Transcervical foley catheter versus laminaria: A randomized controlled trial comparing efficacy and safety in facilitating cervical dilatation in cases of molar pregnancies*

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ABSTRACT

Objective: This study aimed to compare the efficacy and safety of foley catheter versus laminaria in facilitating cervical dilatation among patients with molar pregnancy.

Methods: This was a randomized controlled trial carried out from September 1, 2013 to September 30, 2014. Fifty-two patients with hydatidiform mole were randomly allocated to either the control or treatment group. Laminaria was used in the control group to facilitate cervical dilatation prior to molar evacuation while foley catheter was used in the treatment group. The primary outcome was the rate of successful cervical dilatation. Amount of bleeding, level of pain, presence of foul smelling vaginal discharge, and febrile episode were noted. The two-tailed Wilcoxon rank sum test was used to determine difference between the two groups.

Results: A significantly higher rate of successful cervical dilatation was seen in the foley catheter group (1.6 mm/hr vs 1 mm/hr), as evidenced by shorter duration from placement of mechanical dilator to successful cervical dilatation (9.5 hours vs 12 hours) and the lack of need for insertion of additional cervical dilator (0 vs 1). Compared to laminaria, foley catheter took a significantly shorter time to insert (5 mins vs 1 min) and was significantly less painful (VAS 5 vs VAS 0). Estimated blood loss, relative risk for pelvic pain, febrile episodes, profuse bleeding, and foul smelling discharge did not differ significantly between the two groups.

Conclusion: Foley catheter may be an alternative in facilitating cervical dilatation for molar pregnancies. Foley catheter has the advantage of being readily available, with lower cost and lack of systemic or serious side effects.

Keywords: Hydatidiform mole, laminaria, foley catheter, mechanical induction of labor

INTRODUCTION

Hydatidiform moles are abnormal conceptions with excessive placental, and little or no fetal development.[1] Its incidence varies worldwide, but has been reported to be higher by 7 to 10 times in Southeast Asia compared to Europe or North America.[2] In the Philippines, the national prevalence rate of hydatidiform mole for the years 2002 to 2008 is 2.4/1000 pregnancies.[3]

Suction curettage remains to be the preferred method for molar evacuation regardless of age of gestation and uterine size.[4] If the cervix is unyielding, cervical ripening is done in order to allow insertion of the 12mm cannula used during suction curettage. This process of cervical ripening and dilatation is usually done without anesthesia. Of the various methods used for cervical ripening, mechanical cervical dilatation is preferred because it dilates the cervix pre-operatively without inducing uterine contractions.[1,2,4] The use of oxytocin and prostaglandins is not recommended due to the associated increased risk of trophoblastic deportation and pulmonary embolization as a result of uterine contractions against a closed cervix.

Mechanical dilatation of the cervix is among the oldest methods used to induce labor among women with normal pregnancies. Advantages of mechanical methods over the pharmacological agents include simplicity of the procedure, lower cost, and reduced side effects.[5] Possible complications include endometritis and bleeding.[6] Agents that have been used as mechanical cervical dilators include: (1) hygroscopic dilators, such as laminaria and (2) balloon dilators, such as the foley catheter.[6,7]

Laminaria is made from the stems of the seaweed *Laminaria digitata* or *Laminaria japonica*. The earliest report of its use in obstetrics dates back into the late 1800's.[8] Currently, laminaria is available in sizes ranging from 2 to 10mm in diameter. A stem of laminaria is able to expand up to five times its original diameter.[8,9] Maximal cervical dilatation and softening usually occurs within 12 hours, thereby allowing uterine evacuation.[8,10] Therefore, a 3mm laminaria placed within the endocervical canal may expand up to 15mm in diameter overnight.

The use of transcervical foley catheter (FC) balloon placement was first described by Krause in 1853, and subsequently introduced to obstetric practice by

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Ezimokhai and Nwabineli in 1980.[11] Among its advantages are its efficacy, safety, cost effectiveness, availability, and low incidence of side effects.

Currently, the Philippine Society for the Study of Trophoblastic Diseases endorses the use of laminaria for the cervical dilatation of patients diagnosed with hydatidiform mole who are for suction curettage but presenting with a closed, unyielding cervix.[12] Use of the foley catheter remains unpopular due to fear of inducing profuse vaginal bleeding. Unfortunately, laminaria is not readily available in most parts of the country and its cost has proven quite expensive for patients with hydatidiform mole who are invariably indigent. It is therefore necessary to search for another mechanical method that will be effective, safe, affordable and readily available to patients. The foley catheter seems to be an attractive alternative for this purpose.

