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Leukocytosis during cervical preparation with osmotic dilators for dilation and evacuation

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Abstract

Objectives: To describe leukocytosis trends during cervical preparation with osmotic dilators for second-trimester dilation and evacuation procedures, and to determine whether there is a difference in leukocytosis seen with laminaria versus Dilapan-S.

Methods: We conducted a retrospective cohort study of 986 women presenting for dilation and evacuation from April 2008 through March 2009 at an outpatient clinic network. We included all procedures at ⩾14 weeks' gestation where laminaria or Dilapan-S dilators were used for overnight dilation. All women had routine white blood cell testing during the study period.

Results: There was a median increase of 2.4 $\times$ $10^3/\mu$L white blood cell count (95% confidence interval 2.2–2.7 $\times$ $10^3/\mu$L) from beginning of cervical preparation to the day of procedure (95% confidence interval and p value). Women receiving laminaria (n = 805) versus Dilapan-S (n = 181) had a greater increase in white blood cell count from baseline (median increase 2.7 versus 1.2 $\times$ $10^3/\mu$L, $p < 0.001$), including when adjusting for age, gestational age, parity, baseline white blood cell count, and number of dilators placed.

Conclusion: There is increased leukocytosis during the course of cervical preparation with osmotic dilators, and this is increased with use of laminaria versus Dilapan-S. Rates of clinically recognized infection in second-trimester abortion are low regardless of dilator type used.

Keywords

Dilation and evacuation, abortion, second trimester, leukocytosis, laminaria, Dilapan

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Introduction

Preoperative cervical preparation significantly reduces morbidity associated with second-trimester abortion, including cervical laceration and uterine perforation.[1–3] Dilation and evacuation (D&E) is the most common method of second-trimester abortion and is associated with a less than 1% risk of major complications such as infection.[4,5] Cervical preparation can be accomplished with osmotic dilators or pharmacologic methods. The most commonly used dilators in the United States are laminaria (MedGyn Products, Inc., Addison, IL, USA) and Dilapan-S (HPSRx Enterprises, Salem, VA, USA). Many providers prefer Dilapan-S due to its more rapid and effective dilating properties, but Dilapan-S is often more expensive than laminaria.[6,7] Other providers choose to use a combination of both laminaria and Dilapan-S.[8] Individual clinics and providers have different protocols for type and number of dilators recommended for adequate cervical preparation. Few studies directly compare one type of osmotic dilator to another, and specific protocols for ideal number of dilators are not based on published research.[3]

Some providers have raised concerns regarding a potential increase in maternal infection with osmotic dilators versus pharmacologic cervical ripening agents.[6,9] Theoretically, infection may be increased with use of laminaria in particular, as opposed to the synthetic Dilapan-S, due to the biologic

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origin of laminaria.[3] The package insert for laminaria recommends administering prophylactic antibiotics and advises against leaving laminaria tents in place for more than 24 h.[10] There is no recommendation for the use of prophylactic antibiotics in Dilapan-S labeling.[11] Potentially pathogenic microorganisms have been identified on laminaria tents, though studies to date have not shown an increase in clinical infection.[12,13]

The risk of infection with cervical preparation and D&E is low regardless of the cervical preparation method used. One study comparing infection rates with the use of two types of osmotic dilators found low rates of infection with both laminaria (0.81%) and Dilapan (0.40%), with no statistically significant difference between dilator types.[14] We sought to describe leukocytosis during second-trimester cervical preparation and to determine whether there is an association with other markers of infection. We hypothesized that there would be greater leukocytosis with laminaria versus Dilapan-S, but that rates of clinically recognized infection would be low regardless of the cervical preparation method used.

Methods

Study design

We conducted a retrospective cohort study of women presenting for surgical abortion from April 2008 through March 2009 at an outpatient reproductive health clinic network in Washington State, comprising three freestanding clinics. Second-trimester procedures between 14 and 22 weeks are generally completed in 2 days, with osmotic dilator placement on the first day and a D&E procedure on the next day. Procedures above 22 weeks' gestation are typically completed in 3 days with 2 days of osmotic dilators followed by a D&E procedure on the third day. During the study period, intrafetal digoxin was administered on the day prior to D&E under ultrasound guidance for gestations $\geqslant$20 weeks. All patients received prophylactic antibiotics (doxycycline) beginning with dilator insertion. Vital signs, including temperature, were checked when the patients arrived each day, and at regular intervals during and after each dilator insertion or D&E procedure. Choice of dilator type was primarily based on physician preference; during the study period, majority of physicians transitioned to the use of Dilapan-S. The University of Washington Institutional Review Board approved this study and waived the requirement to obtain informed consent.

