

CERPO

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DIABETES GESTACIONAL

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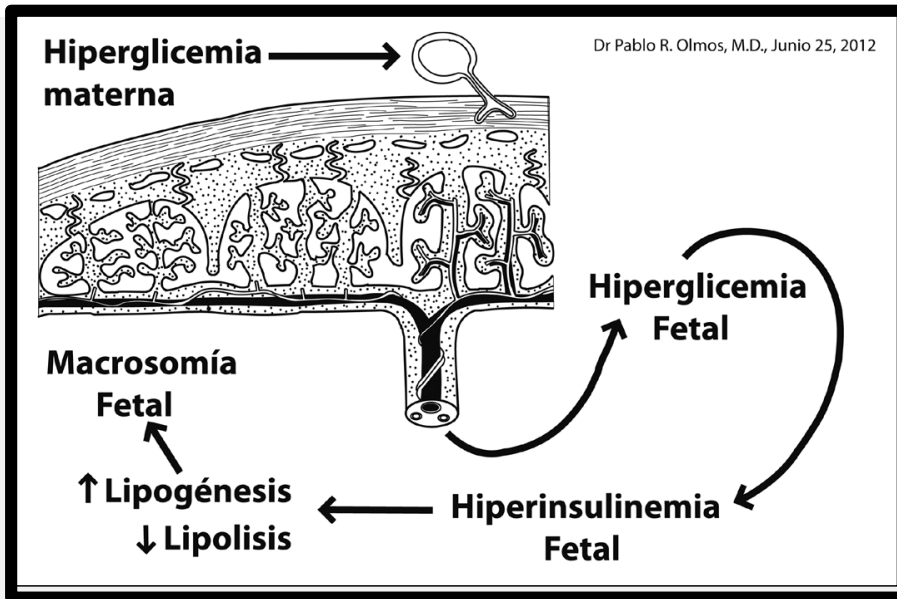
Generalidades

CUALQUIER GRADO DE INTOLERANCIA A LA GLUCOSA DIAGNOSTICADO DURANTE EL EMBARAZO

AUMENTO DE OBESIDAD Y EDAD MATERNA

CHILE : 5,1% DE LAS MUJERES QUE INGRESA A CONTROL PRENATAL TIENE DIABETES Y EL 17% DE LAS QUE SE CONTROLAN EN POLICLINICOS DE ALTO RIESGO

HIPOTESIS DE PEDERSSSEN



INSULINORESISTENCIA(cortisol,
LP, P)

AUMENTO DE DEPOSITO
GRASO

FUNCION PANCREÁTICA
INSUFICIENTE

IMPORTANCIA DE LA DIABETES GESTACIONAL



MATERNO

- PE, PHA , ABORTO , PP CESAREA
- AUMENTO DE DIABETES TIPO 2 A LARGO PLAZO

FETAL

- MACROSOMIA , TRAUMA DEL PARTO, PREMATURIDAD
- COMPLICACIONES PERINATALES
- COMPLICACIONES EN LA VIDA ADULTA?

Generalidades



OBESIDAD AUMENTA DIRECTAMENTE EL RIESGO DE DIABETES GESTACIONAL



DIAGNÓSTICO



Aumento de prevalencia de obesidad ,
reconocer diabetes pregestacional sin
diagnóstico previo al embarazo

Glicemia en ayunas
> o igual a 126

Cualquier glicemia
mayor a 200

Hb glicosilada >6.5
gr /dl

DIAGNÓSTICO



Existe discordancia respecto a los criterios diagnósticos y a la necesidad o no de realizar test de screening y diagnóstico en 1 o 2 pasos

Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study

Associations of maternal A1C and glucose with pregnancy outcomes



ESTUDIO HAPO 2008 REFLEJA UNA CURVA DE RESULTADOS EN RELACIÓN AL AUMENTO DE GLICEMIAS TANTO BASAL COMO POST CARGA DE 75 GRS ... SIN PUNTO DE CORTE DETERMINAR OR 1,75 O DE 2

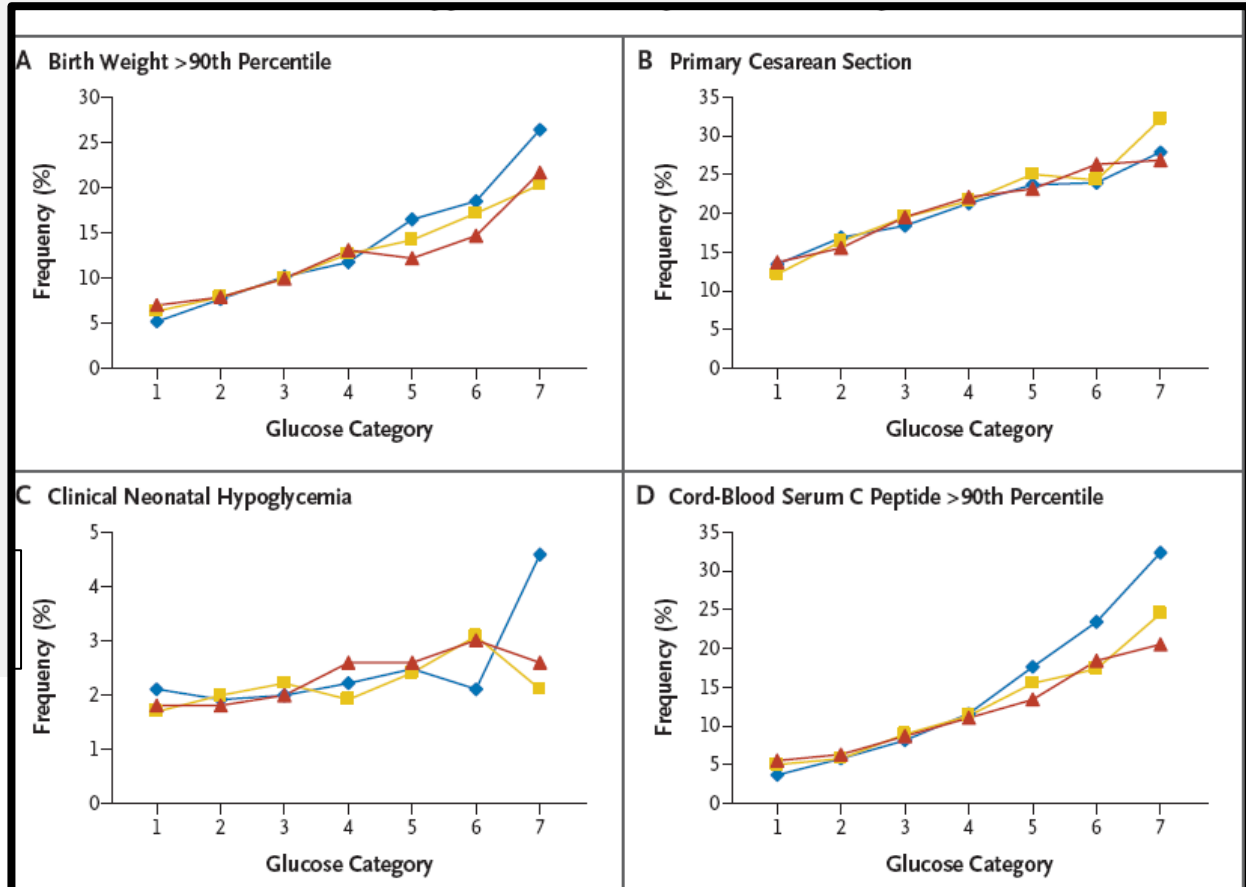
Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study

