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Title

Plasma levonorgestrel levels in non-obese and obese women using a levonorgestrel 52 mg intrauterine system for up to 7 years

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status, income quartile, patient urban-rural designation, hospital geographic region and hospital teaching status. We compared data to visits by women in the same age range without an EC diagnosis. Z-tests were performed to assess any significant differences between groups.

RESULTS: The estimated number of encounters for EC in the ED decreased significantly during the study period. The steepest decline occurred from 2006 (15,039 visits; 95%CI: 11,270 - 18,902) to 2007 (4,370 visits; 95%CI: 3,523 - 5,217). After 2007, visits decreased steadily, reaching 685 visits in 2014 (95%CI: 488 - 881). Overall, this represented a 95% decrease in visits over time. Annual total ED charges decreased from \$6.2M in 2006 to \$0.65M in 2014. When compared to all other ED visits by women aged 15-44 yo in 2014, ED visits for EC were more likely to be by women aged 15-19 yo (30.7% vs 13.3%; $p < .001$), who lived in the Northeast (53.7% vs 17.7%; $p < .001$), lived in large metropolitan areas (64.2% vs 48.1%; $p = 0.010$), or presented to metropolitan teaching hospitals (64.0% vs 54.4%; $p = 0.111$). The proportion of visits for EC by patients who lived in zip codes with average incomes in the lowest and second income quartiles was 29.9% (95%CI: 20.7% - 39.2%), and 36.2% (95%CI: 23.4% - 49.0%), respectively in 2014. Trends by payer showed that patients with private insurance or self-pay status experienced steeper declines in ED visit counts compared to patients with Medicaid, with estimated percent changes of -98%, -98% and -83% between 2006-2014 respectively.

CONCLUSIONS: ED utilization for emergency contraception decreased substantially between 2006-2014, demonstrating the influence of policy on these care seeking patterns. This decrease also led to cost-savings in the ED by reducing utilization. Nonetheless, trends by payer indicate a potential disparity in how women currently access (ED vs other outlets) and can pay for EC. Future policies should ensure that patients seeking care for unintended pregnancy are provided timely and cost-effective care.

Supported by: University of Michigan.

O-104 Tuesday, October 9, 2018 11:00 AM

RETURN OF FERTILITY IN NULLIPAROUS AND PAROUS WOMEN AFTER LEVONORGESTREL 52 MG INTRAUTERINE SYSTEM DISCONTINUATION.

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OBJECTIVE: Evaluate reproductive function in nulliparous and parous women after levonorgestrel (LNG) 52mg intrauterine system (IUS) discontinuation based on time to pregnancy.

DESIGN: Prospective clinical trial.

MATERIALS AND METHODS: Eligible nulliparous and parous women 16-45 years old received the Liletta® IUS in a multicenter trial evaluating efficacy and safety for up to 10 years. Participants who discontinued the IUS within the first 5 years of use and desired pregnancy were contacted every three months for up to 12 months to determine whether pregnancy occurred; pregnancy outcomes were not assessed. We evaluated fertility endpoints in women 16-35 years at study entry. We compared outcomes by parity, gravidity and age using Fisher's exact test, student's t-tests and chi-square test for trend as indicated.

RESULTS: Overall, 132 (86.8%) of 152 women 16-35 years old at study entry who attempted to conceive did so within 12 months. The 12-month conception rates did not differ between nulliparous (70/80 [87.5%]) and par-

Years of IUS Use	Total		Nulliparous		Parous	
	Pregnant	p-value*	Pregnant	p-value*	Pregnant	p-value*
≤1	11/12 (92%)	0.43	3/3 (100%)	0.62	8/9 (89%)	0.29
1+ to 2	27/30 (90%)		11/12 (92%)		16/18 (89%)	
2+ to 3	36/41 (88%)		17/21 (81%)		19/20 (95%)	
3+ to 4	33/42 (79%)		21/25 (84%)		12/17 (71%)	
4+ to 5	25/27 (93%)		18/19 (95%)		7/8 (85%)	

*Chi-square test for trend

ous (62/72 [86.1%]) women ($p = 0.82$) or between nulligravid (60/68 [88.2%]) and gravid (72/84 [85.7%]) women ($p = 0.81$). Pregnancy by the end of 3 and 6 months occurred in 66 (43.4%) and 106 (69.7%), respectively, with a median time to conception of 91.5 days. Median use before discontinuation for the evaluated population was 34 months (range 1.3-59.8 months). Pregnancy rates at 12 months post-discontinuation did not differ by length of IUS use for nulliparous or parous women (Table). The age at IUS discontinuation of women who successfully conceived (29.8±4.0 years) did not differ from women who did not conceive (29.6±4.3 years), $p = 0.84$.

