European Journal of Obstetrics & Gynecology and Reproductive Biology 229 (2018) 70–75

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Full length article

Synthetic osmotic dilators in the induction of labour—An international multicentre observational study

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ARTICLE INFO

Article history:
Received 7 July 2018
Received in revised form 1 August 2018
Accepted 2 August 2018
Available online xxx

Keywords:
Cervical ripening
Dilapan-S
Induction of labour
Synthetic osmotic dilators
Pregnancy
Birth

ABSTRACT

Introduction: To evaluate the effects of synthetic osmotic dilators (Dilapan-S/ Dilasoft) in women who required induction of labour in a large prospective multicentre international observational study.

Materials and methods: Primary outcomes were duration of Dilapan-S/Dilasoft insertion (hours), total induction - delivery interval (hours) and the rate of vaginal deliveries within 24 h (%). Secondary outcomes were the number of dilators inserted, Bishop score increase after extraction of Dilapan-S/ Dilasoft, complications during induction (uterine contractions, uterine tachysystole and hyperstimulation, effect on the fetus) and post induction (infections and neonatal outcomes), agents / procedures used for subsequent induction of labour, immediate rate of spontaneous labours following cervical ripening period, rate of spontaneous vaginal deliveries, rate of instrumental vaginal deliveries and caesarean sections.

RESULTS: Total of 543 women were recruited across 11 study sites, of which, 444 women were eligible for analysis. With Dilapan-S/Dilasoft use of <12 h (n = 188) the overall vaginal delivery rate was 76.6% with 45.7% of these births occurring within 24 h, 66% within 36 h and 75.5% within 48 h from insertion of Dilapan-S/Dilasoft. The mean insertion-delivery interval for this group was 24.3(±10.4) hours. With Dilapan-S/Dilasoft use of >12 h (n = 256), the overall vaginal delivery rate was 64.8%, with 16% of these births occurring within 24 h, 48.4% within 36 h and 54.7% within 48 h from insertion of Dilapan-S/Dilasoft. The mean insertion-delivery interval for this group was 39.1(±29.2) hours. The mean gain in the Bishops score was +3.6(±2.3). The mean number of Dilapan-S/Dilasoft dilators used was 3.8 (±1.1). The overall rate of caesarean section was 30.1%. The overall complication rate was low including infection risk. No adverse neonatal outcome was attributable to the use of Dilapan-S/Dilasoft.

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https://doi.org/10.1016/j.ejogrb.2018.08.004

Conclusion: Dilapan-S/Dilasoft are safe and effective methods for cervical ripening. Their use is associated with low maternal and neonatal complication rates. Future research should aim at level I clinical trials comparing Dilapan-S to other mechanical or pharmacological cervical ripening agents.
Clinical trial registration: https://clinicaltrials.gov/ct2/show/NCT02318173.

Key message

Dilapan-S use of <12 h results in an overall vaginal delivery rate of >75%. It is easy to insert and remove and is safe to use, even in women with previous caesarean sections.

Introduction

The history of induction of labour dates back to Hippocrates' original description of mammary stimulation and mechanical dilatation of cervical canal [1]. Historically, induction was only done in the event of life threatening maternal disease. With the advent of safer and improved methods, the threshold for intervention for induction of labour has reduced.

Based on our expanding knowledge of physiological processes involved in spontaneous labour, the cervix usually undergoes a process of softening, effacement and then dilatation (cervical ripening). Cervical "ripening" is a physiological process occurring throughout the latter weeks of pregnancy and is completed with the onset of labour. There is a continuum from "unripe" to "ripe" or favourable cervix. The nature of the cervix is therefore a crucial organ that may determine a successful vaginal delivery.

Until recently osmotic dilators have been used in the context of cervical ripening prior to surgical termination of pregnancy, particularly at advanced gestations. However, more recently, there has been increasing interest in their use as agents for induction of labour.

In 1964, Edward Bishop devised a five-point scoring scale (maximum score out of 13), which included an assessment of cervical dilation, effacement of the cervix (length), station of the fetus, consistency of the cervix, and position of the cervix to predict the likelihood of a woman entering labour naturally in the near future [2]. The score was modified to become the 'Calder score' or modified Bishop score in 1974 (with minor changes in emphasis), which is now the most commonly used scoring method [3]. A cervix is viewed as unfavourable if the modified Bishop score is less than six.