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Glucose categories (mg/dL)

	<75	75-9	80-4	85-9	90-4	95-9	100-5
Baseline	<75	75-9	80-4	85-9	90-4	95-9	100-5
1-hour	<105	132	155	171	193	211	>212
2-hour	<90	108	125	139	157	177	>178



CRITERIOS DIAGNÓSTICOS

– 2 PASOS (ACOG / ADA / GEDE)

- O'SULLIVAN 140
- TSGO 100 GR GLUCOSA

AYUNA , 60, 120 ,180 MINUTOS

– 1 PASO IADPSG /OPCION ADA / NICE /WHO

- PTGO O TTGO 75 GRS AYUNA , 60 Y 120 MINUTOS

DIAGNÓSTICO



International Association of Diabetes and Pregnancy Study Groups (IADPSG) reporta una prevalencia de 17,8%

Hyperglycemia and Adverse Pregnancy Outcomes (HAPO)

DIAGNÓSTICO



EN CHILE DADA LA PREVALENCIA DE OBESIDAD
NO SE ACEPTARON ESTOS CRITERIOS , DADO
QUE SE ESTIMÓ QUE PODRIA LLEGAR A EXISTIR
UNA PREVALENCIA DE 80% DE DG

DIAGNÓSTICO



Interpretación de los resultados de la PTGO en la mujer embarazada

1er TRIMESTRE DEL EMBARAZO

Glicemia en ayunas (medida antes que comience la PTGO):

- < 100 mg/dl: normal
- Entre 100 y 125 mg/dl, confirmado con un segundo examen realizado dentro de los 7 días: Diabetes gestacional
- \geq 126 mg/dl confirmado con un segundo examen realizado dentro de los 7 días: Diabetes pregestacional.

2do y 3er TRIMESTRE DEL EMBARAZO

Glicemia en ayunas (medida antes que comience la PTGO):

- < 100 mg/dl: normal
- \geq 100 mg/dl: Diabetes gestacional

Glicemia a las 2 horas en una PTGO

- <140 mg/dL a las 2 horas: normal
- \geq 140 mg/dL: Diabetes gestacional



¿QUÉ LOGRAMOS TRATANDO LA DIABETES GESTACIONAL ?

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Multicenter, Randomized Trial of Treatment for Mild Gestational Diabetes

Mark B. Landon, M.D., Catherine Y. Spong, M.D., Elizabeth Thom, Ph.D., Marshall W. Carpenter, M.D., Susan M. Ramin, M.D., Brian Casey, M.D., Ronald J. Wapner, M.D., Michael W. Varner, M.D., Dwight J. Rouse, M.D., John M. Thorp, Jr., M.D., Anthony Sciscione, D.O., Patricia Catalano, M.D., Margaret Harper, M.D., George Saade, M.D., Kristine Y. Yoram Sorokin, M.D., Alan M. Peaceman, M.D., Jorge E. Tolosa and Garland B. Anderson, M.D., for the Eunice Kennedy Shriver Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network*

ABSTRACT

*The NEW ENGLAND
JOURNAL of MEDICINE*

ESTABLISHED IN 1812

JUNE 16, 2005

VOL. 352 NO. 24

Effect of Treatment of Gestational Diabetes Mellitus on Pregnancy Outcomes

Caroline A. Crowther, F.R.A.N.Z.C.O.G., Janet E. Hiller, Ph.D., John R. Moss, F.C.H.S.E., Andrew J. McPhee, F.R.A.C.P., William S. Jeffries, F.R.A.C.P., and Jeffrey S. Robinson, F.R.A.N.Z.C.O.G., for the Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) Trial Group*

ABSTRACT

A Multicenter, Randomized Trial of Treatment for Mild Gestational Diabetes

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Institute of Child Health and Human Development Maternal-Fetal
Medicine Units Network*

ABSTRACT



- 958 MUJERES , RANDOMIZADAS A CONTROL VS TTO .
- OUTCOME PRIMARIO COMPUESTO, SIN DIFERENCIAS
- OUTCOME SECUNDARIO PERINATAL Y MATERNO DISMINUYE PESO FETAL, GEG, >4000 GRS, DISTOCIA DE HOMBROS , CESAREA Y PE



Table 2. Primary Perinatal Outcome.*

Outcome Variable	Treatment Group (N=485)	Control Group (N=473)	Relative Risk (97% CI)	P Value
Gestational age at birth — wk	39.0±1.8	38.9±1.8		0.87
Composite end point — no./total no. (%)†	149/460 (32.4)	163/440 (37.0)	0.87 (0.72–1.07)	0.14
Hypoglycemia‡	62/381 (16.3)	55/357 (15.4)	1.06 (0.73–1.53)	0.75
Hyperbilirubinemia‡	43/450 (9.6)	54/418 (12.9)	0.74 (0.49–1.12)	0.12
Elevated cord-blood C-peptide level‡	75/423 (17.7)	92/403 (22.8)	0.78 (0.57–1.05)	0.07
Stillbirth or neonatal death	0	0		
Birth trauma§	3/476 (0.6)	6/455 (1.3)	0.48 (0.10–2.20)	0.33

