
Prague, 30 May 2017
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Surgical TOP 2nd trimester RCT

Goldberg AB et al.: Cervical Preparation Before Dilation and Evacuation Using Adjunctive Misoprostol or Mifepristone Compared With Overnight Osmotic Dilators Alone: A Randomized Controlled Trial
Obstet & Gynecol 2015;126 (3): 599-609

• 3-arm randomized trial
  – overnight osmotic dilators alone,
  – dilators plus 400 micrograms buccal misoprostol
  – dilators plus 200 mg oral mifepristone during dilator placement

• Primary outcome was dilation and evacuation operative time

• 2 cohorts:
  – 16–18 6/7 weeks of gestation (N=150)
  – 19–23 6/7 weeks of gestation (N=150).

• No difference in operative time in either gestational cohort was found

• In the early cohort, initial dilation was greater with misoprostol than dilators alone, but patients given misoprostol had significantly more pain, fever, and chills.

• In the late cohort, dilation and evacuation procedures were less difficult after mifepristone than misoprostol or dilators alone.

• No difference in operative time. Adjunctive mifepristone facilitates later dilation and evacuation compared with osmotic dilators alone and is better tolerated than misoprostol.
Surgical TOP 1st trimester Clinical Guidelines

Allen RH, Goldberg AB: Society for Family Planning Clinical Guidelines: Cervical dilation before first-trimester surgical abortion (<14 weeks' gestation)
Contraception 93 (2016) 277-291

- Cervical priming in the first trimester with either osmotic dilators or misoprostol may protect against complications such as cervical injury and uterine perforation. The absolute risk of these complications is extremely low.
  - Cervical priming should be considered for all adolescents and is strongly recommended for adolescents at 12 to 14 weeks' gestation.
  - Cervical priming is recommended for all women at 12 to 14 weeks' gestation and for any woman in whom an initial attempt at rigid dilation is difficult.
  - Routine first-trimester cervical priming is not advised because does not confer proven benefit.

- Effective methods of cervical priming include osmotic dilators and misoprostol; the shortest time for efficacy (2 to 4 h) occurs with the use of Dilapan-S, Lamicel and misoprostol.

- Osmotic dilators do not increase the postabortal infection rate in the first trimester.

- Cervical preparation was shown to reduce the need for manual cervical dilatation compared with placebo.
- Misoprostol and isosorbide mononitrate and dinitrate were similarly effective in ripening the cervix, however there was more vomiting with misoprostol.
- Mechanical (Dilapan-S hygroscopic) dilators performed similarly to chemical dilators.
- Large, high-quality trials are required to determine whether the benefits of this treatment outweigh the risks.
Boraas CM, et al.: **Synthetic osmotic dilators with adjunctive misoprostol for same-day dilation and evacuation: a randomized controlled trial**

Contraception 2016 Nov;94(5):467-472

- A randomized, double-blinded, placebo-controlled trial of women 16 0/7 to 20 6/7 weeks gestation desiring D&E.
- Synthetic osmotic cervical dilators (Dilapan-S®) at least 4 h prior to D&E; randomization to 400 mcg buccal misoprostol or placebo 3 h preoperatively, stratified by gestational age.
- The primary outcome was operative time; 36 participants needed
- Secondary outcomes included total procedure time, patient and provider acceptability, baseline cervical dilation and complications.
- Adjunctive buccal misoprostol may not decrease operative times but may decrease complications when combined with synthetic osmotic dilators for cervical preparation for same-day D&E procedures.
- The trial was preliminarily halted
- Caution for the use of synthetic osmotic dilators alone for cervical preparation for same-day D&E at ≥ 19 weeks gestation
- Women strongly preferred same-day cervical preparation (98%).
Medical TOP 2nd and 3rd trimester RCT

Vincienne M, et al.: Comparison of the Induction-to-Delivery Interval in Terminations of Pregnancy with or without Dilapan-S
Fetal Diagn Ther  DOI: 10.1159/000458410

• Retrospective study of TOP in 2010–2012 compared the results from 2 hospitals with different TOP protocols starting at 16 weeks’ gestation, one (164 women) with and one (106 women) without Dilapan-S

• IDI1 = first dose of misoprostol in both centers
  – IDI1 was shorter with dilators (5 h 48 min vs. 10 h 18 min, p< 0.001);
  – the rates of uterine evacuation within 12 and 24 h were higher with dilators (94.5 and 100 vs. 68.9 and 91.5%, p< 0.001)
  – time between first misoprostol dose and amniotomy was shorter with dilators (0 h 47 min vs. 4 h 30 min, p< 0.001).