CONCLUSIONS: After Liletta discontinuation, women have rapid return of normal fertility as demonstrated by time to pregnancy in the year post-removal. Fertility rates after IUS removal do not vary based on parity, gravidity, duration of IUS use or age at discontinuation.

Supported by: Medicines360.

O-105 Tuesday, October 9, 2018 11:15 AM

PLASMA LEVONORGESTREL LEVELS IN NON-OBESE AND OBESE WOMEN USING A LEVONORGESTREL 52 MG INTRAUTERINE SYSTEM FOR UP TO 7 YEARS.

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OBJECTIVE: To evaluate levonorgestrel plasma concentrations for up to seven years in non-obese and obese women using a levonorgestrel (LNG) 52mg intrauterine system (IUS).

DESIGN: Prospective clinical trial.

MATERIALS AND METHODS: Eligible women 16-45 years old received an LNG 52mg IUS (Liletta®) in a multicenter trial evaluating efficacy and safety for up to 10 years. A planned sub-study enrolled 40 participants (19 obese, 21 non-obese) to evaluate LNG concentrations over time at baseline, weeks 1 and 2, and months 1, 3, 6, 9, 12, 18, 24, 30 and 36. Additionally, all study subjects (219 obese and 670 non-obese) began blood sampling every 6 months at month 36. The liquid chromatography-tandem mass spectrometry assay had a lower limit of LNG detection of 25 pg/mL. We compared LNG concentrations in obese and non-obese women at each time point through 84 months (7 years) using an independent-samples t-test.

RESULTS: Plasma LNG concentration was lower in obese compared with non-obese subjects at all time-points through 84 months (Table). All obese users had maximum levels <300 pg/mL at day 30 and thereafter. Maximum LNG concentrations in non-obese LNG 52mg IUS users were 603 pg/mL at week 1, 492 pg/mL at week 14, and <300 pg/mL by 1 year. From 3 to 84 months, LNG concentrations were 21-41% lower in obese subjects ($p < 0.01$ for all months). Average BMI in the obese and non-obese sub-study participants were $38.6 \pm 5.8 \text{ kg/m}^2$ and $24.6 \pm 2.9 \text{ kg/m}^2$, respectively, with ranges of 30.4-49.2 kg/m^2 and 18.9-29.5 kg/m^2 , respectively. Average BMI in the obese and non-obese study subjects beginning sampling at 36 months were similar, with 23.2% of obese subjects having a BMI $\geq 40 \text{ kg/m}^2$.

CONCLUSIONS: Obese women demonstrate lower plasma LNG concentrations throughout seven years of LNG 52mg IUS use. The LNG concentrations in obese and non-obese women may be helpful for patient education

Mean Plasma Levonorgestrel Levels in Levonorgestrel 52mg IUS Users

Time Point (months)	Obese		Non-Obese		P-value
	N	LNG (pg/mL)	N	LNG (pg/mL)	
0.25 (1 week)	19	188 ± 53	21	310 ± 140	<.001
1	19	180 ± 45	21	248 ± 83	.006
6	16	151 ± 40	20	230 ± 67	<.001
12	15	144 ± 52	18	192 ± 36	.006
24	15	116 ± 27	15	178 ± 38	.002
36	219	104 ± 53	670	141 ± 51	<.001
48	182	90 ± 44	550	121 ± 52	<.001
60	95	83 ± 46	250	114 ± 45	<.001
72	65	69 ± 29	133	102 ± 39	<.001
84	47	64 ± 29	94	94 ± 32	<.001

regarding the differences in exogenous hormone exposure between the LNG 52mg IUS and contraceptives that primarily deliver LNG systemically.

Supported by: Medicines360.