Study population

Patients were included in our study if they obtained a D&E at 14 weeks' gestation or greater during the study period and received overnight dilation with either laminaria or Dilapan-S. We excluded patients who received a combination of laminaria and Dilapan-S. Majority of abortion procedures included in this series were in the setting of unintended pregnancy, and none were in the setting of fetal demise or preterm premature rupture of membranes.

Outcomes and covariates of interest

The primary exposure of interest was type of dilator used, with data collected on number of dilators and number of days of preoperative dilation. The primary outcome of interest was change in white blood cell (WBC) count. While it is not a standard practice to obtain complete blood counts (CBCs) during cervical preparation, the clinic network collected this information during the study period of April 2008 to March 2009 for a separate quality improvement project. Additional outcomes of interest included fevers and infectious morbidity (clinical intrauterine infection or additional treatment). We also collected data on demographic characteristics and procedure characteristics. While data on the primary outcome were missing for some patients, all procedures from the study period that met the inclusion and exclusion criteria were included for analysis of secondary outcomes and procedure characteristics.

Statistical analyses

The required sample was determined based on the primary outcome of change in WBC count and primary exposure of type of dilator (laminaria versus Dilapan-S). Assuming a power of 0.8 and alpha 0.05, we required a sample size of 176 per exposure group to detect a 15% greater difference in WBC count. We performed descriptive analyses on the demographic data and reproductive health history of the study population, as well as the WBC counts, procedure characteristics, and other outcomes of interest. We compared patient and procedure characteristics between laminaria and Dilapan-S cohorts using chi square, Wilcoxon rank-sum, and Student's *t* tests. We used a multivariable generalized linear model to adjust for age, gestational age, parity, baseline WBC count, and number of dilators placed. All statistical analyses were performed using STATA SE 13.1.

Results

At the clinic sites, 1068 women underwent D&E between April 2008 and March 2009. We excluded three patients who did not receive dilators and three who experienced extramural deliveries. After excluding patients who received a combination of laminaria and Dilapan-S ($n = 76$), our final data set included 986 patients. This population includes 805 women (81.6%) who received cervical preparation with laminaria and 181 women (18.4%) who received Dilapan-S. Gestational age ranged from 14 weeks 0 days to 25 weeks 5 days by ultrasound measurement.

Available demographic and procedure characteristics are shown in Table 1. There were no significant differences in

Table 1. Demographic and procedure characteristics.

	Total (n = 986)	Laminaria (n = 805)	Dilapan-S (n = 181)	p value
Age in years (mean ± SD)	24.1 ± 6.2	24.1 ± 6.2	23.9 ± 6.2	0.70
History of prior birth (n (%))	721 (73.3)	592 (73.7)	129 (71.3)	0.50
Gestational age in weeks (median (IQR))	18.0 (15.9–20.4)	18.0 (15.9–20.4)	18.0 (15.7–20.7)	0.66
Two days of cervical preparation (n (%))	128 (13.0)	98 (12.2)	30 (16.6)	0.11
Procedure characteristics				
Total dilators placed (median (IQR))	4 (3–5)	4 (3–5)	4 (3–5)	0.67
Procedure time in minutes (median (IQR))	10 (8–15)	10 (8–16)	9 (6–12)	< 0.001
Estimated blood loss in mL (mean ± SD)	49.7 ± 29.4	50.2 ± 29.4	47.5 ± 29.4	0.27
Estimated blood loss ⩾100 mL (n (%))	65 (6.6)	53 (6.6)	12 (6.6)	0.99

SD: standard deviation; IQR: interquartile range.

age, gestational age, and obstetric history between the groups of women receiving laminaria versus Dilapan-S. There were also no differences in total number of dilators placed or estimated blood loss (EBL) between the two groups. There was a small but statistically significant difference in median procedure time, with median procedure times of 10 min (interquartile range (IQR) 8–16 min) in the laminaria group and 9 min (IQR 6–12 min) in the Dilapan-S group ($p < 0.001$).