Table 3. Secondary Neonatal Outcomes.*

Outcome Variable	Treatment Group (N=485)	Control Group (N=473)	Relative Risk (97% CI)	P Value
Birth weight — g	3302±502.4	3408±589.4		<0.001
Birth weight >4000 g — no./total no. (%)	28/477 (5.9)	65/454 (14.3)	0.41 (0.26–0.66)	<0.001
Large for gestational age — no./total no. (%)†	34/477 (7.1)	66/454 (14.5)	0.49 (0.32–0.76)	<0.001
Fat mass — g	427.0±197.9	464.3±222.3		0.003
Preterm delivery — no./total no. (%)‡	45/477 (9.4)	53/455 (11.6)	0.81 (0.53–1.23)	0.27
Small for gestational age — no./total no. (%)§	36/477 (7.5)	29/455 (6.4)	1.18 (0.70–1.99)	0.49
Admission to NICU — no./total no. (%)	43/477 (9.0)	53/455 (11.6)	0.77 (0.51–1.18)	0.19
Intravenous glucose treatment — no./total no. (%)	25/475 (5.3)	31/455 (6.8)	0.77 (0.44–1.36)	0.32
Respiratory distress syndrome — no./total no. (%)	9/477 (1.9)	13/455 (2.9)	0.66 (0.26–1.67)	0.33

Table 4. Maternal Outcomes.*

Outcome Variable	Treatment Group (N=476)	Control Group (N=455)	Relative Risk (97% CI)	P Value
Induction of labor — no. (%)	130 (27.3)	122 (26.8)	1.02 (0.81–1.29)	0.86
Cesarean delivery — no. (%)	128 (26.9)	154 (33.8)	0.79 (0.64–0.99)	0.02
Shoulder dystocia — no. (%)	7 (1.5)	18 (4.0)	0.37 (0.14–0.97)	0.02
Preeclampsia — no. (%)	12 (2.5)	25 (5.5)	0.46 (0.22–0.97)	0.02
Preeclampsia or gestational hypertension — no. (%)	41 (8.6)	62 (13.6)	0.63 (0.42–0.96)	0.01
Body-mass index at delivery†	31.3±5.2	32.3±5.2		<0.001
Weight gain — kg‡	2.8±4.5	5.0±3.3		<0.001

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ABSTRACT



Resultados	Grupo intervenido n (%)	Grupo control (tratamiento habitual)	Riesgo relativo ajustado (IC 95%)	Valor p ajustado (por edad materna, raza o grupo étnico y paridad)
Recién nacidos	506	524		
Cualquier complicación perinatal grave	7 (1%)	23 (4%)	0,33 (0,14-0,75)	P<0,01
Muerte	0	5		0,07
Mortinato	0	3		0,26
Muerte neonatal	0	2		0,50
Distocia hombro	7 (1)	16 (3)	0,46 (0,19-1,09)	0,08
Fractura	0	1 (<1)		0,38
Admisión neonatología	357 (71)	321 (61)		P<0,03
Ictericia que requirió fototerapia	44 (9)	48 (9)	0,93 (0,63-1,37)	0,72
Mujeres	490	510		
Inducción	39%	29%		<0,002
Cesárea	152 (31)	164 (32)	0,97 (0,81-1,16)	0,73
Electiva	72 (15)	61 (12)	1,17 (0,85-1,60)	0,33
Emergencia	80 (16)	103 (20)	0,87 (0,68-1,13)	0,31
Puntaje depresión	13%	17%		P<0,001

Tomado y adaptado de: ACHOIS Trial Group, 2005



Shoulder dystocia

Bevier et al, 1999 (14)	1/35	2/48	6.4	0.69 (0.06–7.27)
Crowther et al, 2005 (6)	7/506	16/524	45.9	0.45 (0.19–1.09)
Landon et al, 2009 (12)	7/476	18/455	47.7	0.37 (0.16–0.88)
Subtotal	1017	1027	100.0	0.42 (0.23–0.77)
Total	15	36		

Heterogeneity: tau-square = 0.00; chi-square = 0.27; $P = 0.87$; $I^2 = 0\%$

Test for overall effect: $Z = 2.83$ ($P = 0.005$)

Neonatal hypoglycemia

Bonomo et al, 2005 (13)	5/150	6/150	4.5	0.83 (0.26–2.67)
Crowther et al, 2005 (6)	35/506	27/524	25.9	1.34 (0.82–2.18)
Gamer et al, 1997 (15)	21/149	13/150	14.4	1.63 (0.85–3.13)
Landon et al, 2009 (12)	62/381	55/357	55.3	1.06 (0.76–1.47)
Subtotal	1186	1181	100.0	1.18 (0.92–1.52)
Total	123	101		

Heterogeneity: tau-square = 0.00; chi-square = 1.96; $P = 0.58$; $I^2 = 0\%$

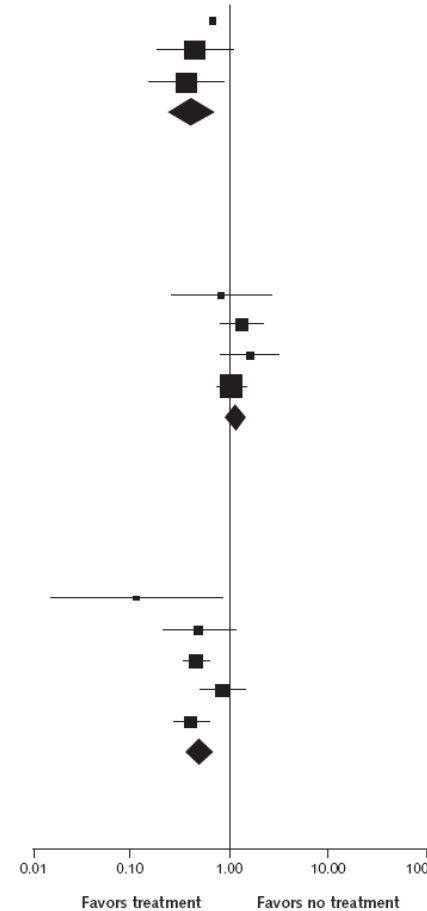
Test for overall effect: $Z = 1.33$ ($P = 0.18$)

Macrosomia (birthweight >4000 g)

Bevier et al, 1999 (14)	1/35	12/48	2.9	0.11 (0.02–0.84)
Bonomo et al, 2005 (13)	8/150	16/150	13.1	0.50 (0.22–1.13)
Crowther et al, 2005 (6)	49/506	110/524	33.1	0.46 (0.34–0.63)
Gamer et al, 1997 (15)	24/149	28/150	23.7	0.86 (0.53–1.42)
Landon et al, 2009 (12)	28/477	65/454	27.2	0.41 (0.27–0.63)
Subtotal	1317	1326	100.0	0.50 (0.35–0.71)
Total	110	231		

