

Título: Traducción y comentarios sobre el artículo “Ensayo Randomizado sobre el Scratching Endometrial antes de Fertilización In Vitro”

Nombre revisor: Irene Fares. Hospital Rey Juan Carlos.

1. - Artículo Original:

Lensen S, Wilkinson J, Sadler L.. A Randomized Trial of Endometrial Scratching before In Vitro Fertilization. N Engl J Med. 2019 May 2;380(18):1777-1778. doi: 10.1056/NEJMc1902642.

PMID:31042838

2.- Resumen del Artículo:

2.1 Introducción:

La tasa de recién nacido vivo tras técnicas de reproducción sigue siendo modesta, con porcentajes en algunos estudios de 25-30% por ciclo iniciado.

El scratching endometrial, que consiste en obtener una muestra endometrial con una cánula, se ha propuesto como una estrategia para mejorar los resultados de las técnicas de reproducción. Se postula que el daño endometrial puede mejorar las tasas de implantación por mecanismos inmunológicos e inflamatorios.

Con anterioridad ha habido estudios que defienden esta teoría en pacientes con fallos de implantación, pero posteriormente se publicó un estudio bien diseñado que mostraba la falta de efectividad o incluso tasas menores de gestación.

A pesar de la evidencia, en una reciente encuesta en UK, Australia y Nueva Zelanda, revelaba que el 83% de los clínicos seguían recomendándolo.

Por ello se realizó este estudio, donde se quiere investigar si el scratching endometrial (realizado como toma de biopsia endometrial) aumenta las posibilidades de recién nacido vivo en pacientes que van a realizar FIV.

2.2 Metodología

Se realizó una aleatorización 1:1. Las pacientes candidatas eran aquellas que iban a realizar transferencia de embriones ya fuera tras estimulación ovárica o criotransferencia (no candidatas pacientes que fueran a realizar ovodonación).

Las pacientes a las que se les realizó scratching, debía realizarse entre el día 3 del ciclo previo a la realización de la estimulación y el día 3 del ciclo (considerando primer día de ciclo, primer día de menstruación).

El scratching se realizó con una cánula de 3mm

El objetivo principal se definió como recién nacido vivo.

Los objetivos secundarios fueron: gestación clínica, bioquímica, gestación múltiple, ectópico, aborto espontáneo, muerte fetal, resultados maternos y neonatales....

2.3 Resultados:

Se reclutaron pacientes entre junio de 2014 y junio de 2017 en 13 ciudades de 5 países.

Inicialmente fueron elegibles 3627 pacientes, pero finalmente hubo 690 a las que se les realizó scratching y 674 que formaban el grupo control.

En la siguiente tabla se pueden ver las características demográficas de las pacientes

Table 1. Demographic and Clinical Characteristics of the Participants.*

Characteristic	Endometrial Scratch (N = 690)	Control (N = 674)
Median age (IQR) — yr†	35 (32–38)	35 (32–38)
Body-mass index — median (IQR)‡	23.7 (21.5–27.7)	23.9 (21.5–27.1)
Smoking status — no. (%)		
Current smoker	13 (1.9)	10 (1.5)
Former smoker	145 (21.0)	158 (23.4)
Never smoked	522 (75.7)	495 (73.4)
Missing data	10 (1.4)	11 (1.6)
Median duration of subfertility (IQR) — mo§	43 (30–60)	42 (29–60)
Cause of subfertility — no. (%)		
Ovulation disorder	75 (10.9)	86 (12.8)
Male factor	239 (34.6)	237 (35.2)
Tubal factor	78 (11.3)	80 (11.9)
Endometriosis	55 (8.0)	53 (7.9)
Unexplained	209 (30.3)	193 (28.6)
PGD or PGS	5 (0.7)	3 (0.4)
Same-sex couple	13 (1.9)	13 (1.9)
Other	15 (2.2)	8 (1.2)
Missing data	1 (0.1)	1 (0.1)
Type of subfertility — no. (%)		
Primary	382 (55.4)	352 (52.2)
Secondary	307 (44.5)	321 (47.6)
Missing data	1 (0.1)	1 (0.1)
No. of previous embryo transfers — no. of participants (%)¶		
0	325 (47.1)	301 (44.7)
1	156 (22.6)	173 (25.7)
2	109 (15.8)	90 (13.4)
≥3	100 (14.5)	110 (16.3)
No. of previous unsuccessful embryo transfers — no. of participants (%)¶		
0	350 (50.7)	332 (49.3)
1	174 (25.2)	171 (25.4)
2	85 (12.3)	89 (13.2)
≥3	81 (11.7)	82 (12.2)

* There were no significant between-group differences. Percentages may not total 100 because of rounding. IQR denotes interquartile range, PGD preimplantation genetic diagnosis, and PGS preimplantation genetic screening.

