

SiM(Scratch in Miscarriage) study

Pilot Randomised Controlled trial of the effect of endometrial scratch in recurrent miscarriage on pregnancy outcomes

Valarmathy Kandavel MBBS DGO MRCOG

Clinical Fellow in Reproductive Medicine

UHCW NHS Trust and Tommy's National centre for miscarriage research

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Background to the study

- Recurrent miscarriages are defined as three or more consecutive pregnancy losses < 24 weeks
- Currently patients are offered specialist referral after 3 consecutive miscarriages
- Psychological and social implications for the couple
- 39,800 miscarriages had a hospital stay between 2012 – 2013 with cost implications for the NHS

What is known so far

- Common listed causes for miscarriages

Genetic- mostly first trimester

Clotting disorders- acquired and inherited

Anatomical- Cervical weakness, uterine abnormalities

Medical disorders- thyroid

- Few effective treatment options

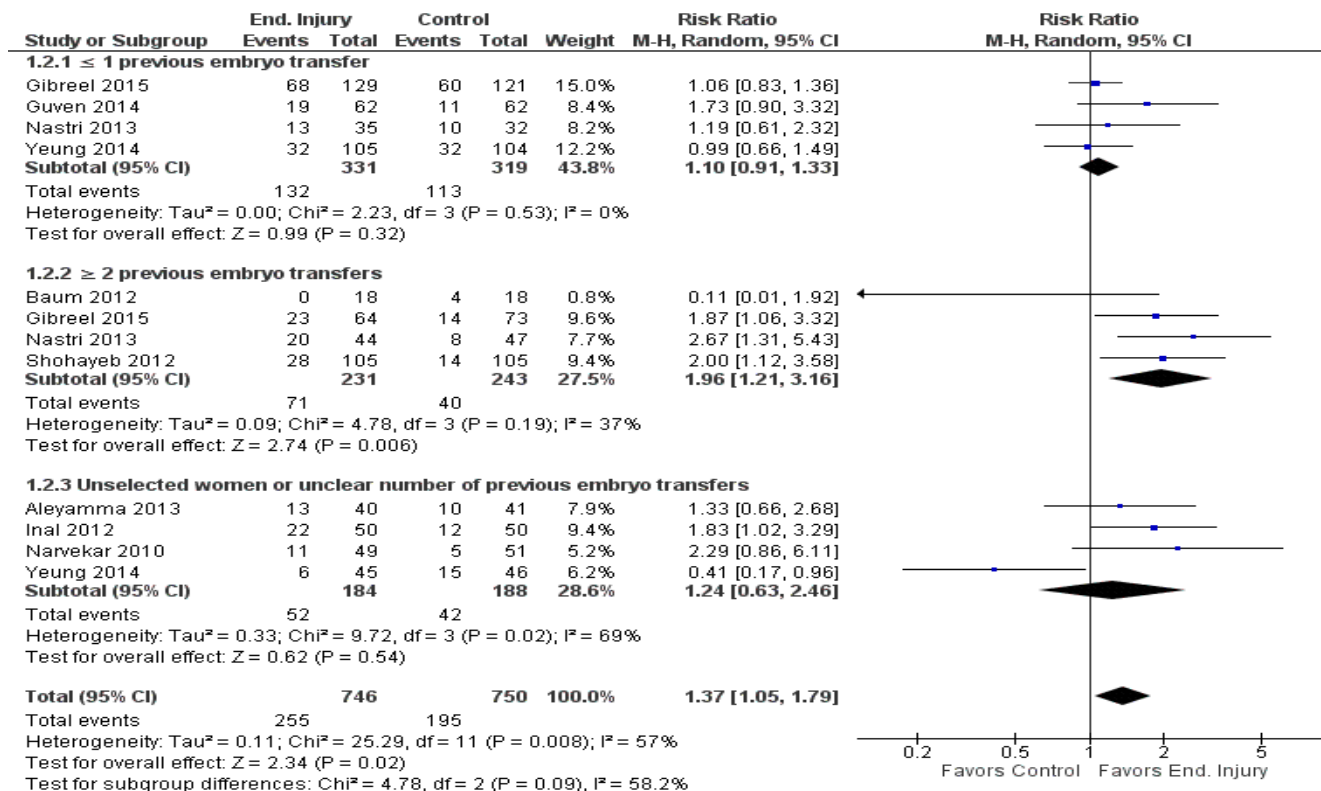
Our approach

- Miscarriage can be due to a primary endometrial problem
- Failed pregnancies are due to impaired decidualisation
- Aim to optimise the environment for implantation
- Significant difference in the decidualisation markers in women with recurrent miscarriages

