

# Randomised comparison of the nitric oxide donor isosorbide mononitrate with prostaglandin E2 gel for cervical ripening prior to the induction of labour at term

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<b>Registration date</b> 18/12/2002	<b>Overall study status</b> Completed	<input type="checkbox"/> Protocol
<b>Last Edited</b> 10/09/2009	<b>Condition category</b> Pregnancy and Childbirth	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data

**Plain English summary of protocol**  
Not provided at time of registration

## Contact information

**Type(s)**  
Scientific

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## Additional identifiers

**EudraCT/CTIS number**

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**

01/02A

## **Study information**

**Scientific Title**

### **Study objectives**

Double blind trial comparing isosorbide mononitrate with prostaglandin E2 for pre-induction cervical ripening in nulliparous women. Women were randomised to receive vaginally either IMN tablets (40mg) or PGE2 gel (2mg), up to two doses 16 hrs apart. The aims of the study were to test the following hypotheses:

1. IMN (40mg) is as effective as PGE2 gel (dinoprostone 2 mg) for cervical ripening prior to the induction of labour at term.
2. IMN (40mg) is associated with a lower incidence of uterine hyperstimulation than PGE2 gel (dinoprostone 2mg) for cervical ripening prior to the induction of labour at term.
3. IMN (40mg) is associated with a zero incidence of abnormal fetal heart rate (FHR) patterns, vaginal bleeding, uterine hypertonus and hypotension requiring treatment, and thus would be safe to use in an outpatient setting.

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

Not provided at time of registration

### **Study design**

Randomised controlled trial

### **Primary study design**

Interventional

### **Secondary study design**

Randomised controlled trial

### **Study setting(s)**

Hospital

### **Study type(s)**

Treatment

### **Participant information sheet**

### **Health condition(s) or problem(s) studied**

Obstetrics and gynaecology

## **Interventions**

Randomised to one of two treatment groups on up to two occasions:

1. Isosorbide mononitrate tablet 40 mg administered vaginally (n = 200)
2. Prostaglandin gel (dinoprostone) 800 ug administered vaginally (n = 200).

Each treatment given on up to two occasions: after recruitment and 16 h later. If Bishop score found to be more than 6, cervical ripening agent will be withheld and fetal membranes ruptured to induce labour.

Women who go into labour during the ripening process will be managed according to an 'active management of labour' protocol, and further ripening agents withheld.

## **Intervention Type**

Other

## **Phase**

Not Specified

## **Primary outcome measure**

The study examined primary outcomes of safety and efficacy. The cervical ripening effect of each agent was assessed as change in modified Bishop score at each treatment insertion (16 hours and 24 hours) over pre-randomisation modified Bishop score. Frequency and duration of uterine contractions was assessed at 2, 4, 6, 16, 18, 20, 22 and 24 hours, in order to calculate the incidence of uterine hyperstimulation (defined as uterine tachysystole [more than 5 uterine contractions per 10 minutes for at least 20 minutes] with or without FHR changes).<sup>14</sup> We also recorded the frequency of events during ripening that would be hazardous for mother or baby if cervical ripening had been performed on an outpatient basis (any of: abnormal FHR patterns, maternal hypotension requiring treatment, uterine hypertonus or vaginal bleeding). Abnormal FHR patterns were assessed by cardiotocography performed from 30 minutes prior to drug administration until one hour after, and then at 6, 15.5, 17 and 24 hours or continuously once uterine contractions ensued. Cardiotocograph tracings were rated normal, suspicious or pathological according to the Royal College of Obstetricians and Gynaecologists guidelines on the use of electronic fetal monitoring.<sup>13</sup> On conclusion of the trial, the abnormal FHR patterns were reviewed by an independent Obstetrician whilst blind to treatment allocation. Hypotension requiring treatment was assessed by maternal pulse and blood pressure measurements at 1, 2, 6, 16, 17 and 24 hours using an automated device (Dinamap®, Critikon Company, Tampa, Fla). Vaginal bleeding during the cervical ripening period (first drug treatment to 24 hours) was prospectively ascertained by examination or patient enquiry. All primary outcomes were ascertained during the first 24 hour study period, during treatment solely with either IMN or PGE2, and prior to rescue treatment with PGE2 where applied.

## **Secondary outcome measures**

1. The incidence of maternal side effects over the preceding 6 hours (assessed by a structured questionnaire at 6, 16 and 22 hours)
2. The timings and maternal outcomes of the subsequent labour
3. Fetal outcomes

4. Maternal satisfaction with cervical ripening treatment (measured by a visual analogue score [VAS] prior to discharge from hospital), 5. Preference for inpatient or outpatient cervical ripening  
6. Any events requiring hospital admission or referral.

**Overall study start date**

01/10/2001

**Completion date**

30/11/2003

## **Eligibility**

**Key inclusion criteria**

Consenting pregnant women admitted to Glasgow Royal Maternity Hospital for cervical ripening prior to the induction of labour at term who fulfil the criteria:

1. Singleton fetus
2. Cephalic presentation greater than or equal to 38 completed weeks gestation
3. Modified cervical (Bishop) score of less than or equal to 6

**Participant type(s)**

Patient

**Age group**

Adult

**Sex**

Female

**Target number of participants**

400

**Key exclusion criteria**

1. Patients with any of the contraindications listed in the British National Formulary to PGE2 (active cardiac, pulmonary, renal or hepatic disease, placenta praevia or unexplained vaginal bleeding during pregnancy and ruptured membranes, major cephalopelvic disproportion or fetal malpresentation, history of Caesarean section or major uterine surgery, untreated pelvic infection and fetal distress) or IMN (hypersensitivity to nitrates, hypotensive conditions and hypovolaemia, hypertrophic obstructive cardiomyopathy, aortic or mitral stenosis, cardiac tamponade, constrictive pericarditis, marked anaemia and closed-angle glaucoma).
2. Other exclusion criteria were delivery mandatory within the next 48 hours in the maternal or fetal interest, one or more births >23 weeks gestation, age <16 years, or ruptured fetal membranes.

**Date of first enrolment**

01/10/2001

**Date of final enrolment**

30/11/2003

# Locations

## Countries of recruitment

Scotland

United Kingdom

## Study participating centre

Department of Obstetrics & Gynaecology

Glasgow

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# Sponsor information

## Organisation

The Sir Jules Thorn Charitable Trust (UK)

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## Sponsor type

Charity

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# Funder(s)

## Funder type

Charity

## Funder Name

The Sir Jules Thorn Charitable Trust (UK)

# Results and Publications

Publication and dissemination plan  
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary  
Not provided at time of registration

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	01/04/2006		Yes	No