Dilapan-S®

EXECUTIVE SUMMARY

A randomized trial of synthetic osmotic cervical dilator for induction of labor versus dinoprostone vaginal insert (SOLVE trial)

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Objective:

- To compare the efficacy, maternal and neonatal safety, and maternal satisfaction of DILAPAN-S with dinoprostone (10mg controlled release vaginal pessary).

Materials and methods:

- An open-label, superiority, randomized controlled trial in four English hospitals.
- 674 women were randomized (337 to the DILAPAN-S group and 337 to the dinoprostone group).
- The trial did not reach its planned sample size of 860 due to restrictions on research during the Covid-19 pandemic.
- Up to five DILAPAN-S dilators (according to the protocol) were inserted and left for a minimum of 12 hours and up to a maximum of 24 hours. If the cervix remained unfavorable after the first series (Bishop score <6) a second (then third) series of dilators were placed for an additional 12-24 hours.
- Dinoprostone was administered high up into the posterior vaginal fornix. Each series of dinoprostone remained in place for up to 24 hours or up to 32 hours, according to local hospital policy.
- If spontaneous labor had not started, amniotomy was conducted after the Bishop score was ≥6. Oxytocin infusion using a syringe pump was used as per hospital protocols, commencing no sooner than 30 minutes after the removal of the last series of DILAPAN-S or dinoprostone and with continuous fetal monitoring.
- The primary outcome was failure to achieve vaginal delivery (i.e. Cesarean delivery).
- Secondary outcome measures included maternal and neonatal adverse events, and maternal satisfaction.

Results:

- Nulliparous represented 79.8 % of participants in the DILAPAN-S group and 80.7 % in the dinoprostone group.
- **Failure to achieve vaginal delivery (i.e. Cesarean delivery):** 37.4 % in the DILAPAN-S group vs 34.3 % in the dinoprostone group.
- **First round cervical ripening success rate** (*defined as Series 2 not required*)**:** 78.9 % in the DILAPAN-S group vs 69.0 % in the dinoprostone group.
  - **Slow progress** or **failure to ripen** was reported as a reason for unsuccessful first rounds in **55** women in the DILAPAN-S group compared to **71** women in the dinoprostone group.
  - **Intervetion fell out** in **0** women in DILAPAN-S compared to **13** women in dinoprostone.

Complications during cervical ripening: 7.6 % in the DILAPAN-S group vs 22.6 % in the dinoprostone group.
  - **Uterine tachysystole:** 0.4 % in DILAPAN-S vs 5.0 % in dinoprostone
  - **Uterine hyperstimulation with non-reassuring FHR:** 0 % in DILAPAN-S vs 4.3 % in dinoprostone
  - **Effect on fetus (CTG):** 2.4 % in DILAPAN-S vs 11.3 % in dinoprostone
- Further, 1 case of neonatal death, 3 cases of hypoxic ischemic encephalopathy and 1 case of placental abruption occurred solely in the dinoprostone group.
- **Use of analgesia during cervical ripening:** 51.2 % in the DILAPAN-S group vs 66.3 % in the dinoprostone group (p<0.0001), from which
  - Oral opioids: 21.4 % vs 43.9 %
  - Pethidine: 6.2 % vs 17.5 %
- **Time between removal of last series of intervention to amniotomy (mean):** 30.3 hours in the DILAPAN-S group vs 31.1 hours in the dinoprostone group
- **Amniotomy undertaken for induction of labor:** 70.2 % in the DILAPAN-S group vs 42.6 % in the dinoprostone group (p < 0.0001)
- **Oxytocin required for induction of labor:** 62.7 % in the DILAPAN-S group vs 39.3 % in the dinoprostone group (p < 0.0001)
- There were substantially better outcomes for DILAPAN-S regarding maternal satisfaction during cervical ripening period.

Maternal satisfaction		**DILAPAN-S**	**Dinoprostone**
How much pain did you have while the drug/device was being put in place?	Wong Baker Pain Scale (0-10 points)	Mean 4.3	Mean 4.7
		Median 4	Median 4
Were you able to perform daily activities such as walking, dressing, hygiene, shower?	Always	155 (76.0 %)	104 (46.9 %)
Were you able to get some relaxing time?	Always	108 (52.9 %)	62 (27.9 %)
Were you able to get some sleeping time?	Always	97 (48.0 %)	49 (22.1 %)
Were contractions frequent?	Not at all	73 (37.1 %)	28 (12.7 %)
Were contractions intense?	Not at all	87 (44.2 %)	34 (15.5 %)
Did you feel any discomfort with the drug/device in place?	Not at All	92 (46.2 %)	59 (22.7 %)
Please rate the overall pain that you had while the drug/device was in place.	Wong Baker Pain Scale (0-10 points)	Mean 3.1	Mean 5.6
		Median 3	Median 6

Key take away messages:

- Due to **demands on the clinical service** not all women were able to receive a timely amniotomy once a favorable cervix had been achieved, **potentially pausing or reversing the physiological process of cervical ripening**.
- Women undergoing cervical ripening with DILAPAN-S have similar vaginal delivery rates compared to dinoprostone but with fewer instances of **uterine tachysystole**, **hyperstimulation** and adverse effects on the fetus.
- More women in the DILAPAN-S group reported better **satisfaction** in terms of ability to perform their desired daily activities such as walking, dressing, hygiene, shower, ability to sleep, relax, and reported less frequent and lower intense **uterine contractions** as well as **lower pain scores** both within the insertion procedure and during the ripening period.
- There was **a lower need for re-insertion** of DILAPAN-S, by approximately 10 %.
- The trial indicated DILAPAN-S capability to prevent or minimize risk of complications and serious adverse reactions.
- **Significantly less women needed analgesia** during the cervical ripening process in the DILAPAN-S group, **strong opioid analgesics** in particular.
- Mean number of **4.7** dilators being inserted for **19 hours** in average enabled progress of about **3.2 points** in Bishop score when assessing the favorability of the cervix for labor.
- **Intrauterine growth restriction** and **reduced fetal movements** represent a group of women with reduced fetal reserve where DILAPAN-S would be a benefit as it is associated with a lower risk of uterine hyperstimulation.
- This would suggest that DILAPAN-S could also be used for cervical ripening as an **outpatient procedure**.
- Majority of women in the DILAPAN-S group underwent amniotomy after cervical ripening which confirms DILAPAN-S predictability and provides an opportunity to schedule IOL procedure more properly.

NOTE BELOW:

Occurrence of Cesarean section (37.4 % vs 34.3 %) should be seen in relation to high proportion of Nulliparous participants (79.8 % vs 80.7 %) and delayed amniotomies due to demands on the clinical service.