OBJECTIVES

General Objectives

To compare the efficacy and safety of transcervical foley catheter versus laminaria in facilitating cervical dilatation in cases of molar pregnancies.

Specific Objectives

1. To determine the time duration needed to insert a transcervical foley catheter versus laminaria
2. To compare the rate of cervical dilatation among patients who had transcervical foley catheter versus laminaria insertion
3. To compare the time duration from placement of mechanical dilator to successful cervical dilatation of the two treatment groups
4. To compare the need for additional insertion of the mechanical dilator
5. To compare the safety of the two treatment groups using the following parameters:

    a. presence of pain during administration and while awaiting cervical dilatation
    b. amount of blood loss during insertion of the mechanical dilator
    c. amount of blood loss from insertion to time of successful cervical dilatation
    d. presence of foul smelling vaginal discharge
    e. presence of febrile morbidities

MATERIALS AND METHODS

Study Design

This was a randomized controlled trial approved by the University of the Philippines Manila, Philippine General Hospital research technical and ethical review board.

Patient Population

All patients diagnosed with hydatidiform mole, admitted at the Section of Trophoblastic Diseases, Department of Obstetrics and Gynecology, Philippine General Hospital, University of the Philippines Manila, from September 2013 to September 2014 for suction curettage, and presenting with a closed, unyielding cervix were eligible for inclusion in the study.

Patients with cervical pathology or has undergone previous surgery involving the cervix that will prevent the insertion of the mechanical dilator were excluded from the study. Likewise, patients with mullerian anomalies, genital tract infection or were unable to give consent were excluded.

Sample Size Computation

Sample size was based on number of patients diagnosed with hydatidiform mole admitted for suction curettage at the Section of Trophoblastic Diseases, Department of Obstetrics and Gynecology, Philippine General Hospital, University of the Philippines Manila for the year 2012. The following formula was used for the computation:

Population size (for finite population correction factor or fpc) *(N)*:	86
Hypothesized % frequency of outcome factor in the population *(p)*:	50%+/-10
Confidence limits as % of 100 (absolute +/- %) *(d)*:	10%
Design effect (for cluster surveys-DEFF):	1

$$\text{Sample size } n = [DEFF*Np(1-p)]/\ [(d^2/Z^2_{1-\alpha/2}*(N-1)+p*(1-p)]$$

Calculated sample size was 46 subjects. To account for a possible 10% dropout rate, a new sample size was computed as: 46/(1-0.10) = 51.1 (rounded off to 52), with 26 patients per treatment group. This achieved a 95% confidence level, with 10% margin of error, at 0.05 and 0.01 alpha levels of significance.

Description of Study Procedure

Patients who met the inclusion criteria were recruited to participate in the study. Consent was obtained using the informed consent process. The following demographic and clinical data were obtained and recorded in a patient data form: age, gravidity, parity, corpus size, baseline hemoglobin and serum beta human chorionic gonadotrophin (βHCG).

Patients were randomly assigned to the control or treatment group using a table of computer generated random numbers. Laminaria was used in the control group to facilitate cervical dilatation prior to molar

evacuation while transcervical F16 foley catheter was used in the treatment group. A research assistant did the randomization and the principal investigator inserted either modality. Patients randomized into the laminaria group received MedGyn sterile laminaria size small, 3mm in diameter. The patient's perineum and vagina were prepped with antiseptic and a sterile speculum was inserted to visualize the cervix. After cleansing the cervix with antiseptic, the anterior lip of the cervix was clamped with an allis forceps to straighten the endocervical canal. Then an ovum forceps was used to introduce the laminaria into the endocervical canal. The vaginal canal was then packed with sterile gauze to keep the laminaria in place. Each patient was evaluated 12 hours after insertion of the laminaria, unless there was bleeding, to determine cervical dilatation. If the cervix has not dilated after 12 hours, another laminaria was inserted until cervical dilatation was achieved.