• IDI2 = dilator placement if used, and otherwise first dose of misoprostol
  – IDI2 was longer with dilators (18 h 24 min vs. 10 h 18 min, p < 0.001)
  – Rate of evacuation within 24 h did not differ significantly.

• Dilapan-S acts on cervical ripening and dilatation, thereby allowing early amniotomy.

• Prospective multicenter randomized trial (DILATOP) is about to begin; its purpose is to assess the efficacy and safety of Dilapan-S as well as women’s satisfaction with it.
GynecologieObstetrique&Fertilite (2016), http://dx.doi.org/10.1016/j.gyobfe.2016.04.001

• Comparison of two methodologies AROM and then administration of Cytotec or a cytotec first and then possibly to do a AROM ...
• Dilapan-S was placed in both arms as the standard of care but was not the subject of examination ...
Missed miscarriage Case Reports (Russian activity)

Barinov SV, et al.: Use of the Dilapan-S osmotic dilator in missed miscarriage in patients with severe comorbidities

- **Dr. Ugo Cerletti published 1 case report on successful use of ECT in human in 1937. ECT has become the most popular healing method between 1940 and 1960**
- Two case reports of missed miscarriage in women with severe comorbidities.
- Dilapan-S was placed for 12 hours resulting in induced miscarriage without any other pharmacological augmentation.
- Dilapan-S impacts the cervical tissue and results in cervical dilation via the promotion of endogenous prostaglandin release as the result of collagen degradation.
- Dilapan-S not only causes the dilation of the cervical canal, but in some cases independently facilitates induced abortion.
Gupta JK, et al.: **Efficacy and Safety of Synthetic Osmotic Dilators prior to Medical or Surgical Abortion: International Observational E-Registry**

Oral presentation at 25th EBCOG Conference, 17–21 May 2017, Antalya, Turkey

- Application of synthetic osmotic dilators is a safe and efficient method of cervical priming prior to surgical as well as medical termination of pregnancy.

- Insertion of 2-3 osmotic dilators for time interval of 4-7 hours provided effective cervical priming in majority of women.

- Fast mode of action enables one-day procedures in majority of surgical (84%) as well as medical (81%) abortions.

- No serious adverse outcomes including infectious complications associated with the use of synthetic osmotic cervical dilators were reported.
Future clinical evidence

Cervical priming prior to TOP

- **Laminaria Compared to Dilapan-S for Cervical Preparation Before Dilation and Evacuation at 18-24 Weeks of Gestation**
  - PI: Planned Parenthood of New York City, Inc.
  - 180 subjects randomized; recruitment completed

- **Mifepristone Versus Osmotic Dilator Insertion for Cervical Preparation Prior to Surgical Abortion at 15-18 Weeks (SaMi2)**
  - PI: Boston University
  - Comparison of mifepristone + misoprostol use vs osmotic dilator use for cervical preparation
  - Randomization of 50 subjects, recruitment completed

- **Same-day Cervical Preparation With Dilapan-S™ Plus Buccal Misoprostol Compared to Overnight Dilapan-S™ Before Dilation and Evacuation at 16 to 20 Weeks' Gestation: A Randomized Controlled Trial**
  - PI: Planned Parenthood of New York City, Inc.
  - Randomization of 92 subjects; recruitment ongoing
Cervical priming prior to TOP / conclusions

• In late 1\textsuperscript{st} and 2\textsuperscript{nd} trimester Dilapan-S offers excellent efficacy in cervical dilation and is evaluated as superior to misoprostol.

