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Induction of labor compared to dilation and evacuation for postmortem analysis

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Abstract

Objective—To evaluate the ability to obtain autopsy and cytogenetics after midtrimester termination.

Methods—A retrospective cohort study of women undergoing termination, via induction or dilation and evacuation (D&E), at 16 0/7-23 6/7 weeks from 2002-2011 was performed. Exclusion criteria were elective termination, preterm labor, PPRM and no autopsy or cytogenetic exam performed. The ability to obtain cytogenetics and autopsy as well as complications rates were compared between the 2 groups with Chi-square tests.

Results—Of the 469 women who met the inclusion criteria, 158 had an induction and 312 had a D&E. The induction of labor group had higher mean gestational ages, $p < 0.01$. Successful autopsy was more likely in the induction group, 94.3%, vs. D&E group, 34.7%, $p = 0.01$. There was no difference in ability to obtain cytogenetics between the two groups, 89.1% in the induction group and 92.3% in D&E group, $p = 0.4$. There was a difference in the total complication rates between the groups, 9.8% (26) in the induction versus 6.4% (20) in the D&E group, $p < 0.01$; however, there was no difference in major complications.

Conclusions—Midtrimester terminations by induction were more likely to have successful autopsies when compared to D&E. The ability to obtain cytogenetics was similar regardless of termination mode.

Introduction

Advances in prenatal diagnosis and ultrasound are allowing fetal abnormalities to be diagnosed earlier in pregnancy. Women may opt to terminate their pregnancy based on a multitude of reasons, including chromosomal abnormalities, fetal anomalies diagnosed by ultrasound, or intrauterine fetal demise. These complications affect approximately 0.6-3% of all pregnancies.¹⁻³ Both autopsy and cytogenetics can be obtained as part of the postmortem examination; each may provide important information about the diagnosis and recurrence risk. Previously, studies have shown that the ability to obtain cytogenetics after induction of labor ranges from 35-73% and rates as high as 99% for dilation and evacuation (D&E) have

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been reported.⁴⁻⁶ These studies, however, failed to directly compare rates of cytogenetic analysis between the two modes typically used for midtrimester termination.

One advantage of an induction of labor is a morphologically intact fetus for autopsy. In a study comparing the prenatal diagnosis to autopsy results, 33% of cases had their prenatal diagnosis refined when additional information was obtained from the postmortem examination.⁷ This study highlights the importance of obtaining postmortem information for accurate diagnosis of fetal abnormalities. There is conflicting data on the ability to obtain an autopsy after D&E. Several studies that assessed the association between prenatal ultrasound and postmortem examination excluded D&E specimens.^{8,9} Another study reported that a composite assessment of postmortem information after D&E, consisting of radiographic studies, autopsy, cytogenetics and DNA analysis, was able to confirm the antenatal diagnosis in all 60 cases.¹⁰ This discrepancy demonstrates the need for more information regarding autopsies on D&E specimens.

Based on a decision analysis, Cowett et al reported that D&E is a less costly and more effective way of completing a midtrimester termination.¹¹ In addition, studies have shown advantages to a D&E, including less morbidity, more effectiveness and lower overall complication rates as compared to induction of labor.¹²⁻¹⁴

Our hypothesis was that after induction of labor, as compared to D&E, there is a higher likelihood that postmortem information would be available. The primary objective of our study was to assess the ability to obtain autopsy and cytogenetic analysis, comparing two different modes of termination, induction of labor and D&E. The secondary objective of the study was to compare procedural complications between the two modes of termination.