A French 16 foley catheter was used for patients randomized into treatment group. Patients underwent the same preparation as the laminaria group. Using an ovum forceps, the foley catheter was inserted through the endocervical canal into the potential space between the molar products and the isthmus of the uterus. After proper placement was ensured, the catheter balloon was inflated with 20 ml of sterile saline solution. This attained a balloon diameter of 15 mm to 20mm. Traction was applied to the catheter until the balloon was taut against the internal cervical os. The catheter was then connected to a urinary bag filled with 500mL of water placed to gravity over the end of the bed to maintain traction. Cervical dilatation was assumed successful once there was spontaneous expulsion of the foley catheter out of the vagina. For cases where no spontaneous expulsion occurred, foley catheter remained in situ for 24 hours. Repeat internal examination was done when there was vaginal bleeding or pelvic pain. At the 24th hour, when the foley catheter had not fallen out, the foley catheter was removed and cervix was assessed if it was able to accommodate the 12mm suction cannula. If the cannula met resistance, this was deemed "failed cervical priming" and laminaria was inserted.

All procedures were done without anesthesia. For cases where transcervical foley catheter insertion failed, use of laminaria was also considered. These patients were excluded from the study.

All patients were placed on "nothing per orem" at the start of the procedure. They were also asked to remain supine for the duration of the procedure of cervical dilatation, except when with urge to void. Vital signs were monitored hourly. For each patient, the following data were obtained and recorded in the patient data form:

1. time duration of insertion of mechanical dilator
2. intensity of pain during insertion of mechanical dilator
3. amount of blood loss during insertion and from the time of insertion to removal of laminaria or spontaneous expulsion of foley catheter
4. time duration from placement of mechanical dilator to successful cervical dilatation
5. need to insert additional pieces of laminaria
6. presence of profuse vaginal bleeding, pelvic pain, foul smelling vaginal discharge, and febrile episode

Description of Outcome Measures

The primary outcome of the study was the rate of successful cervical dilatation, expressed in mm/hr. This was derived by dividing the cervical dilatation measured in millimeters, which corresponded to the diameter of foley catheter balloon expelled or diameter of expanded laminaria, by the number of hours it took to attain successful cervical dilatation, which corresponded to the time duration from placement of mechanical dilator to successful cervical dilatation. Successful cervical dilatation was confirmed following easy insertion of the 12 mm cannula at start of suction curettage. The secondary outcomes included were the following:

1. time duration of insertion of mechanical dilator expressed in minutes
2. intensity of pain during insertion of mechanical dilator measured using the visual analog scale (VAS), with 0 having no pain and 10 having the worst excruciating pain.
3. amount of blood loss during insertion and from the time of insertion to removal of laminaria or spontaneous expulsion of foley catheter. For patients in laminaria group, blood loss was based on number of 4 inches x 4 inches gauze inserted as vaginal pack after laminaria insertion, which was soaked with blood upon laminaria removal. A 4 inches x 4 inches gauze fully soaked with blood was estimated to contain around 5cc of blood. For patients in the FC group, blood drained through the foley catheter into the urine bag, and the estimated blood loss was equivalent to the volume of fluid in the urine bag less the initial 500mL water placed for traction. For patients who had profuse vaginal bleeding, either following spontaneous foley catheter expulsion or laminaria removal, the estimated blood loss was based on the number of dry sheet soaked with blood. A 70 cm x 180 cm dry sheet fully soaked with blood was estimated to contain around 1000cc of blood.
4. time duration from placement of mechanical

dilator to successful cervical dilatation expressed in hours

5. need to insert additional pieces of laminaria. This was considered when the cervix was assessed to still be closed or unable to accommodate the 12 mm suction cannula after foley catheter expulsion or after laminaria removal
6. presence of profuse vaginal bleeding, pelvic pain, foul smelling vaginal discharge and febrile episode.

Data Analysis

Descriptive statistics were used to compute for percentages (%), means, standard deviations (SD), median differences, and interquartile ranges (IQR) for the socio-demographic and clinical characteristics of the sample population, as well as the primary and secondary outcomes of the study. Only two data variables (corpus size and hemoglobin) had statistically normal distribution. For these variables, unpaired T-test was used to determine differences between the two groups based on the outcome measures set by the study. The remaining variables were not normally distributed, hence a non-parametric analysis, the Wilcoxon rank sum test, was used to determine differences between the two treatment arms. For analysis of the relative risk of occurrence of profuse vaginal bleeding, pelvic pain, foul smelling vaginal discharge, and febrile episode, Fischer's exact test was used. All tests of significance were carried out at 0.05 and 0.01 alpha levels of significance, with 95% confidence interval.