Baseline (prior to initial cervical dilator placement) median WBC count was $9.5 \times 10^3/\mu L$ (IQR 8.0–11.2) and median WBC count on procedure day was $12.0 \times 10^3/\mu L$ (IQR 9.8–14.6), with a net increase of $2.4 \times 10^3/\mu L$ ($p < 0.001$). Almost one-fourth (23.8%) of the patients had an elevated WBC count on the day of the procedure greater than $14.8 \times 10^3/\mu L$, which is the upper limit of the normal WBC range in the second trimester of pregnancy.[15] For patients who received 2 days of cervical preparation, there was a further increase in WBC count from the second day of cervical preparation to the day of the procedure, with a median increase in WBC count of $4.2 \times 10^3/\mu L$ over the course of the 3-day procedures ($p < 0.001$). For the subset of patients receiving 2 days of cervical preparation for whom these data were available, baseline WBC count was $9.5 \times 10^3/\mu L$ (IQR 7.9–11.3), WBC count on the second day was $11.7 \times 10^3/\mu L$ (IQR 10.1–13.3), and the WBC count on the procedure day was $14.8 \times 10^3/\mu L$ (IQR 12.1–18.1).

There was no difference in median baseline WBC values between groups receiving laminaria versus Dilapan-S ($9.5 \times 10^3/\mu L$ versus $9.2 \times 10^3/\mu L$, $p = 0.12$; Figure 1). The increase from baseline WBC count to WBC count on the day of procedure was greater for patients receiving laminaria versus Dilapan-S (2.7 versus $1.2 \times 10^3/\mu L$, $p < 0.001$), as was the proportion with elevated WBC count $>14.8 \times 10^3/\mu L$ (26.9% versus 11.8%, $p < 0.001$). For patients who had 2 days of cervical preparation, the increase in WBC count was also more pronounced in patients receiving laminaria versus Dilapan-S (6.0 versus $3.3 \times 10^3/\mu L$, $p < 0.001$).

The increase in WBC count was also greater for the laminaria group versus Dilapan-S group when adjusting for age, gestational age, parity, baseline WBC count, and total number of dilators placed ($p < 0.001$; Table 2). A larger increase in WBC count was also associated with greater gestational age ($p < 0.001$) and greater number of dilators placed ($p < 0.001$) in this same multivariable model.

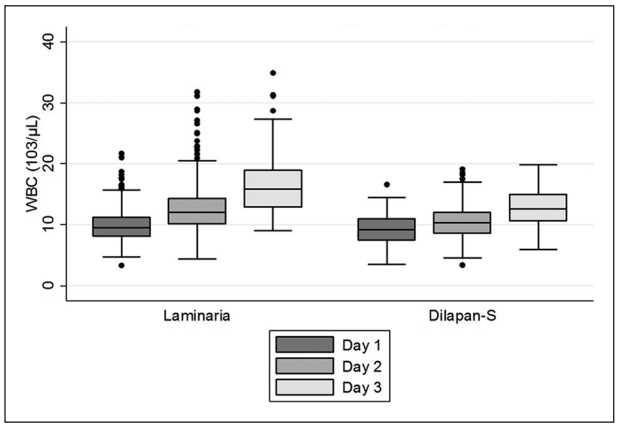

Figure 1. Leukocytosis trend during cervical preparation.

Mean temperature was 98.4° Fahrenheit at baseline and on the procedure day. There were no significant differences in mean temperature between patients receiving laminaria versus Dilapan-S during the course of cervical preparation. No patients were febrile (temperature ⩾ 100.4° Fahrenheit) at baseline, while 25 (2.4%) became febrile during the course of cervical preparation and abortion (Table 3). While a greater number of patients receiving laminaria became febrile compared to those receiving Dilapan-S (3.0% versus 0.6%, $p = 0.06$), this was not statistically significant. Six patients (0.6%) were treated for clinically suspected intrauterine infection, based on individual provider assessment of patient symptoms and clinical exam findings.

Discussion

Our findings demonstrate that a natural leukocytosis occurs during the course of cervical preparation, in the absence of clinically recognized infection. There was a significant increase in WBC count, which was greater with an additional day of cervical preparation and with a larger number

Table 2. Multivariable linear regression model for white blood cell (WBC) count ($\times 10^3/\mu L$) on procedure day.