Materials and Methods

This was a retrospective cohort study from the University of Illinois Hospital and Health Sciences System. Institutional Review Board approval was obtained prior to starting the study. The obstetric database and electronic medical record were searched to identify women who underwent midtrimester terminations from July 1, 2002-October 31, 2011. Data were ascertained from all women, ages 18-45 years undergoing either an induction of labor or D&E at 16 0/7-23 6/7 weeks gestation at a single institution. Gestational age was determined by the best obstetric dating, either the earliest ultrasound or LMP. Women with an intrauterine fetal demise (IUFD) were included. Exclusion criteria were elective termination, preterm labor, previable preterm premature rupture of membranes. These exclusion criteria were chosen as these women were less likely to undergo postmortem examination. Additionally, those women who did not have an autopsy or cytogenetics performed were excluded. Demographic variables included age, gravity, parity and gestational age at termination. Ultrasounds or cytogenetic analyses done prior to the termination of pregnancy were reviewed and documented. The indications for termination were categorized into chromosome abnormalities, fetal anomalies, IUFD, and other (i.e., perinatal infection and conjoined twins). If a woman had multiple indications for termination of pregnancy, only one was recorded as the reason for termination. Labor induction method was at the discretion of the attending physician and misoprostol was most commonly used.

For those women undergoing D&Es, they were performed in the hospital's operating rooms, with laminaria placement the day prior to the procedure.

Whether a woman had an autopsy and/or cytogenetics was assessed from the medical record. The autopsy report and cytogenetic analysis of the fetus were then reviewed and assessed for accuracy and completeness. If the specimen for fetal analysis was received by pathology, this was counted as requested autopsy specimen. If any information could be ascertained from the autopsy report, this was counted as a successful autopsy. If, however, no meaningful information could be obtained from the autopsy report (i.e., "fragmented fetus" or "products of conception") this was counted as an unsuccessful autopsy. If the specimen for karyotype (i.e., placenta, fetal biopsy, etc) was received in the cytogenetics laboratory, this was counted as a requested cytogenetics specimen. Placental tissue was the most common specimen submitted for analysis. This was typically submitted to the cytogenetics lab directly from the pathology department, after the specimen was received there first. If the specimen failed to grow in culture and the cytogenetics report was documented as such, this was counted as an unsuccessful cytogenetics attempt. As our center has only recently started to perform microarrays for genetic analysis, these results were not included in the analysis. The cytogenetics lab had a single director during the study period. Different pathologists completed the autopsies during the study period and a perinatal pathologist was employed by the university after 2009.

Complications for each procedure were assessed. They were divided into major complications (e.g., uterine perforation, hysterectomy or blood transfusion) and minor complications (e.g., retained placenta, cervical laceration requiring repair, EBL > 500 mL or change in admission status such as from an outpatient to an inpatient hospitalization).

Demographics, indication for termination, successful autopsy and cytogenetics rates, and complications were compared using two sample t-tests or Wilcoxon rank sum tests for continuous variables according to distribution and Chi-square or Fisher exact tests for categorical variables between the D&E and induction of labor groups. Logistic regression was used to calculate odds ratios and 95% CI for the outcome variables controlling for gestational age grouped in two week increments (16 0/7 – 17 6/7 weeks as referent) and mode of termination. A p-value<0.05 was considered statistically significant. Statistical analysis was performed using SAS software (version 9.2, Cary, N.C.).

A review of the literature on midtrimester terminations suggests that approximately 70% of cases will have a successful autopsy after an induction.⁷ Using a beta of 0.8 and an alpha of 0.05, the sample size for each group would be 121 women to detect a 15% difference between the groups.

Results

In total, 1029 women underwent midtrimester termination during the study period; 474 had an induction of labor and 555 had a D&E. Of these, 208 from the IOL and 225 from the D&E group were excluded (elective termination, preterm premature rupture of membranes, and/or preterm labor). An additional 126 were further excluded from the analysis because

there was no attempt to perform an autopsy or cytogenetics. After all exclusion criteria were applied, the total study group was 470, with 158 in the induction group and 312 in the D&E group. (Figure 1)

Among the study patients, there was a significant difference between maternal age, gestational age, parity, and the indication for the termination between the two groups, $p < 0.05$ (Table 1). The most common indication for termination was fetal anomalies, 71.5% ($n=113$) for induction and 65.4% ($n=204$) for D&E. Other indications for termination included chromosomal abnormalities, 8.2% for induction and 30.5% for D&E and fetal demise, 19.6% for induction and 3.2% for D&E.