RESULTS

Fifty-two patients were enrolled in the study from September 2013 to September 2014. Twenty-six patients were randomly assigned to the FC group and the other 26 patients were randomly assigned to the laminaria group. One patient in each group was excluded from analysis because these patients' cervices spontaneously opened before any intervention (either laminaria or foley catheter) was instituted. Another patient from the FC group was withdrawn from the study and excluded from analysis because of failed transcervical foley catheter insertion. Therefore, the FC group included 24 patients, while the laminaria group included 25 patients, for a total of 49 patients.

There were no significant differences in the socio-demographic and clinical data between the two groups. Data are summarized in Table 1.

Significantly higher rate of successful cervical dilatation was seen in the FC group as evidenced by a shorter time duration from its placement to successful cervical dilatation and the lack of need for insertion of additional cervical dilator. The time duration of placement of foley catheter was significantly shorter and pain intensity during its insertion was also significantly lower. Parameters to assess efficacy in facilitating cervical dilatation that were evaluated in the study are presented in Table 2.

The relative risk of occurrence of pelvic pain, febrile episodes, profuse vaginal bleeding and foul smelling vaginal discharge did not differ significantly between the two groups. Parameters to assess safety of each modality that were evaluated in the study are presented in Table 3.

DISCUSSION

The best modality for cervical ripening in cases of hydatidiform mole remains controversial. No one method has proven to be superior over another. However, clinical

Table 1. Socio-demographic Variables and Baseline Laboratory Values

	Laminaria (n = 25)	**Foley Catheter (n = 24)**	**p-value[a] (two-tailed)**
Age (years)	24 (7)	24 (8)	.55
Gravidity	2 (2)	2 (2)	.98
Parity	1 (2)	0 (2)	.82
Corpus size (cm)	17.9, 2.9	17.8, 3.2	.92[b]
Hemoglobin (mg/dL)	108.5, 17.5	113.2, 17.8	.36[b]
βHCG (IU/L)	472, 900 (616, 350)	309, 500 (560,801)	.47

Values were expressed as mean, SD or median (IQR)

* Significant difference at 0.05 alpha level, **at 0.01 alpha level

[a] Statistical analysis used was Wilcoxon rank sum test

[b] Statistical analysis used was unpaired T-test

Table 2. Cervical Dilatation Data

	Laminaria (n = 25)	Foley Catheter (n = 24)	p-value[a] (two-tailed)
Rate of Cervical Dilatation (mm/hr)	1 (0.8)	1.6 (0.9)	0.00**
Time Duration of Insertion of Dilator (min)	5 (2)	1 (2)	0.00**
Pain Intensity During Insertion of Dilator (VAS)	5 (2)	0 (2)	0.00**
Estimated Blood Loss During Insertion of Dilator (mL)	2.5 (3)	0 (3)	.26
Estimated Blood Loss From Insertion of Dilator to Successful Cervical Dilatation (mL)	15 (190)	50 (75)	.06
Time Duration From Placement of Dilator to Successful Cervical Dilatation (hours)	12 (21)	9.5 (6)	0.00**
Additional Pieces of Laminaria Inserted (number)	1 (2)	0 (0)	0.00**

Values were expressed as median (IQR)
*Significant difference at 0.05 alpha level, **at 0.01 alpha level
[a] Statistical analysis used was Wilcoxon rank sum test

Table 3. Signs and Symptoms Reported During Cervical Dilatation

	Laminaria (n = 25)	Foley Catheter (n = 24)	Relative Risk (95% CI)	p-value[a] (two-tailed)
Febrile episodes (%)	2 (8.0 %)	1 (4.2 %)	0.96 (0.83-1.11)	.52
Pelvic pain (%)	6 (24.0 %)	7 (29.2 %)	1.07 (0.77-1.50)	.75
Profuse vaginal bleeding (%)	7 (28.0 %)	5 (20.8 %)	0.91 (0.66-1.25)	.75
Foul-smelling vaginal discharge (%)	1 (4.0 %)		0.96 (0.89-1.04)	.66