Endometrial scratch

- Intentional minor damage to the endometrium performed with the objective of improving reproductive outcomes.
- Highly debated current topic of interest
- Has shown benefits in Cochrane reviews in both women undergoing IVF and those trying other methods
- However the trials are of poor quality

Cochrane review of IVF patients



Proposed mechanisms of action

- Induce decidualisation
- Provoke wound healing
- Backward development hypothesis
- Increase in stem cell population
- Modulation of gene expression of IP factors
- Usually a cluster of events which promotes implantation

Miscarriage and endometrial scratch

- Earliest evidence is from Karrow et al 1971
- May work by improving decidualisation, recruitment of stem cells, synchronicity
- Selection of relatively lower risk patients will help in evaluation of effectiveness
- Not been evaluated in patients with RM
- Randomised trial of endometrial scratch vs control

Study details

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- Obtained ethics approval on 26/10/15, Ref: 15/WM/0295
- Sponsor- University of Warwick
- 1x substantial amendment approved on 13th April 2016
- Approval for recruitment until 01/09/2017
- Registered on clinicaltrials.gov NCT02681627
- BJOG citation under clinical trials-May 2016

Clinical trials

Clinicians keen to keep up-to-date regarding clinical studies that are currently recruiting may find the following informative.

SIM (Scratch in Miscarriage) study (SIM)	
Registration	http://clinicaltrials.gov/ct2/show/NCT02681627
Description	This phase 1, pilot, randomised controlled trial aims to determine whether endometrial scratch with a Wallace catheter during the luteal phase improves the live birth rate in women with recurrent miscarriage.
Outcome measures	Primary: Live birth rate after 24 weeks of gestation. Secondary: Miscarriage until 23 rd weeks of gestation; pregnancy complications; acceptability of the intervention.
Study site	Coventry and Warwick, UK. Anticipated study end date: September 2017.

Study Details

Inclusion criterion	Exclusion criterion
<p>Age 18- 42 years 2 or more idiopathic miscarriages No medical or surgical co-morbidities Able to consent Actively trying for pregnancy</p>	<p>Conditions needing treatment during pregnancy Uterine anomalies Inability to tolerate internal examinations Previous entry into the trial</p>

Outcome measures

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Primary-

Live birth after 24 weeks (Pregnancy achieved within 3 cycles after randomisation)

Secondary

- Miscarriages until 23+6 including the type, gestation, management including ectopic (reassurance scans from 6 weeks)
- Pregnancy complications such as PTL,SGA,PET (telephone interview 6 weeks postnatal and hospital notes)
- Acceptability of the procedure by patient questionnaire (completed within 4 weeks of procedure)

Flow diagram

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Consent

- History, Explain trial
- Consent if eligible and willing to participate

Ovulation

- Ovulation testing at home, use of contraception
- Appointment 7- 10 days after Ovulation

Randomisation

- Pregnancy test, consent for procedure
- TVS, Speculum ,scratch(intervention) or touching of cervix(control)
- Patient is blinded to the procedure

Recruitment

- Recruitment from RM clinic, EPAU and self referral
- 1st patient consented- 04/12/15, randomised on 30/12/2015
- Ongoing recruitment for 14 months (till date), target of 110 patients
- 116 women have consented to the study(8-9/month)
- 93 women have been randomised

Statistical plan

- Randomisation by sequential envelopes
- Due to pilot/feasibility study, we will test the null hypothesis of equal birth rates at two-sided 20% significance level [Schoenfeld, 1980].
- The completed questionnaires of women in the intervention group will be used to assess acceptability(set at 95%)
- To assess efficacy, we will compare the birth rates for the intervention and control arms using a chi-squared test. It will be considered worthwhile, to conduct a larger study if the p-value is less than 0.2.

Summary

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- Pilot study for women aged 18-42 after 2 or more miscarriages testing if endometrial scratch prevents miscarriages
- On-going recruitment near target
- Accumulation of tissue bank samples with further lab work and in conjunction with the SIMPLANT study
- Aim is to plan for a larger RCT if the pilot study is proven to be acceptable and shows a difference
- SiM after SECOND Miscarriage

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