O-106 Tuesday, October 9, 2018 11:30 AM

POST HOC ANALYSIS OF A RANDOMIZED PLACEBO-CONTROLLED PILOT STUDY ON THE EFFECT OF AMPHORA®, AN ACID-BUFFERING VAGINAL GEL, ON VAGINAL PH BY BASELINE VAGINAL PH LEVEL.



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OBJECTIVE: High vaginal pH may increase a woman's risk of bacterial vaginosis (Linhares et al. *Am. J. Obstet. Gynecol* 2011). The objective of this study was to determine the change and duration of change in vaginal pH with intravaginal administration of single doses of an acid-buffering gel (Amphora) by baseline vaginal pH level.

DESIGN: This was a Phase I, randomized, placebo-controlled, double-blind, multicenter study.

MATERIALS AND METHODS: The primary study randomized 105 women to receive a single intravaginal dose of one of three Amphora doses (3, 4 or 5 g), universal placebo gel (UPG 4 g) or no treatment. Subjects were admitted for overnight stay in the domiciliary unit. Vaginal pH measurements were taken prior to treatment (baseline) and 1, 6, 12 and 24 hours post-treatment. Subjects were then discharged and asked to measure vaginal pH daily on Days 2-6 post-treatment. On Day 7, subjects returned to the clinic and clinic staff measured subjects' vaginal pH. In this post-hoc analysis, the effect on vaginal pH was examined in women who were assigned to one of the following treatment groups: Amphora 5 g, UPG or no treatment. The mean change in vaginal pH was calculated at multiple intervals from baseline to Day 7 post-treatment. Change in vaginal pH and the duration of this change were determined according to baseline vaginal pH (pH <5 and pH ≥ 5).

RESULTS: Subjects in the Amphora treatment group experienced a decrease in vaginal pH at all time points from Day 0, 1 hour post-treatment, to Day 7, regardless of baseline vaginal pH (Table 1). When stratified by baseline vaginal pH (pH <5 and pH ≥ 5), significant decreases in pH from baseline were seen in both sub-groups at nearly all time points through Day 6, though the magnitude of the decrease was greater in women with higher baseline vaginal pH. When compared to UPG or no treatment, women with higher baseline vaginal pH had significantly greater decreases through Day 4 while in the lower vaginal pH group, these differences were only significant through the first 24 hours.

CONCLUSIONS: Amphora lowered the vaginal pH in subjects regardless of baseline vaginal pH levels, though this effect was most pronounced in subjects with baseline vaginal pH levels ≥ 5. This analysis will help guide future studies on the impact of Amphora on vaginal pH.

References:

Linhares IM, et al. Contemporary perspectives on vaginal pH and lactobacilli. *Am J Obstet Gynecol*. 2011;204:120.e1-5.

Supported by: This study was sponsored by Evoform, Inc. (San Diego, CA), a wholly owned subsidiary of Evoform Biosciences, Inc. Medical writing assistance was provided by PharmaWrite, LLC (Princeton, NJ), and was funded by Evoform, Inc.

O-107 Tuesday, October 9, 2018 11:45 AM

PRODUCT ACCEPTABILITY AND ASSESSMENT OF GENITOURINARY DISCOMFORT IN A PHASE 3 TRIAL COMPARING AN ACID-BUFFERING CONTRACEPTIVE VAGINAL GEL (AMPHORA®) TO NONOXYNOL-9.



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OBJECTIVE: To present data on product acceptability and genitourinary discomfort when using Amphora®, an investigational acid-buffering contraceptive vaginal gel, vs. nonoxynol-9 (Conceptrol®).

DESIGN: This was a multicenter, open-label, randomized phase 3 trial conducted over 6 months (representing 183 days or 7 menstrual cycles) assessing efficacy and safety of Amphora; women in the Amphora group could participate for an additional 6 cycles for a maximum of 13 cycles.

MATERIALS AND METHODS: Amphora, which was delivered in 5 mL doses, is a water-based, petroleum-free gel with active ingredients of citric acid, potassium bitartrate and L-lactic acid. Nonoxynol-9 (4% concentration) was delivered in 2.5 mL volume. Acceptability of study product and mild genitourinary discomfort (secondary endpoints) were measured by questionnaires. The acceptability questionnaire was administered at visits after Cycles 1, 7 and 13. P values were based on the CMH statistical test with the Row Mean Score Method using the numeric value of the response. The discomfort questionnaire was administered after Cycles 1, 3, 7, 10 and 13, and included the woman's and her partner's discomfort.