	Coefficient[a] (95% CI)	*p* value
Laminaria versus Dilapan-S	2.09 (1.55–2.63)	<0.001
Covariates		
Gestational age (weeks)	0.29 (0.17–0.41)	<0.001
First pregnancy	0.42 (−0.10 to 0.93)	0.11
Patient age (years)	−0.01 (−0.05 to 0.02)	0.47
Total number of dilators	0.15 (0.06–0.25)	0.001
Baseline WBC count	0.77 (0.69–0.86)	<0.001

CI: confidence interval.
[a]Coefficient for laminaria versus Dilapan-S refers to increase in the WBC count on the procedure day for laminaria versus Dilapan-S when all covariates are held constant. Coefficient for all additional covariates refers to increase in WBC count on the procedure day for each unit increase in the covariate when all other variables are held constant.

Table 3. Characteristics of febrile versus afebrile patients.

	Febrile (*n* = 25)	Afebrile (*n* = 961)	*p* value
Type of dilators placed			0.06
Dilapan-S	1 (4.0)	180 (18.7)	
Laminaria	24 (96.0)	781 (81.3)	
Gestational age in weeks (median (IQR))	20.7 (17.6–23.4)	18.1 (15.9–20.4)	0.002
Two days of cervical preparation (*n* (%))	13 (52.0)	115 (11.1)	<0.001
Increase in WBC count ($\times 10^3/\mu L$) (median (IQR))	7.2 (3.7–10.4)	2.3 (0.8–4.3)	<0.001
Evidence of clinical infection	3 (12.0)	3 (0.3)	<0.001

IQR: interquartile range; WBC: white blood cell.

of cervical dilators. As expected, infection rates were low regardless of dilator type. Leukocytosis in the absence of infection has been well-documented in pregnancy, and particularly during labor. The average WBC count is increased in pregnancy primarily due to increased number of neutrophils in circulation.[16] In labor, leukocytosis has been shown to increase in a linear fashion dependent on the length of labor.[17] It is reasonable that this same increase in WBC count occurs during cervical preparation for second-trimester abortion. We demonstrated an overall increase in median WBC count of $2.4 \times 10^3/\mu L$ during the course of cervical preparation. Based on these data, treatment for intrauterine infection based solely on an elevated WBC count is not indicated, given the natural leukocytosis identified in these subjects over the course of their cervical preparation prior to abortion.

In addition to an overall increase in WBC count with cervical preparation, we also demonstrated that the increase is greater with the use of laminaria compared to Dilapan-S, including when controlling for gestational age, parity, and total number of dilators placed. However, it remains unknown whether or not laminaria is associated with an increased infection risk compared to Dilapan-S. We demonstrated a low infection rate overall and this study was not powered to detect a difference in clinical infection rates between dilator types.

Our study is limited by the unavailability of some patient characteristics, including race, ethnicity, body mass index, and significant comorbidities. The choice between laminaria and Dilapan-S was primarily based on provider preference and may have introduced bias. As clinical infection rate is low in abortion care in general, we were not powered to determine a difference in clinical infection rates between the two groups, and it remains to be determined how well increased leukocytosis correlates with clinical infection risk, if at all. In addition, while patients typically return to this same clinic for follow-up care or complications, it is possible that patients may have presented to a different facility for subsequent infection or other complication.

Our study is strengthened by the inclusion of a large number of patients from three clinic sites and multiple physicians. We had the unique opportunity of a study period during which CBCs were collected routinely for almost all patients during the course of their cervical preparation and procedure.

Conclusion

Both laminaria and Dilapan-S are effective osmotic dilators for cervical preparation, and we saw no clinically significant differences in procedure characteristics or blood loss. A previous study has demonstrated that Dilapan-S is superior in achieving greater cervical dilation in a shorter amount of time.[8] Our study adds to this literature by demonstrating a greater increase in WBC count with laminaria versus Dilapan-S. Nonetheless, providers can be reassured that the risk of clinical infection is low regardless of dilator type used.

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Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

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Informed consent

Our Institutional Review Board granted a waiver for informed consent for this study, as this was a retrospective chart review where data were abstracted and de-identified.

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