† Data on age were missing for 1 participant in the endometrial-scratch group.

‡ The body-mass index is the weight in kilograms divided by the square of the height in meters. Data were missing for 18 participants in each group.

§ Data on the duration of subfertility were missing for 8 participants in the endometrial-scratch group and 2 participants in the control group.

¶ Double-embryo or triple-embryo transfer was considered to be one embryo transfer.

Las características de los ciclos fueron similares en ambos grupos como se puede ver en las siguientes tablas:

Table 1. Demographic and Clinical Characteristics of the Participants.*

Characteristic	Endometrial Scratch (N=690)	Control (N=674)
Median age (IQR) — yr†	35 (32–38)	35 (32–38)
Body-mass index — median (IQR)‡	23.7 (21.5–27.7)	23.9 (21.5–27.1)
Smoking status — no. (%)		
Current smoker	13 (1.9)	10 (1.5)
Former smoker	145 (21.0)	158 (23.4)
Never smoked	522 (75.7)	495 (73.4)
Missing data	10 (1.4)	11 (1.6)
Median duration of subfertility (IQR) — mo§	43 (30–60)	42 (29–60)
Cause of subfertility — no. (%)		
Ovulation disorder	75 (10.9)	86 (12.8)
Male factor	239 (34.6)	237 (35.2)
Tubal factor	78 (11.3)	80 (11.9)
Endometriosis	55 (8.0)	53 (7.9)
Unexplained	209 (30.3)	193 (28.6)
PGD or PGS	5 (0.7)	3 (0.4)
Same-sex couple	13 (1.9)	13 (1.9)
Other	15 (2.2)	8 (1.2)
Missing data	1 (0.1)	1 (0.1)
Type of subfertility — no. (%)		
Primary	382 (55.4)	352 (52.2)
Secondary	307 (44.5)	321 (47.6)
Missing data	1 (0.1)	1 (0.1)
No. of previous embryo transfers — no. of participants (%)¶		
0	325 (47.1)	301 (44.7)
1	156 (22.6)	173 (25.7)
2	109 (15.8)	90 (13.4)
≥3	100 (14.5)	110 (16.3)
No. of previous unsuccessful embryo transfers — no. of participants (%)¶		
0	350 (50.7)	332 (49.3)
1	174 (25.2)	171 (25.4)
2	85 (12.3)	89 (13.2)
≥3	81 (11.7)	82 (12.2)

* There were no significant between-group differences. Percentages may not total 100 because of rounding. IQR denotes interquartile range, PGD preimplantation genetic diagnosis, and PGS preimplantation genetic screening.

† Data on age were missing for 1 participant in the endometrial-scratch group.

‡ The body-mass index is the weight in kilograms divided by the square of the height in meters. Data were missing for 18 participants in each group.

§ Data on the duration of subfertility were missing for 8 participants in the endometrial-scratch group and 2 participants in the control group.

¶ Double-embryo or triple-embryo transfer was considered to be one embryo transfer.

Table 3. Characteristics of Frozen Embryo Transfer Cycle.*

Characteristic	Endometrial Scratch (N=201)	Control (N=193)
Stimulation protocol — no. (%) [†]		
Natural	106 (52.7)	94 (48.7)
Stimulated	30 (14.9)	34 (17.6)
Programmed	57 (28.4)	56 (29.0)
Missing data	8 (4.0)	9 (4.7)
Insemination method — no. (%)		
IVF	85 (42.3)	89 (46.1)
ICSI or IVF–ICSI split	110 (54.7)	98 (50.8)
Missing data	6 (3.0)	6 (3.1)
Status with respect to embryo transfer — no. (%)		
No embryo transfer	12 (6.0)	22 (11.4)
Embryo transfer	189 (94.0)	169 (87.6)
Single	163 (81.1)	141 (73.1)
Double	26 (12.9)	28 (14.5)
Missing data	0	2 (1.0)
Day of embryo transfer — no./total no. (%) [‡]		
2	7/189 (3.7)	7/169 (4.1)
3	23/189 (12.2)	21/169 (12.4)
≥5	158/189 (83.6)	140/169 (82.8)
Missing data	1/189 (0.5)	1/169 (0.6)