RESULTS: A total of 2,935 women were randomized and used at least one application of study drug (1,458 in the Amphora group and 1,477 in the nonoxynol-9 group). By Cycle 7, significantly more women in the Amphora group strongly liked or somewhat liked the product compared to those in the nonoxynol-9 group (83.5% vs. 79.8%, respectively; P=0.010) (Table 1). Acceptability remained high with Amphora users after Cycle 13 (88.2%). Approximately 11% of women reported mild genitourinary discomfort after Cycle 7 (10.9% Amphora; 11.8% nonoxynol-9), mostly due to itching, irritation and burning. Results were similar in the Amphora extension study with 11.6% and 6.6% of women reporting mild genitourinary discomfort after Cycles 10 and 13, respectively. Discomfort was reported in only 1.5% of partners at Cycle 7 (1.6% in the Amphora group and 1.5% in the nonoxynol-9 group) and in approximately 1% of partners of Amphora users after both Cycles 10 and 13. The most common adverse events in the Amphora and nonoxynol-9 treatment groups were similar and included bacterial vaginitis (11.0% and 11.5%, respectively), vulvovaginal mycotic infection (10.7% and 11.4%) and urinary tract infection (9.6% and 13.1%).

CONCLUSIONS: Amphora contraceptive vaginal gel was acceptable and comfortable to most women and their partners.

Supported by: This study was sponsored by Evoform, Inc. (San Diego, CA), a wholly owned subsidiary of Evoform Biosciences, Inc. Medical writing assistance was provided by PharmaWrite, LLC (Princeton, NJ), and was funded by Evoform, Inc.

TABLE 1. Mean change (SD) in vaginal pH from baseline at each treatment timepoint

Baseline pH	Amphora 5 g		UPG 4 g		No Treatment	
	pH <5 (n=12)	pH ≥ 5 (n=10)	pH <5 (n=10)	pH ≥ 5 (n=10)	pH <5 (n=13)	pH ≥ 5 (n=8)
Day 0 - 1 hr	-0.15 (0.25)	-0.80 (0.50) ^a	0.03 (0.31)	-0.64 (0.55) ^a	0.05 (0.25)	-0.52 (0.48) ^a
Day 0 - 12 hr	-0.57 (0.40) ^{a,b,c}	-0.97 (0.67) ^{a,b,c}	-0.05 (0.46)	0.01 (0.65)	0.05 (0.33)	-0.05 (0.37)
Day 0 - 24 hr	-0.43 (0.35) ^{a,c}	-1.05 (0.55) ^{a,b,c}	-0.13 (0.33)	-0.13 (0.39)	0.28 (0.75)	0.00 (0.34)
Day 2	-0.16 (0.25)	-0.52 (0.51) ^{a,b}	0.00 (0.31)	0.46 (0.83)	-0.02 (0.42)	0.01 (0.46)
Day 3	-0.25 (0.27) ^a	-0.57 (0.52) ^{a,b,c}	-0.10 (0.29)	0.21 (0.85)	-0.02 (0.42)	0.14 (0.57)
Day 4	-0.21 (0.26) ^a	0.57 (0.57) ^{a,b,c}	-0.05 (0.26)	0.26 (0.93)	0.02 (0.39)	0.14 (0.35)
Day 5	-0.25 (0.27) ^{a,c}	0.47 (0.56) ^a	-0.25 (0.33) ^{a,c}	-0.24 (0.54)	0.09 (0.38) ^b	0.07 (0.84)
Day 6	-0.44 (0.37) ^{a,c}	-0.47 (0.64) ^a	-0.13 (0.30)	-0.27 (0.61)	0.02 (0.41)	-0.05 (0.87)
Day 7	-0.18 (0.26)	-0.10 (0.68)	0.09 (0.72)	-0.41 (0.46) ^a	0.13 (0.41)	-0.38 (0.55)

^aP<0.05 vs Baseline; ^bP<0.05 vs UPG; ^cP<0.05 vs No treatment.