Values were expressed as n (%)
*Significant difference at 0.05 alpha level, **at 0.01 alpha level
[a] Statistical analysis used was Fischer's exact test

experience has dictated that mechanical methods are far more advantageous than other modalities. In a Cochrane database of systematic review on mechanical methods of cervical ripening, mechanical methods, in the form of laminaria and intracervical foley catheter were shown to be more effective than oxytocin and prostaglandins in facilitating cervical dilatation with less associated side effects.[7]

Laminaria, being an osmotic or hygroscopic dilator, expands as it draws water from cervical tissues, thereby gently and gradually dilating the cervix. Also by drawing water from proteoglycan complexes in cervical tissue, the complexes dissociate, allowing the cervix to soften and dilate. It has been further hypothesized that the gradual mechanical stretching provides a stimulus for the local release of prostaglandins, cytokines, and elastase, which are thought to be important in cervical ripening.[8] On the other hand, the mechanical dilation with a foley catheter works by a number of mechanisms. One mode of action is by direct stretching of the cervix by local endocervical pressure. Another mechanism of action is by triggering a local inflammatory response that releases matrix metalloproteinases and endogenous prostaglandin E2, which in turn softens the cervix. There is also the theory advanced by Embrey and Mollison in 1967, which proposes that the mechanical action of the foley catheter balloon may cause rupture of decidual cells and their lysosome contents triggering the release of the lytic enzyme phospholipase A. This acts on phospholipids to form arachidonic acid, which in turn is converted to prostaglandin E2 then prostaglandin A2 which improves the consistency and effacement of the cervix.[13]

Several local studies have been performed demonstrating the efficacy of transcervical foley catheter and laminaria for cervical ripening. Mochtar compared the efficacy of prostaglandin E1 and laminaria as cervical

primers prior to evacuation of failed first trimester pregnancy. Their study concluded that laminaria achieved cervical dilatation faster than vaginal misoprostol, and that laminaria was associated with reduced cost and side effects.[14] Gayoma-Gonzales and Quevedo, on the other hand, compared the efficacy of a Fr 16 transcervical foley catheter inflated with 20cc of sterile water and intravaginal prostaglandin E1 for cervical ripening in cases of missed abortion and intrauterine fetal death. They demonstrated that the two modalities showed equal efficacy in dilating the cervix.[15]

In this study, transcervical foley catheter and laminaria were effective and safe in achieving cervical dilatation among patients with hydatidiform mole presenting with unfavorable cervices. However, the foley catheter facilitated a significantly faster rate of successful cervical dilatation compared to laminaria.

The most common complication of laminaria is pain during insertion. Less frequent side effects reported are anaphylaxis and retained fragments.[14,20,21] Since laminaria are made from seaweed stems, there were concerns that it may harbor infectious organisms. However, due to modern sterilization techniques, studies have shown that infectious morbidity is not increased by their use.[8,20] There is no report on the incidence of bleeding following the use of laminaria.

A number of series reported very few side effects of cervical ripening with foley balloon catheter, the most common of which was discomfort at insertion. One study reported cervical laceration as a rare complication.[17] The most important concern with leaving the catheter in situ for more than 24 hours is that of sepsis while the most feared complication after spontaneous expulsion of the balloon catheter is profuse vaginal bleeding. [18,22,15]

The findings of our study did not support any of these concerns for both modalities. For the laminaria group, there were 7 reports of profuse vaginal bleeding, 2 febrile episodes, and 1 report of foul-smelling discharge. There was no report of anaphylaxis or retained fragments. The most common subjective complaint with this modality was pain during insertion.

Discomfort during insertion of foley catheter was not observed in this study. There was 1 febrile episode but no report of cervical laceration. Profuse vaginal bleeding following spontaneous expulsion of the balloon catheter occurred less than expected, surprisingly, occurring more with the laminaria group.

In our study, in both FC group and laminaria group, pelvic pain occurred in 24-29 % of patients following cervical dilatation. This is consistent with the concept that myometrial preparedness and contractility is correlated with cervical dilatation in as much as both the cervix and myometrium are under a mutual endocrine-paracrine regulation.

CONCLUSION

Foley catheter may be an alternative in facilitating cervical dilatation among patients with hydatidiform mole, when laminaria is not readily available because both are equally effective. Foley catheter has the advantage of simplicity, low cost, availability, lack of systemic or serious side effects and causes only minimal discomfort.

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