Heterogeneity: tau-square = 0.07; chi-square = 7.94; $P = 0.09$; $I^2 = 50\%$

Test for overall effect: $Z = 3.84$ ($P < 0.001$)



OBJETIVOS METABOLICOS



Glicemia capilar	Metas
Antes del desayuno	60-90 mg/dL
Antes de otras comidas	60-105 mg/dL
1 hora después de las comidas	< 140 mg/dL
2 horas después de las comidas	< 120 mg/dL
Durante la noche	60-99 mg/dL
Hb A1c en DPG	< 6,0 %

HbA1c : medición mensual .. Tiende a bajar por hemodilucion del embarazo

EL 70 % -80% DE LAS PACIENTES CON DMG SE CONTROLA CON ESTILO DE VIDA Y DIETA

OBJETIVOS METABOLICOS



Regimen con 175 gr de HC

71 grs de proteina

28 grs de fibra

4 comidas 2 colaciones

Monitoreo de HGT en ayunas y PP por 2
semanas

IMC pregestacional	Feto único (kg)	Embarazo múltiple (kg)
BAJO PESO	12,5 -18	-
NORMOPESO	11,5-16	17-25
SOBREPESO	7-11,5	14 - 23
OBESIDAD	5-9	11-19

USO DE METFORMINA



- MECANISMOS DE ACCION

1- Mejora la sensibilidad a insulina

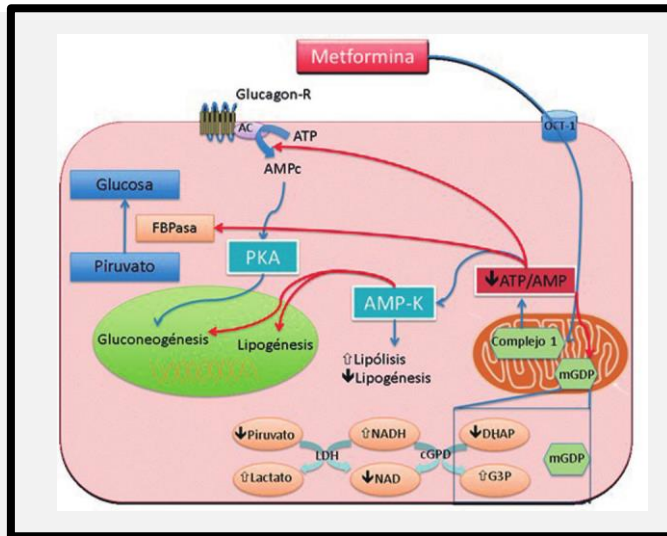
2- Reduce la gluconeogénesis hepática

3.- Aumenta la captación de glucosa en tejidos periféricos

4.- reduce la insulina en ayunas en 40%



USO DE METFORMINA



LA METFORMINA PASA LIBREMENTE POR LA PLACENTA
ACTUALMENTE ES CONSIDERADO FÁRMACO CLASE B DE FDA
A PESAR DE ESTO, EN EEUU AUN NO SE USA EN DIABETES Y EMBARAZO POR LA FALTA DE INFORMACIÓN DE SU USO A LARGO PLAZO EN NIÑOS EXPUESTOS

USO DE METFORMINA



- EN MUJERES OBESAS NO DIABÉTICAS EMBARAZADAS EL RIESGO DE

DIABETES GESTACIONAL 3.1

PREECLAMPSIA 2.1

MACROSOMIA 2.3

USO DE METFORMINA



Podemos mejorar resultados perinatales usando metformina en mujeres obesas ?

Lancet Diabetes Endocrinol. 2015 Oct; 3(10): 778–786.

PMCID: PMC4673088

doi: 10.1016/S2213-8587(15)00219-3: 10.1016/S2213-8587(15)00219-3

PMID: [26165398](https://pubmed.ncbi.nlm.nih.gov/26165398/)

Effect of metformin on maternal and fetal outcomes in obese pregnant women (EMPOWaR): a randomised, double-blind, placebo-controlled trial



Effect of metformin on maternal and fetal outcomes in obese pregnant women (EMPOWaR): a randomised, double-blind, placebo-controlled trial

- ESTUDIO MULTICENTRICO
- TOLERANCIA NORMAL PREVIO
- IMC 30
- 223 PLACEBO 226 CONTROL Dosis de 500 A 2500 MGRS DE METFORMINA VS PLACEBO DESDE LAS 12 A 16 SEM.



Effect of metformin on maternal and fetal outcomes in obese pregnant women (EMPOWaR): a randomised, double-blind, placebo-controlled trial

- **OUTCOME PRIMARIO : Z SCORE PESO RECIEN NACIDO**
- **NO EXISTIÓ DIFERENCIAS EN OUTCOME PRIMARIO**



Effect of metformin on maternal and fetal outcomes in obese pregnant women (EMPOWaR): a randomised, double-blind, placebo-controlled trial