The cervix is a unique organ composed of collagen (type1,3,4), blood vessels, fibroblasts, elastin and minimal smooth muscle [4]. Cervical ripening at a microstructural level is associated with reduction in the number of cross linkages between the collagen helices, with a resultant "soft" cervix. Enzymatic actions via matrix metalloproteases, proteases, and collagenases alters the balance of proteoglycans and glycosaminoglycans within the extracellular matrix [5,6]. In addition, there is increased vascularity as well hypertrophy of the cervical glands and stroma. Mechanical methods, including osmotic dilators are predominantly thought to physically dilate the cervix and induce endogenous prostaglandins (PG) release which in turn results in cervical ripening described above [7].

Dilapan-S is a second-generation osmotic hygroscopic dilator made from an anisotropic xerogel AQUACRYL®. It is a synthetic gel rod (sterile), which acts by absorbing fluid from the cells of the cervical canal, resulting in reversible cell wall dehydration and softening. The increase in volume of the rod(s), in turn by mechanical stretch, effects endogenous PG release with resultant cervical ripening. It is currently US FDA approved and CE certified. Like Dilapan-S, Dilasoft is made from patented AQUACRYL hydrogel and uses the same mechanism of action. Dilasoft was developed on special request of the Japanese market and is currently sold mainly in the Japan market, CE marked (2010), Nintei approved (2009). When compared with mechanical dilatation using balloon catheters, the mechanism utilised by inflatable balloon catheters may result in tissue injury, inflammation and scarring as the lack of hydraulic permeation to dehydrate the cervical cells of results in the cells being burst or damaged [8].

The most common pharmacological agents use for cervical ripening are prostaglandin-based preparations such as controlled release pessaries or inserts, gels, tablets and occasionally oral solutions. The common prostaglandins used include PGE2 (dinoprostone) and PGE1 (misoprostol). Prostaglandins increase cell membrane permeability, and decrease osmotic pressure [9], however they are associated with significant side effects such as uterine hyperstimulation, uterine rupture in previous caesarean sections, postpartum haemorrhage, fetal heart rate changes or fetal hypoxia [10].

Common mechanical methods include membrane sweeping, amniotomy, osmotic dilators and balloon catheters.

The general perceived advantages of mechanical methods over pharmacologic agents include comparable efficacy with low risk of uterine hyperstimulation [11] and fetal distress, low risk of drug related side effects such as nausea, vomiting, diarrhoea and fever [10] and potential economic and storage benefits.

Limited evidence is available with regards to the use of osmotic dilators in the context of pre-induction cervical ripening for term pregnancies. Small historical randomised controlled trials comparing Dilapan-S to intracervical prostaglandin gel have found a statistically significant decrease in uterine contractions and hyperstimulation in the group of women that received Dilapan-S [12,13].

The goal of this study was to evaluate the effects of Dilapan-S in women who required induction of labour in a large prospective multicentre international observational study.

Methods

Study design and population

After obtaining an ethics approval from each participating study site, an international, multicentre, non-interventional, observational study was conducted with 11 study sites in 7 countries (the United Kingdom, Germany, Czech Republic, India, Russia, Slovakia and the United States of America).

In the study, 2 types of synthetic osmotic dilators were used: Dilapan-S (n = 276) and Dilasoft (n = 168). They are essentially the same product and for the study report, we have used the term Dilapan-S by combining the data for the two types.

The primary outcomes were duration of Dilapan-S/Dilasoft insertion (hours), total induction – delivery interval (hours) and the rate of vaginal deliveries within 24 h (%). Secondary outcomes were the number of dilators inserted, Bishop score increase after extraction of Dilapan-S/Dilasoft, complications during induction (uterine contractions, uterine tachysystole and hyperstimulation, effect on the fetus) and post induction (infections and neonatal outcomes), agents / procedures used for subsequent induction of labour, immediate rate of spontaneous labours following cervical