauterine. Both pregnancies in PDF-treated females occurred in nulliparous females - a group considered high-risk for failure. One progressed normally to term and one underwent spontaneous abortion.

CONCLUSIONS: A single transcervical treatment with PDF prevented pregnancy in most baboons. Pregnancy occurred in PDF-treated females considered at high risk of failure due to nulliparity.

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P-495 Wednesday, October 16, 2019 6:30 AM

PRE-REMOVAL PLASMA LEVONORGESTREL LEVEL AND RETURN OT FERTILITY AFTER LEVONORGESTREL 52 MG INTRAUTERINE SYSTEM DISCONTINUATION. Michael A. Thomas, MD,[a] Gretchen S. Stuart, MD, MPH,[b] Carolyn L. Westhoff, MD, MSc,[c] David L. Eisenberg, MD, MPH,[b] Andrea I. Olariu, MD, PhD,[b] Mitchell D. Creinin, MD[d] [a]University of Cincinnati, West Chester, OH; [b]Affiliation not provided; [c]Columbia University, New York, NY; [d]University of California - Davis, Sacramento, CA.

OBJECTIVE: Evaluate return of fertility after levonorgestrel (LNG) 52 mg intrauterine system (IUS) discontinuation according to pre-removal serum levonorgestrel levels.

DESIGN: Prospective clinical trial.

MATERIALS AND METHODS: Nulliparous and parous women 16-45 years old received the Liletta® LNG 52 mg IUS in an IRB-approved multicenter trial to evaluate efficacy and safety for up to 10 years. Participants in a pharmacokinetics sub-study had frequent plasma LNG evaluations over the first 3 years of the trial. All study subjects, beginning at 3 years of LNG IUS use, had plasma LNG evaluations every 6 months and at IUS removal (if no level had been obtained in the prior 3 months). Women who desired pregnancy were followed for up to 12 months for pregnancy occurrence. This analysis compares LNG concentrations at IUS discontinuation between women who did and did not conceive and evaluates time to conception, using Fisher's exact and Mann Whitney U tests as indicated. We evaluated outcomes in women aged 16-35 years at study entry who had LNG levels within 90 days prior to or the day of IUS removal.

RESULTS: The analysis cohort includes 76 women who conceived and 19 women who did not conceive within 12 months of IUS removal. The majority of plasma LNG levels had been obtained on the IUS removal day in both groups (60/76 [79%] vs. 16/19 [84%], respectively, p=0.76). The ages of the women who conceived and did not conceive were 25.5 ± 3.1 and 25.2 ± 3.6 years. The proportion of nulliparous women in the two groups was similar (60/76 [79%] vs. 12/19 [63%], respectively, p=0.23). Fewer women who conceived had a body mass index (BMI) ≥30 kg/m^2 (9/76 [12%] vs. 7/19 [37%], respectively, p=0.02) although the median BMI among women who conceived and did not conceive was similar (23.7 vs. 24.9 kg/m^2, respectively, p=0.11). Median duration of use was 4.3 (range 2.0-7.6) and 4.0 (range 2.0-6.4) years, respectively. Median LNG levels were higher among women who conceived than among those who did not (Table). Eight women conceived within one month and another 34 women by the end of 3 months. Median LNG levels among the 42 women who conceived within 3 months (124.5 pg/mL) after IUS discontinuation were similar to the 34 women who conceived at 4-12 months (103.5 pg/mL), p=0.23.

Median LNG levels (pg/mL)

	conceived	did not conceive	p-value
overall	109.5 (n=76)	78.2 (n=19)	<0.01
non-obese	123 (n=67)	99.4 (n=12)	0.09
obese	86.8 (n=9)	59.7 (n=7)	0.06

Obese = BMI ≥ 30 kg/m^2

CONCLUSIONS: Plasma LNG levels were higher among women who conceived after LNG 52 mg IUS discontinuation compared to women who did not conceive. We found no evidence that higher LNG levels impact the ability to conceive or time to conceive following LNG 52 mg IUS removal.

SUPPORT: Medicines360.

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SELF-ADMINISTERED VAGINAL LIDOCAINE *IN-SITU* GEL PRIOR TO INTRAUTERINE DEVICE INSERTION IS AN EFFECTIVE ANALGESIC IN WOMEN WITH NO PREVIOUS VAGINAL DELIVERY. Ahmed M. Abbas, MD,[a] Noura H. Abd Ellah, PhD,[b] Meret Ayad, MSc,[a] Mohamed Abdellah, MD.[a] [a]Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt; [b]Department of Pharmaceutics, Faculty of Pharmacy, Assiut University, Assiut, Egypt.

OBJECTIVE: Long-acting reversible contraception methods are highly effective for reduction of the unplanned pregnancy rate. The intrauterine device (IUD) can provide reliable, effective and long term contraception for many women. However, the insertion procedure can be associated with a troublesome degree of pain that prevent some women from choosing its use. Our objective is to assess the analgesic effect of self-administered vaginal lidocaine *in-situ* gel in pain relief during IUD insertion in women with no previous vaginal delivery.

DESIGN: Randomized, double-blind, placebo-controlled trial (Clinicaltrials.gov: NCT03166111).

MATERIALS AND METHODS: Reproductive-aged women who previously delivered only by cesarean section (CS) requesting Multiload-375 Copper IUD insertion were counseled to participate. Eligible women category 1 or 2 based on WHO guidelines were recruited and randomized (1:1) to lidocaine in-situ gel vs. placebo using a permuted block schedule. Each woman was supplied by a syringe filled with 5 ml lidocaine or placebo in-situ gel to be self-administered vaginally 10 minutes prior to insertion. The primary outcome was the difference in pain scores during IUD insertion using a 10-cm Visual Analogue Scale (VAS). A 2 cm difference in VAS score between both arms was considered a clinically significant difference. The secondary outcomes included the difference in pain scores during cervical tenaculum placement, uterine sound insertion and 15 minutes post-procedure, ease of insertion score and need for additional analgesia. Mann Whitney and Fisher's exact tests were used for the analysis of the outcomes.

RESULTS: The final analysis included 105 women randomized to lidocaine in-situ gel group (n=54) or placebo (n=51). Both arms were similar regarding age, parity, BMI, and a number of previous CS. Lidocaine in-situ gel group reported significantly lower pain scores during uterine sound insertion (median[IQR]: 3.5 [2-5] vs 6[5-8], p<0.001), IUD insertion (median[IQR]: 3.5[2-4.25] vs 5.5[4.75-8], p=0.002) and 15 minutes post-insertion (median[IQR]: 1.5[1-1.75] vs 4[2-4], p=0.03). No difference between scores during tenaculum placement (median[IQR]: 2.5[1.5-3] vs 3[2-4], p=0.07). The ease score of IUD insertion was significantly higher in the lidocaine group (median[IQR]: 8[7-9] vs. 6[5.25-8], p=0.001). No difference regarding the need for additional analgesia.

CONCLUSIONS: Self-administered vaginal lidocaine in-situ gel 10 minutes prior to copper IUD insertion is effective in pain reduction in women with no previous vaginal delivery.

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