• Dilapan-S is suitable for one-day D&E procedure.

• In late 1\textsuperscript{st} trimester abortions, 1-3 rods of Dilapan-S for 4 hours ensures adequate cervical priming.

• In 2nd trimester abortions, 2-4 rods of Dilapan-S for 4 hours ensures adequate cervical priming.

• **Dilapan-S provides an effective and beneficial cervical priming in medical terminations (misoprostol) of pregnancy including missed miscarriage.**

• Insertion of Dilapan-S for 12 hours not only causes the dilation of the cervical canal, but in some cases independently facilitates induced abortion.
Current and future clinical evidence in Induction of labor (IOL) 2016, 2017, ....

Prague, 30 May 2017
Daniela Gdovinová
Maier JT, et al: Cervical Ripening with an Osmotic Dilator (Dilapan-S) in Term Pregnancies – An Observational Study
Journal of Gynecology and Neonatal Biology, Open Access, Volume 1: Issue 3

- 60 out of 83 patients were nulliparae; 12 out of 83 patients had a previous cesarean section.
- Average time from cervical ripening to delivery was 1.5 days (36 hours)
- 60.2% of patients delivered spontaneously,
- 4.8% by ventouse/forceps and
- 34.9% by secondary cesarean section
- A longer duration of cervical ripening and labor induction was associated with a significantly higher rate of delivery by ventouse or cesarean section (14.3% vs. 4.8% and 42.9% vs. 34.9% respectively).
- No adverse fetal or maternal outcomes were noted.
- The application of Dilapan-S is cost-effective as patients can be seen in outpatient care. The device is efficient and safe.
- It is an attractive option for physicians and patients to lower the cesarean section rate by facilitating VBAC.
Current clinical evidence

Cervical ripening prior to IOL

DOI: 10.15761/COGRM.1000154

- 63 women were enrolled in this study (Dilapan-S n=26, intracervical n=20, intravaginal n=19).
- No difference in caesarean delivery rate was identified when comparing mechanical induction methods to pharmacologic induction methods.
- The intracervical PEG2 had the shortest induction to delivery time in comparison to intravaginal PEG2 and mechanical induction with Dilapan-S.
- With intracervical PEG2 high levels of uterine hyperstimulation (25%) were detected which all required pharmacological intervention with Ferenterol.
- Intravaginal PEG2 only rarely caused uterine hyper stimulation, whereas Dilapan-S showed no hyper stimulation at all.
- Dilapan-S is an ideal candidate for women with a prior caesarean section due to the current contraindications of the pharmacological induction agents.
- Potentially, for outpatient cervical ripening Dilapan-S might also be a candidate.
Current clinical evidence

Cervical ripening prior to IOL

Gupta JK, et al.: Efficacy and Safety of Synthetic Osmotic Dilators prior to Induction of Labor: International Observational E-Registry

Oral presentation at 25th EBCOG Conference, 17–21 May 2017, Antalya, Turkey

- The use of synthetic osmotic dilators for cervical ripening leads to high vaginal delivery rates.
- **Significantly better efficacy outcomes when the cervical dilator was left in situ up to 12 hours then longer duration of insertion time.**
- Synthetic osmotic cervical dilators did not lead to serious maternal and neonatal adverse effects including infectious complications.
- **This method was effective and may lead to lower rates of cesarean section in high risk pregnancies and potential use in the outpatient setting when no maternal or fetal pathology is suspected, resulting in lower health costs.**
- Level 1 clinical trials are needed to compare osmotic synthetic dilators to other methods => Randomized CT
Current clinical evidence

Cervical ripening prior to IOL

Hasegawa J, et al.: The use of balloons for uterine cervical ripening is associated with an increased risk of umbilical cord prolapse: population based questionnaire survey in Japan


- **Prolapse of the umbilical cord during labor was observed** in 88 (0.005%) of 1,891,189 deliveries not associated with the use of balloons for cervical ripening and in **93 (0.064%) of 146,271 deliveries associated with the use of balloons for cervical ripening.**

- All types of balloons were significantly associated with the occurrence of prolapse of the umbilical cord.

