ESCOLA DE MEDICINA
PUCRS

Antihipertensivos como e quando usar, prós e contras

Rede Brasileira de Estudos sobre Hipertensão na Gravidez - RBEHG

I Congresso Brasileiro sobre Hipertensão na Gravidez

Carlos Eduardo Poli de Figueiredo.

Online, 22/05/2021 09:50-10:10. cepolif@pucrs.br

REDE BRASILEIRA DE ESTUDOS SOBRE HIPERTENSÃO NA GRAVIDEZ 2020

DECLARAÇÃO DE CONFLITO DE INTERESSES

Professor da Escola de Medicina da PUCRS - Chefe do Serviço de Nefrologia da PUCRS.
Pesquisador do Centro de Pesquisas Clínicas da PUCRS – Pesquisas com a indústria Farmacêutica e Ministério da Saúde
Consultor, advisory board ou palestrante : Agências de fomento como CAPES, CNPq e FAPESP, e da Baxter, Fresenius, Astrazeneca e Alexion.

SEM conflitos relacionados a apresentação de hoje.

Nefrologista com ADMIRAÇÃO pelos colegas da Obstetrícia e honrado pelo convite de participar da RBEHG.

Roteiro

Conflitos de interesse

PUCRS | ESCOLA DE MEDICINA

Fisiopatologia e tratamento

Posição da RBEHG

Diretrizes Brasileiras de HAS

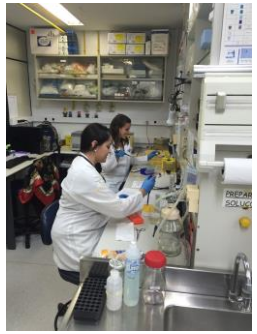
Outras diretrizes