Most women (94.3%) in the induction group had a successful autopsy compared to only 34.7% in the D&E group, $p < 0.01$. The ability to obtain cytogenetics was not different between the two groups, 89.1% in the induction group vs. 92.3% in the D&E group, $p=0.4$ (Table 2).

Major complications, defined as uterine perforation, hysterectomy and blood transfusion, were not different between the two groups. Total complications, however, were increased in the induction group, 9.8% compared vs. 6.4% in the D & E group. Minor complications were also increased in the induction (9.0%) vs. D&E group (5.1%), $p < 0.01$ (Table 2). There were no cases of endometritis reported in either group.

A logistic regression was performed to evaluate the ability to obtain successful autopsy and cytogenetics, in relation to gestational age and mode of termination (Table 3). Termination mode and increasing gestational age were significant predictors of successful autopsy whereas neither were significant predictors of cytogenetic results.

Discussion

We evaluated the ability to obtain post-mortem examinations after a termination of pregnancy, specifically comparing induction of labor to D&E. The ability to achieve successful autopsy occurred more often in the induction group compared to D&E, whereas the ability to obtain cytogenetics was not significantly different between the two groups.

Other studies have reported on the correlation between an antenatal ultrasound diagnosis and postmortem autopsy result. These studies report a wide range of concordance with the prenatal diagnosis (44-100%).^{7,8, 10,15-18} This emphasizes the importance of an autopsy even when the diagnosis is made prenatally, as additional information may be acquired in the postmortem examination. Although some studies have shown the ability to confirm prenatal diagnosis after D&E, this is not consistently reported in the literature.¹⁰ Sun et al found that after D&E, only 28% of postmortem findings were able to reliably correlate with the prenatal ultrasound findings due to fragmented fetal parts. In contrast, 82% of fetuses examined after induction of labor had a reliable correlation with antenatal ultrasound findings.¹⁹ Other studies exclude D&Es in the analysis of perinatal autopsies.^{8,9}

Cytogenetics is also an important part of the evaluation for termination of pregnancy due to its ability to predict recurrence risks. Other studies have shown a 40-99% success rate of

cytogenetic analysis after termination of pregnancy.^{5,6,20} In our study, there was a high likelihood of acquiring cytogenetics regardless of termination mode.

Overall, we found low complication rates for both procedures, 9.8 % and 6.4% for induction of labor and D&E, respectively. Other studies have shown higher complication rates of 24%-44% for induction of labor.¹²⁻¹⁴ D&E complication rates have been reported as 3%-11%, which is consistent with our study.¹²⁻¹⁴ Retained placenta after induction was frequently the cause of the increased complications in other studies; however, as retained placenta usually does not have long term complications for the patient, we deemed it a minor complication. If manual removal and dilation and curettage for retained placenta were deleted from the complication rates, the induction complication rate would decrease to 3%, identical to that for D&E.¹³ Although our minor complication rates were increased in our induction group, the majority of complications in the induction group, 92.3%, were related to retained placenta. By including total complications, as well as classifications of major and minor complications, a more accurate clinical representation of issues that can arise during a termination of pregnancy is described. In experienced hands, women can choose either procedure with minimal risk for complications.

At our institution, midtrimester terminations were performed by two divisions in the department of obstetrics and gynecology. In this single center, however, all providers practiced non directive counseling for both procedures and therefore the risks, benefits and alternatives were equally reviewed. As both the maternal fetal medicine and family planning divisions have fellowship programs and are intricately involved in the counseling, there is formal training in counseling and providing care for these patients.

A limitation of this study is that more women in the D&E group had a pathologic examination performed. This was influenced by the procedure being performed in the operating room, with the fetus treated as a surgical specimen. Currently, all D&E specimens are sent to pathology from the operating room. While they make note of any prenatal diagnosis, they would not specifically state whether an autopsy was requested. This could confound our findings as a larger number of women would seem to have had an autopsy, when in reality this was not the case. The pathology department evaluated autopsies in a similar fashion regardless of whether it was an induction or labor or D&E specimen. Due to the retrospective nature of this study, whether or not patients specifically requested an autopsy could not be clearly determined by the chart review, thus arrival in the pathology department was the surrogate marker.