	Placebo group		Metformin group		Adjusted mean difference or ratio (95% CI)	p value
	Mean (SD)	N	Mean (SD)	N		
Maternal biochemistry at 36 weeks' gestation						
Fasting glucose (mmol/L)	4.42 (0.48)	151	4.35 (0.45)	143	-0.060 (-0.163 to 0.043)	0.25
2 h glucose (mmol/L)*	5.96 (1.46)	148	5.70 (1.32)	142	-0.251 (-0.565 to 0.062)	0.12
Fasting insulin (pmol/L)	208.98 (91.12)	131	227.73 (170.50)	127	1.005 (0.901 to 1.120)	0.93
HOMA-IR score†	5.98 (2.89)	131	6.30 (4.78)	123	0.974 (0.865 to 1.097)	0.67
C-reactive protein (mg/L)	9.20 (7.10)	150	7.47 (4.62)	140	0.860 (0.743 to 0.996)	0.04
Cholesterol (mmol/L)	6.32 (1.44)	144	6.33 (1.74)	139	1.004 (0.954 to 1.056)	0.88
HDL (mmol/L)	1.70 (0.38)	145	1.76 (0.43)	138	0.051 (-0.040 to 0.142)	0.27
LDL (mmol/L)	3.57 (1.13)	126	3.77 (1.25)	118	1.064 (0.982 to 1.152)	0.13
Triglycerides (mmol/L)	2.79 (0.84)	146	2.76 (0.88)	140	0.993 (0.926 to 1.064)	0.82
Interleukin-6 (mmol/L)	3.86 (4.10)	131	2.93 (1.37)	127	0.847 (0.754 to 0.952)	0.01
Leptin (ng/mL)	105.0 (52.4)	131	106.6 (58.8)	127	1.005 (0.902 to 1.120)	0.93
Serum cortisol (nmol/L)	821.7 (232.9)	131	867.0 (225.5)	127	1.062 (0.999 to 1.128)	0.05
NEFA (mmol/L)	0.47 (0.18)	131	0.46 (0.19)	127	0.947 (0.859 to 1.044)	0.27
PAI-1 to PAI-2 ratio	3.20 (2.61)	131	2.97 (2.79)	128	0.913 (0.771 to 1.081)	0.29
Cord-blood biochemical outcomes						
Glucose (mmol/L)	3.89 (1.24)	79	4.06 (1.08)	74	1.067 (0.974 to 1.170)	0.16
Insulin (pmol/L)	76.05 (52.02)	47	79.24 (61.12)	57	1.060 (0.767 to 1.463)	0.72
HOMA-IR score†	1.92 (1.39)	38	1.91 (2.00)	41	1.012 (0.701 to 1.462)	0.95
C-reactive protein (mg/L)‡	4.32 (19.55)	78	2.36 (2.29)	73	..	0.74
Anthropometric variables						
Maternal weight gain during pregnancy (kg)	7.23 (4.91)	156	6.70 (6.00)	143	-0.680 (-1.863 to 0.503)	0.26
Ponderal index (mass [g]/height ³ [cm])§	2.60 (0.41)	143	2.67 (0.50)	130	1.032 (0.996 to 1.069)	0.08
All variables, except for maternal glucose and HDL, and neonatal C-reactive protein, were log-transformed for the statistical analysis and converted back to original scale for this table. HOMA-IR=homeostatic model assessment of insulin resistance. NEFA=non-esterified fatty acids. PAI=plasminogen activator inhibitor. *After a 75 g oral glucose challenge. †Fasting glucose (mmol/L)×insulin (μIU/L)/22.5. ‡Kruskal-Wallis non-parametric test used. §Livebirths only; we removed outliers outside SD 6 and log-transformed data for the statistical analysis; results were back-transformed for this table.						

Table 3: Secondary outcomes

METFORMINA EN PACIENTES DIABETICAS



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Metformin versus Insulin for the Treatment of Gestational Diabetes

Janet A. Rowan, M.B., Ch.B., William M. Hague, M.D., Wanzhen Gao, Ph.D.,
Malcolm R. Battin, M.B., Ch.B., and M. Peter Moore, M.B., Ch.B.,
for the MiG Trial Investigators*

METFORMINA EN PACIENTES DIABETICAS



- Y qué pasa con los resultados neonatales si adicionamos metformina a mujeres diabéticas pregestacionales durante el embarazo ?

Metformin versus Insulin for the Treatment of Gestational Diabetes

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- ENROLÓ 751 MUJERES A METFORMINA O TTO HABITUAL MAS PLACEBO , INCLUYENDO INSULINA
- OUTCOME PRIMARIO NEONATAL COMPUESTO: HIPOGLICEMIA NEONATAL , SDR, NECESIDAD DE FOTOTERAPIA , APGAR MENOR A 7, PP< 37 SEM
- OUTCOME SECUNDARIOS: GLICEMIA Y PESO MATERNOS, GEG , ANTROPOMETRIA RN

Metformin versus Insulin for the Treatment of Gestational Diabetes

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Table 2. Primary Outcome and Additional Neonatal Complications.*

Outcome	Metformin Group (N=363) no. (%)	Insulin Group (N=370) no. (%)	Relative Risk (95% CI)	P Value
Primary composite outcome	116 (32.0)	119 (32.2)	0.99 (0.80–1.23)	0.95
Recurrent blood glucose level <46.8 mg/dl†	55 (15.2)	69 (18.6)	0.81 (0.59–1.12)	0.21
Any blood glucose level <28.8 mg/dl	12 (3.3)	30 (8.1)	0.41 (0.21–0.78)	0.008
Respiratory distress‡	12 (3.3)	16 (4.3)	0.76 (0.37–1.59)	0.47
Transient tachypnea	7 (1.9)	8 (2.2)		
Respiratory distress syndrome	4 (1.1)	5 (1.4)		
Sepsis	1 (0.3)	5 (1.4)		
Pulmonary hypertension	0	2 (0.5)		
Phototherapy	29 (8.0)	31 (8.4)	0.95 (0.59–1.55)	0.85
Birth trauma§	16 (4.4)	17 (4.6)	0.96 (0.49–1.87)	0.90
Mild	16 (4.4)	15 (4.1)		
Moderate or severe	0	2 (0.5)		
5-Min Apgar score <7¶	3 (0.8)	1 (0.3)	3.06 (0.32–29.26)	0.37
Preterm birth (<37 wk of gestation)	44 (12.1)	28 (7.6)	1.60 (1.02–2.52)	0.04
Iatrogenic (indicated)	18 (5.0)	13 (3.5)	1.41 (0.70–2.84)	0.33
Spontaneous	26 (7.2)	15 (4.1)	1.77 (0.95–3.28)	0.07
Additional neonatal complications				
Admission to level 2 or 3 neonatal intensive care unit	68 (18.7)	78 (21.1)	0.89 (0.66–1.19)	0.43
>24-Hr stay in neonatal intensive care unit	46 (12.7)	45 (12.2)	1.04 (0.71–1.53)	0.83
	<i>mean ±SD</i>			
pH of umbilical-cord or scalp blood	7.27±0.07	7.26±0.07		0.32

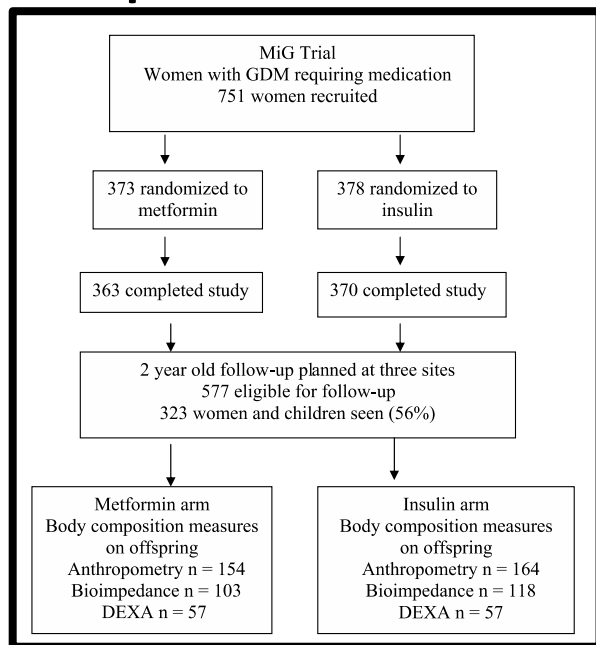
EL OUTCOME PRIMARIO
COMPUESTO FUE SIMILAR
EN LOS DOS GRUPOS, CON
EXCEPCIÓN DE
**HIPOGLICEMIA NEONATAL
SEVERA**
EN RELACIÓN A
METFORMINA FUE MEJOR
ACEPTADA POR LAS MADRES
, LAS QUE LA USARON
REQUIRIERON MENORES
DOSIS DE INSULINA Y UN
46% DE LAS CON USO DE
METFORMINA REQUIRIÓ
INSULINA ADEMÁS