- A total of 39% of cases of umbilical cord prolapse occurred during manual or spontaneous balloon removal, while 53% of cases occurred after a while not directly associated with balloon removal.

- **The risk of umbilical cord prolapse was significantly increased during the use of balloons for cervical ripening,** especially in cases involving the use of disk-type and ball-type balloons filled with large amounts of water.
Future clinical evidence

Cervical ripening prior to IOL

Chodankar R, Sood A, Gupta JK; An overview of the past, current and future trends for cervical ripening in induction of labour
The Obstetrician & Gynaecologist, DOI: 10.1111/tog.12395

• There is limited evidence with regard to the use of osmotic dilatators in the context of preinduction cervical ripening.

• An RCT has compared the use of Dilapan-S and Laminaria japonica for this purpose. The study concluded that use of Dilapan-S was preferable as its use was associated with a shorter induction–delivery interval and fewer dilatators were necessary to obtain significant cervical ripening.

• Other RCTs comparing the use of Dilapan-S and PGE2 found a statistically significant increase in the rate of uterine contractions and hyperstimulation associated with the use of prostaglandins PGs.

• The evidence from the International Dilapan-S E-Registry so far has shown no risk of hyperstimulation or associated fetal heart rate FHR abnormalities with Dilapan-S use.

• It has been proposed that Dilapan-S may be potentially used as an outpatient agent for induction of labour.
RCT clinical program to confirm clinical profile of Dilapan-S in IOL

- **RCT Dilapan-S vs PGE2 (1:1)**
  - Propess (N=430) vs Dilapan-S (n=430)

- **RCT clinical program of Dilapan-S**

- **RCT Dilapan-S vs Foley catheter (1:1)**
  - Baloon catheter (n=210) vs Dilapan-S (n=210)

**Primary outcome:** not reach of vaginal delivery within 36 hours
- Hypothesis of superiority of Dilapan-S over Propess by 8%
- Including of patients questionnaire of tolerability and satisfaction

**Primary outcome:** vaginal delivery rate
- Double hypothesis of non-inferiority of Dilapan-S vs Foley catheter or superiority of Dilapan-S
- Including of patients questionnaire of tolerability and satisfaction
Future clinical evidence
Cervical ripening prior to IOL

- **An RCT of a Induction of Labor in Women With Unfavorable Cervix: Dilapan Versus Foley Bulb**
  - PI: The University of Texas Medical Branch, Galveston
  - Randomization of 420 subjects; 120 subjects recruited

- **An RCT of a Synthetic Osmotic Cervical Dilator for Induction of Labour in Comparison to Dinoprostone Vaginal insErt (SOLVE)**
  - PI: Birmingham Women's NHS Foundation Trust
  - Multicentre; randomization of 860 subjects; recruitment starts in May 2017

- **What After the First Propess: A Randomised Comparative Prospective Study**
  - PI: South Warwickshire NHS Foundation Trust
  - Randomization of 330 subjects (no treatment / vaginal PGE2 tablet / Dilapan-S)
  - 3 arm randomized trial; 11 subjects recruited

- **A comparison between the effect of Dilapan-S, extra amniotic normal saline infusion and oral misoprostol in term pregnancies**
  - PI: Akbarabadi Hospital - Labor ward, Iran
  - 3 arm randomized trial; 120 subjects (40 subjects in each arm)
Cervical ripening prior to IOL / conclusions

- Dilapan-S (3-5 rods) and other mechanical methods offer at least similar or higher efficacy as pharmacological agents.

- **Shorter duration of cervical ripening (up to 12 hours) provides significantly higher rate of achieved vaginal deliveries than longer duration time (12-24 hours).**

- No higher risk of maternal / neonatal morbidity including infectious complications has been recorded with Dilapan-S.
  - Dilapan-S offers minimal risk of uterine hyperactivity and fetal distress.

- Data confirm efficacy and safety of the use of Dilapan-S in women with C. section in medical history and other higher risk conditions.

- Dilapan-S is already considered by some clinicians as the optimal choice for out-patient cervical ripening.
Thank you for your attention