If there is extensive autolysis, it can be difficult to perform autopsies in cases of IUFD; however, we had a higher percentage of patients undergoing termination for IUFD in the induction of labor group, 19.6% compared to 3.2% with D&E. Because of the larger numbers of IUFD in the induction of labor group, this should not have affect the results of our study in favor of induction of labor.

The strengths of our study include the large number of midtrimester terminations that were included. Also, a single author performed all the data collection to ensure all the reports

were reviewed in a standard, systematic fashion, with random checks for accuracy of the collection.

When women undergo mid-trimester termination of pregnancy for fetal abnormalities or intrauterine fetal demise, they desire information regarding etiology and recurrence risks. As there are two different options for termination, it is important for the provider to be able to accurately counsel women regarding the information obtained from either procedure. In this study we showed that with induction of labor, autopsy was more likely to be obtained whereas the ability to obtain cytogenetics were similar between the two groups.

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What is known about this topic?

-- Postmortem examination, including autopsy and cytogenetic, can be used to confirm or add information to a prenatal diagnosis.

--D&E has been shown to have fewer complications than IOL, but the ability to obtain autopsy is controversial

What does our study add?

--This study compares the two modes of termination and their ability to obtain autopsy and cytogenetics.

Figure 1.
Flow chart of patients included in the study.

Table 1

Demographic data and indication for midtrimester termination.

Variable (mean $\pm$ standard deviation) or % (n)	Induction of labor n = 158	Dilation and evacuation n = 312	p-value
Age (years)	27.3 $\pm$ 6.7	30.2 $\pm$ 7.3	< 0.01
Gestational age (weeks)	20.8 $\pm$ 1.8	20.1 $\pm$ 2.1	< 0.01
Gravidity	3.2 $\pm$ 1.9	3.0 $\pm$ 1.9	0.34
Parity	1.5 $\pm$ 1.5	1.2 $\pm$ 1.3	0.10
Indication for termination			< 0.01
Chromosome abnormalities	8.2% (13)	30.5% (95)	
Fetal anomalies	71.5% (113)	65.4% (204)	
Fetal demise	19.6% (31)	3.2% (10)	
Other	0.6% (1)	1.0% (3)	

Table 2

Postmortem analysis and complications by mode of termination

Outcome (% , n)	Induction of labor	Dilation and evacuation	p-value
Postmortem analysis			
Autopsy	94.3% (116/123)	34.7% (108/311)	0.01
Cytogenetics	89.1% (98/110)	92.3% (108/117)	0.4
Type of Complication	n = 158	n = 312	p-value
Major	0.8 % (2)	1.3% (4)	0.9
Uterine perforation	(0)	0.6% (2)	0.6
Hysterectomy	(0)	0.3% (1)	0.7
Blood transfusion	1.3% (2)	0.3% (1)	0.6
Minor	9.0% (24)	5.1% (16)	<0.01
EBL > 500 mL	(0)	3.8% (12)	0.02
Change in admission status	(0)	0.6% (2)	0.6
Retained placenta	9.0% (24)	(0)	<0.01
Cervical laceration	(0)	0.6% (2)	0.6
Overall	9.8% (26)	6.4% (20)	<0.01

Table 3

The association between gestational age and mode of termination on the ability to obtain autopsy and cytogenetics

Variable	Autopsy		Cytogenetics	
	OR	95% CI	OR	95% CI
Gestational age				
16 0/7 - 17 6/7	1.0	Referent	1.0	Referent
18 0/7 - 19 6/7	1.96	0.82-4.54	0.27	0.03-2.5
20 0/7 - 21 6/7	4.20	1.85-9.1	0.27	0.03-2.27
22 0/7 - 23 6/7	4.55	1.92-11.1	0.33	0.04-2.94
Termination mode				
Induction	1.0	Referent	1.0	Referent
Dilation and evacuation	0.03	0.01-0.07	1.38	0.55-3.46