Metformin in Gestational Diabetes: The Offspring Follow-Up (MiG TOFU)



Body composition at 2 years of age

- ¿Qué ocurrió a largo plazo con los niños expuestos a metformina durante este estudio?



RESULTS—The children were similar for baseline maternal characteristics and pregnancy outcomes. In the metformin group, compared with the insulin group, children had larger mid-upper arm circumferences (17.2 ± 1.5 vs. 16.7 ± 1.5 cm; $P = 0.002$) and subscapular (6.3 ± 1.9 vs. 6.0 ± 1.7 mm; $P = 0.02$) and biceps skinfolds (6.03 ± 1.9 vs. 5.6 ± 1.7 mm; $P = 0.04$). Total fat mass and percentage body fat assessed by bioimpedance ($n = 221$) and DEXA ($n = 114$) were not different.

CONCLUSIONS—Children exposed to metformin had larger measures of subcutaneous fat, but overall body fat was the same as in children whose mothers were treated with insulin alone. Further follow-up is required to examine whether these findings persist into later life and whether children exposed to metformin will develop less visceral fat and be more insulin sensitive. If so, this would have significant implications for the current pandemic of diabetes.

Diabetes Care 34:2279–2284, 2011

AUMENTO DE GRASA CORPORAL TOTAL

METFORMINA Y DIABETES



Y EN PACIENTES OBESAS EMBARAZADAS , SIN DIABTES ... ¿METFORMINA DISMINUYE MACROSOMÍA?

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Metformin versus Placebo in Obese Pregnant Women without Diabetes Mellitus

Argyro Syngelaki, Ph.D., Kypros H. Nicolaidis, M.D., Jyoti Balani, M.D.,
Steve Hyer, M.D., Ranjit Akolekar, M.D., Reena Kotecha, M.D.,
Alice Pastides, M.D., and Hassan Shehata, M.D.

NO HAY
DISMINUCIÓN DE
MACROSOMÍA , SI
UNA MENOR
GANANCIA
PONDERAL Y
MENOR
ASOCIACIÓN PE

¿QUÉ SUCEDE AL COMPARAR METFORMINA GLIBENCLAMIDA E INSULINA?



BMJ 2015;350:h102 doi: 10.1136/bmj.h102 (Published 21 January 2015)

Page 1 of 12

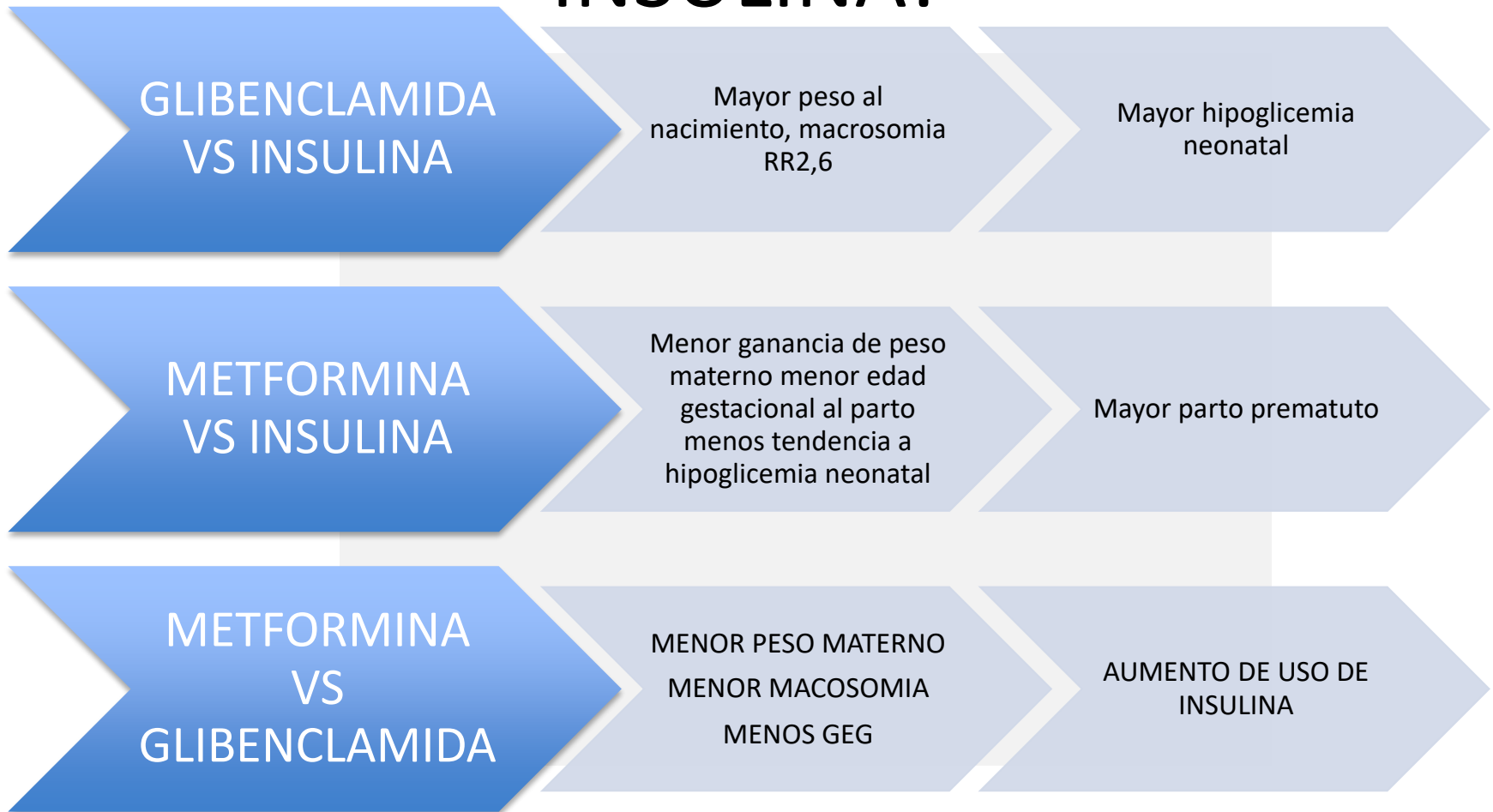
RESEARCH

Glibenclamide, metformin, and insulin for the treatment of gestational diabetes: a systematic review and meta-analysis

 OPEN ACCESS

Montserrat Balsells *registrar in endocrinology and nutrition*¹, Apolonia García-Patterson *registrar*

¿QUÉ SUCEDE AL COMPARAR METFORMINA GLIBENCLAMIDA E INSULINA?