* Data include participants who planned to undergo or who underwent a frozen-embryo transfer during the trial period, including 67 women (33 in the endometrial-scratch group and 34 in the control group) who underwent randomization as planning a fresh IVF cycle but who instead underwent a freeze-all cycle and subsequent frozen-embryo transfer within the 3-month trial period. Not included are 2 women in the endometrial-scratch group who underwent randomization as planning a frozen-embryo transfer but who instead underwent an IVF cycle with fresh-embryo transfer within the 3-month trial period. There were no significant between-group differences. Percentages may not total 100 because of rounding.

[†] A stimulated cycle involved administration of FSH, clomiphene, or letrozole. A programmed cycle involved administration of estrogen and progesterone, usually with a gonadotrophin-releasing hormone antagonist. A natural cycle did not involve any of these medications. However, all three types of cycles may have involved luteal-phase support.

[‡] The denominator is the number of women who underwent embryo transfer.

A un total de 1118 pacientes se le realizó transferencia de embriones, un 82% en el grupo scratching y un 78% en el grupo control.

De las 690 del grupo scratching, se les realizó el mismo a un 92.9%

La tasa de recién nacido vivo fue de 26.1% en el grupo scratching frente a un 26.1% en el grupo control.

Table 4. Trial Outcomes (Intention-to-Treat Analysis).*

Outcome	Endometrial Scratch (N = 690)	Control (N = 674)	Adjusted Odds Ratio (95% CI)†
	<i>number (percent)</i>		
Live birth‡	180 (26.1)	176 (26.1)	1.00 (0.78–1.27)
Single	168 (24.3)	167 (24.8)	
Twin	11 (1.6)	9 (1.3)	
Triplet	1 (0.1)	0	
Biochemical pregnancy‡	273 (39.6)	269 (39.9)	0.98 (0.79–1.22)
Clinical pregnancy‡			
≥1 Gestational sac	217 (31.4)	210 (31.2)	1.01 (0.80–1.27)
≥1 Heartbeat	195 (28.3)	194 (28.8)	0.97 (0.76–1.23)
Ectopic pregnancy§	3 (0.4)	3 (0.4)	0.98 (0.18–5.32)
Multiple pregnancy§	15 (2.2)	12 (1.8)	1.22 (0.57–2.67)
Twin	14 (2.0)	11 (1.6)	
Triplet	1 (0.1)	1 (0.1)	
Ongoing pregnancy§	181 (26.2)	183 (27.2)	0.96 (0.76–1.23)
Miscarriage§	36 (5.2)	30 (4.5)	1.17 (0.10–1.94)
Stillbirth	0	2	NC
Termination§	1	2	0.48 (0.02–4.98)

* Data were imputed in one case: one woman with no pregnancy-test result was assumed to not be pregnant. Biochemical pregnancy is defined by a positive pregnancy test. Multiple pregnancy is defined by any scan with more than one heartbeat or gestational sac at the stage of clinical pregnancy (approximately 6 weeks). Miscarriages are losses of clinical pregnancy before 20 weeks, excluding ectopic pregnancy. Stillbirths are all losses of clinical pregnancy at or after 20 weeks (not including loss of one fetus in multiple pregnancies). Terminations are losses of an intrauterine pregnancy, through intervention by medical, surgical, or unspecified means. CI denotes confidence interval, and NC not able to be calculated.

† Confidence intervals have not been adjusted for multiple testing, and inferences drawn from the intervals may not be reproducible.

‡ The odds ratio was adjusted for both stratification factors: recruiting site and type of embryo transfer planned (fresh or frozen).

§ The odds ratio was adjusted for the type of embryo transfer planned (fresh or frozen) but not for recruiting site.

No hay ninguna evidencia de beneficio del scratching endometrial en pacientes con una transferencia fallida o con pacientes con al menos 2 transferencias fallidas.

3.- Comentario:

El presente estudio es un estudio grande, multicéntrico y randomizado.

El scratching endometrial no resulta en mayores tasas de recién nacido vivo. Tampoco en el análisis por subgrupos se consigue identificar ningún subgrupo de pacientes que se pueden beneficiar de este procedimiento.

El procedimiento se asoció con dolor moderado y escasos resultados adversos.