¿QUÉ SUCEDE AL COMPARAR METFORMINA GLIBENCLAMIDA E INSULINA?



Conclusions At short term, in women with gestational diabetes requiring drug treatment, glibenclamide is clearly inferior to both insulin and metformin, while metformin (plus insulin when required) performs slightly better than insulin. According to these results, glibenclamide should not be used for the treatment of women with gestational diabetes if insulin or metformin is available.

USO DE CORTICOIDES PARA MADURACION



SE RECOMIENDA MONITORIZAR
INTENSIVAMENTE GLICEMIAS 12 HORAS
POSTERIOR A LA ADMINISTRACIÓN DE
CORTICOIDES

USO DE CORTICOIDES PARA MADURACION



Antenatal Corticosteroids for Women at Risk of Late Preterm Delivery

Cynthia Gyamfi-Bannerman, MD, MSc, Elizabeth A. Thom, PhD, Sean C. Blackwell, MD, Alan T.N. Tita, MD, PhD, Uma M. Reddy, MD, MPH, George R. Saade, MD, Dwight J. Rouse, MD, David S. McKenna, MD, Erin A.S. Clark, MD, John M. Thorp Jr., MD, Edward K. Chien, MD, MBA, Alan M. Peaceman, MD, Ronald S. Gibbs, MD, Geeta K. Swamy, MD, Mary E. Norton, MD, Brian M. Casey, MD, Steve N. Caritis, MD, Jorge E. Tolosa, MD, MSCE, Yoram Sorokin, MD, J. Peter VanDorsten, MD, and Lucky Jain, MD, MBA

LA MADURACIÓN DE 34 A 37 SEMANAS
DISMINUYE EL SDR DE 14 % A 11% **PERO**
EXCLUYÓ DIABETICAS PREGESTACIONALES
NO ES RECOMENDABLE USO DE CORTOIDES
POSTERIOR A LAS 37 SEMANAS

INDUCCION EN MACROSÓMICOS



Induction of labour versus expectant management for large-for-date fetuses: a randomised controlled trial

Michel Boulvain, Marie-Victoire Senat, Franck Perrotin, Norbert Winer, Gael Beucher, Damien Subtil, Florence Bretelle, Elie Azria, Dominique Hejaiej, Françoise Vendittelli, Marianne Capelle, Bruno Langer, Richard Matis, Laure Connan, Philippe Gillard, Christine Kirkpatrick, Gilles Ceysens, Gilles Faron, Olivier Irion, Patrick Rozenberg, for the Groupe de Recherche en Obstétrique et Gynécologie (GROG)

Summary

Background Macrosomic fetuses are at increased risk of shoulder dystocia. We aimed to compare induction of labour with expectant management for large-for-date fetuses for prevention of shoulder dystocia and other neonatal and maternal morbidity associated with macrosomia.

Methods We did this pragmatic, randomised controlled trial between Oct 1, 2002, and Jan 1, 2009, in 19 tertiary-care centres in France, Switzerland, and Belgium. Women with singleton fetuses whose estimated weight exceeded the 95th percentile, were randomly assigned (1:1), via computer-generated permuted-block randomisation (block size of four to eight) to receive induction of labour within 3 days between 37⁰ weeks and 38⁶ weeks of gestation, or expectant management. Randomisation was stratified by centre. Participants and caregivers were not masked to group assignment. Our primary outcome was a composite of clinically significant shoulder dystocia, fracture of the clavicle, brachial plexus injury, intracranial haemorrhage, or death. We did analyses by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT00190320.

Findings We randomly assigned 409 women to the induction group and 413 women to the expectant management group, of whom 407 women and 411 women, respectively, were included in the final analysis. Mean birthweight was 3831 g (SD 324) in the induction of labour and 4118 g (392) in the expectant group. Induction of labour significantly reduced the risk of shoulder dystocia or associated morbidity (n=8) compared with expectant management (n=25; relative risk [RR] 0.32, 95% CI 0.15–0.71; p=0.004). We recorded no brachial plexus injuries, intracranial haemorrhages, or perinatal deaths. The likelihood of spontaneous vaginal delivery was higher in women in the induction group than in those in the expectant management group (RR 1.14, 95% CI 1.01–1.29). Caesarean delivery and neonatal morbidity did not differ significantly between the groups.

Interpretation Induction of labour for suspected large-for-date fetuses is associated with a reduced risk of shoulder dystocia and associated morbidity compared with expectant management. Induction of labour does not increase the risk of caesarean delivery and improves the likelihood of spontaneous vaginal delivery. These benefits should be balanced with the effects of early-term induction of labour.

LA INDUCCION DE
MACROSOMICOS
ENTRE LAS 37 Y 38,6
SEMANAS
DISMINUYE EL
RIESGO DE TRAUMA
EN EL PARTO SIN
AUMENTAR LA TASA
DE CESÁREA



CONCLUSIONES

LA DIABETES GESTACIONAL ES UNA ENFERMEDAD DE ALTA PREVALENCIA

SU PREVENCIÓN Y MANEJO TIENE EFECTOS MATERNOS A CORTO Y LARGO PLAZO

EXISTEN MÚLTIPLES CRITERIOS DIAGNÓSTICOS PARA DG , ESTO DEPENDE DE LAS POLÍTICAS DE SALUD APLICADAS

LA GLICEMIA MATERNA SE CORRELACIONA DIRECTAMENTE CON RESULTADOS NEONATALES



CONCLUSIONES

LA MAYORIA DE LAS PACIENTES CON DG PUEDE CONTROLARSE CON ESTILO DE VIDA Y REGIMEN METFORMINA ES UNA ALTERNATIVA PARA EL CONTROL DE DIABETES GESTACIONAL , SOLA O ASOCIADA A INSULINA

GLIBENCLAMIDA , FRENTE A LA EVIDENCIA ACTUAL NO ES UNA ALTERNATIVA RECOMENDABLE

BIBLIOGRAFIA



- 1-Landon MB, Spong CY, Thom E, Carpenter MW, Ramin SM, Casey B, et al. A multicenter, randomized trial of treatment for mild gestational diabetes. *N Engl J Med* 2009;361:1339e48.
- 2-Brown J, Martis R, Hughes B, Rowan J, Crowther CA. Oral anti-diabetic pharmacological therapies for the treatment of women with gestational diabetes. *Cochrane Database Syst Rev*
- 3-Farrar D, Tuffnell DJ, West J, West HM. Continuous subcutaneous insulin infusion versus multiple daily injections of insulin for pregnant women with diabetes. *Cochrane Database Syst Rev* 2016;6:CD00554
- 4-Werner EF, Hauspurg AK, Rouse DJ. A cost-benefit analysis of low-dose aspirin prophylaxis for the prevention of preeclampsia in the United States. *Obstet Gynecol* 2015;126:1242–1250
- 5-Villamor E, Cnattingius S. Interpregnancy weight change and risk of adverse pregnancy outcomes: a population-based study. *Lancet* 2006; 368:1164–1170

BIBLIOGRAFIA



- 6-Sutton AL, Mele L, Landon MB, Ramin SM, Varner MW, Thorp Jr JM, et al. Delivery timing and cesarean delivery risk in women with mild gestational diabetes mellitus. *Am J Obstet Gynecol* 2014;211:244.e1e7.
- 7-Karmon A, Levy A, Holcberg G, Wiznitzer A, Mazor M, Sheiner E. Decreased perinatal mortality among women with diet-controlled gestational diabetes mellitus. *Int J Gynaecol Obstet* 2009;104:199e202.
- 8-Gyamfi-Bannerman C, Thom EA, Blackwell SC, Tita AT, Reddy UM, Saade GR, et al. Antenatal betamethasone for women at risk for late preterm delivery. *N Engl J Med* 2016;374:1311e20.
- 9-Sotiriadis A, Makrydimas G, Papatheodorou S, Ioannidis JP. Corticosteroids for preventing neonatal respiratory morbidity after elective caesarean section at term. *Cochrane Database Syst Rev* 2009:CD006614.
- 10-Stutchfield P, Whitaker R, Russell I. Antenatal Steroids for Term Elective Caesarean Section Research Team. Antenatal betamethasone and incidence of neonatal respiratory distress after elective caesarean section: pragmatic randomised trial. *BMJ* 2005;331:662.
- 11-Crowther CA, Hiller JE, Moss JR, F.C.H.S.E. McPhee AJ, Jeffries WS, Robinson JS, F.R.A.N.Z.C.O.G. for the Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) Trial Group. Effect of Treatment of Gestational Diabetes Mellitus on Pregnancy Outcomes — *N Engl J Med* 2005;352(24):2477-2486
- 12-Mukhopadhyay A, Farrell T, Fraser RB, Ola B. Continuous subcutaneous insulin infusion vs intensive conventional insulin therapy in pregnant diabetic women: a systematic review and metaanalysis of randomized, controlled trials. *Am J Obstet Gynecol* 2007; 197:447.
-

BIBLIOGRAFIA



- 12- GUÍA DE DIABETES Y EMBARAZO MINSAL CHILE
- 13.-DIABETES IN PREGNANCY DAVID R MACCANCE BEST PRACTICE & RESEARCH CLINICAL OBSTETRICS AND GYNAECOLOGY 29 (2015) 685E699
- 14-American Diabetes Associa- tion. 13. Management of diabetes in pregnancy: Standards of Medical Care in Diabetesd2018. Diabetes Care 2018;41(Suppl. 1):S137–S143
- 15- DIABETEES IN PREGNANCY CLINICAL PRACTICE GUIDELINE J Obstet Gynaecol Can 2016;
- 16.- METFORMIN IN PREGNANCY MECHANISM AND CLINICAL APLICATIONS *Int. J. Mol. Sci.* **2018**, *19*, 1954; doi:10.3390/ijms19071954
- 16—METFORMIN USE IN PREGANANCY: PROMISES UNCERTAINTIES *Diabetologia* (2017) 60:1612–1619 DOI 10.1007/s00125-017-4351-y
- 17 Carolyn Chiswick, MBChB,a Rebecca M Reynolds, Prof, PhD,b Fiona Denison, MD Effect of metformin on maternal and fetal outcomes in obese pregnant women (EMPOWaR): a randomised, double-blind, placebo- controlled trial
- Lancet Diabetes Endocrinol. 2015 Oct; 3(10): 778–786.
- 18-Management of diabetes from preconception to the postnatal period: summary of NICE guidance
- BMJ 2008;336:714-7 ,doi:10.1136/bmj.39505.641273.AD

BIBLIOGRAFIA



- 18– LYNN P. LOWE, PHD1, BOYD E. METZGER, MD2 ALAN R. DYER, PHD1 Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study,,Associations of maternal A1C and glucose with pregnancy outcomes , DIABETES CARE, VOLUME 35, MARCH 2012 ,care.diabetesjournals.org
- 19.-Metformin in Gestational Diabetes: The Offspring Follow-Up (MiG TOFU) Body composition at 2 years of age ,JANET A. ROWAN, MBCHB1 ELAINE C. RUSH, PHD2 VICTOR OBOLONKIN, care.diabetesjournals.org
- DIABETES CARE, VOLUME 34, OCTOBER 2011 ,2279
- 20.-Janet A. Rowan, M.B., Ch.B., William M. Hague, M.D., Wanzhen Gao, Ph.D., Metformin versus Insulin for the Treatment of Gestational Diabetes ,MIG TRIAL, n engl j med 358;19 www.nejm.org may 8, 2008
- 21.-Argyro Syngelaki, Ph.D., Kypros H. Nicolaidis, M.D., Jyoti Balani, M.D., Metformin versus Placebo in Obese Pregnant Women without Diabetes Mellitus n engl j med 374;5 nejm.org February 4, 2016
- 22.-Actualización en diabetes gestacional Gemma Sesmilo , BCNatal – Centre de Medicina Maternofetal i Neonatologia de Barcelona ,Hospital Clínic i Hospital Sant Joan de Déu Universitat de Barcelona .