Impacto dos anti-hipertensivos e opções

~~Puerpério~~

~~Longo-prazo~~

Conclusões

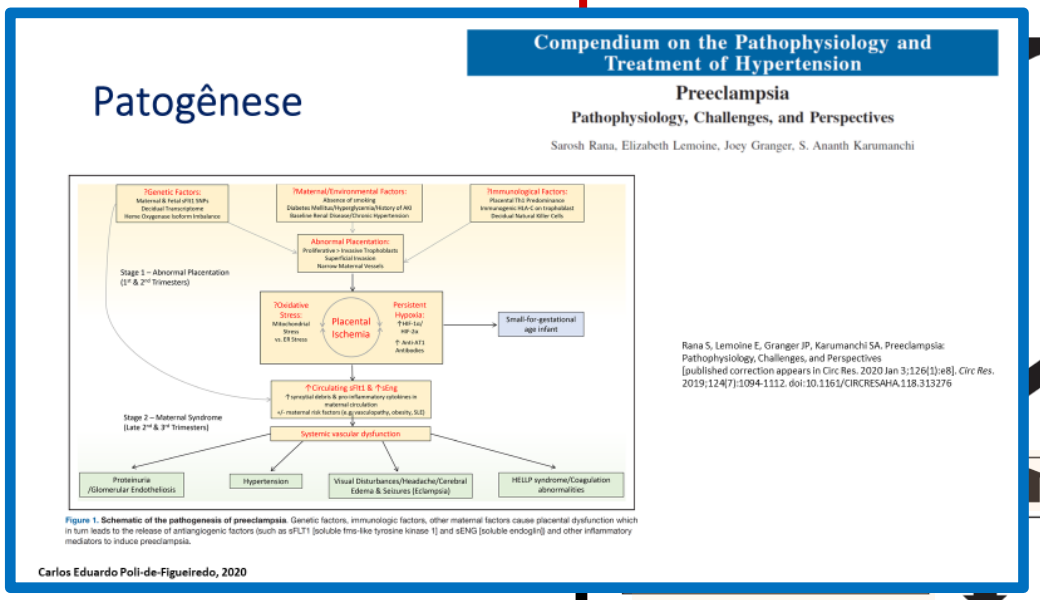


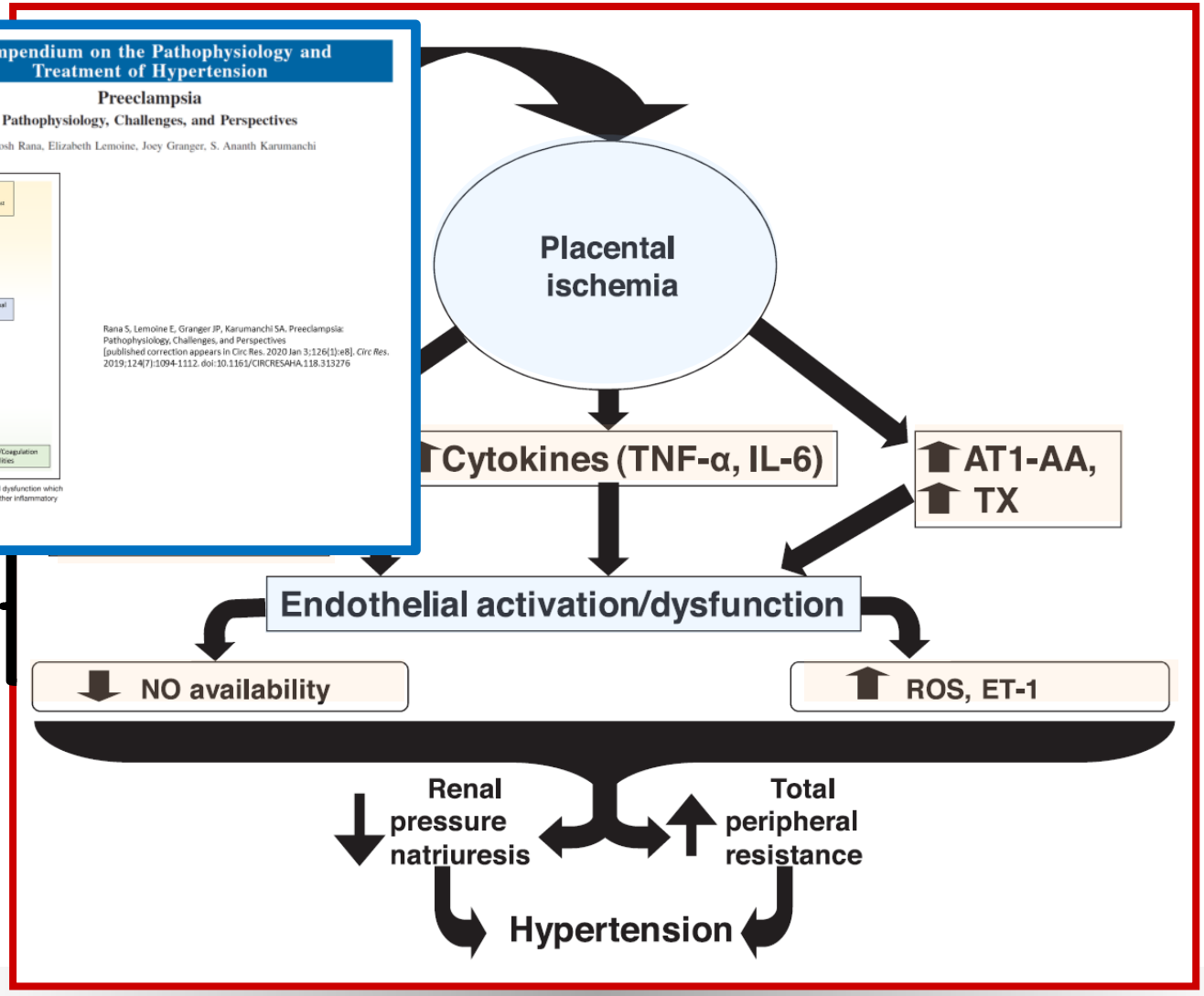
Am J Physiol Heart Circ Physiol 294: H541–H550, 2008.
First published November 30, 2007; doi:10.1152/ajpheart.01113.2007.

Invited Review

Pathophysiology of hypertension during preeclampsia: linking placental ischemia with endothelial dysfunction

Jeffrey S. Gilbert, Michael J. Ryan, Babbette B. LaMarca, Mona Sedeek, Sydney R. Murphy, and Joey P. Granger





Proteinuria
Systemic dysfunction

Am J Physiol Heart Circ Physiol 294: H541–H550, 2008.
First published November 30, 2007; doi:10.1152/ajpheart.01113.2007.

Invited Review

Tratamento

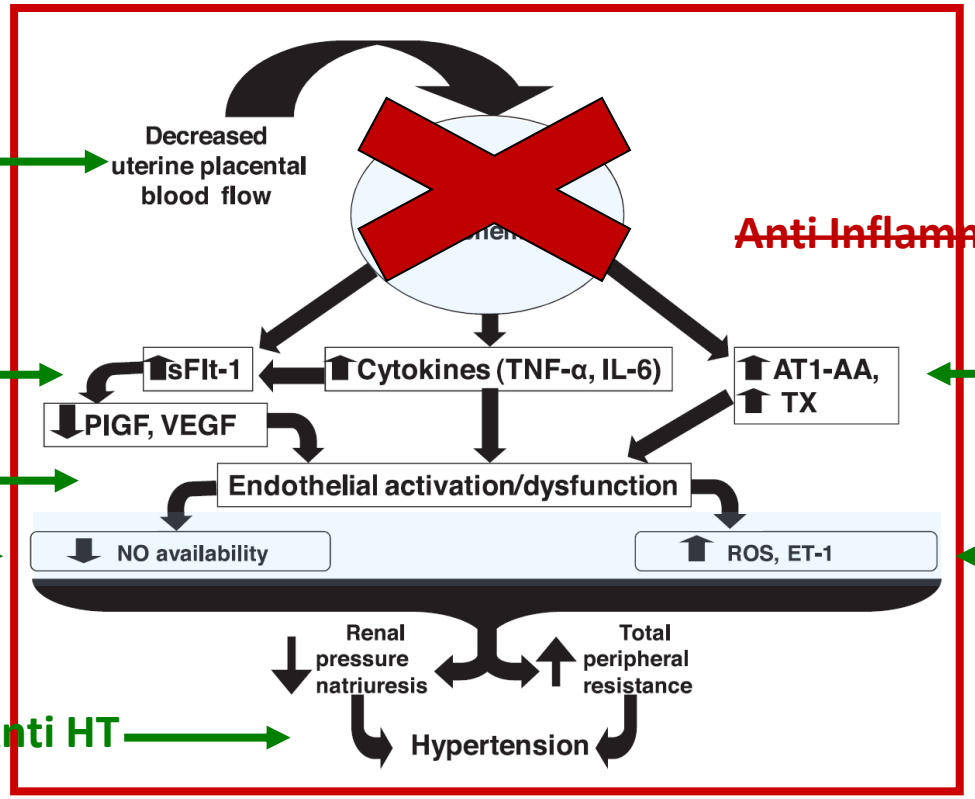
Pathophysiology of hypertension during preeclampsia: linking placental ischemia with endothelial dysfunction

Jeffrey S. Gilbert, Michael J. Ryan, Babbette B. LaMarca, Mona Sedeek, Sydney R. Murphy, and Joey P. Granger

Prevention (AAS, Ca, ~~Vit, BP control,...~~)

Apheresis
VEGF
PDE5 inhibit

L-Arg



~~Anti Inflammatories~~

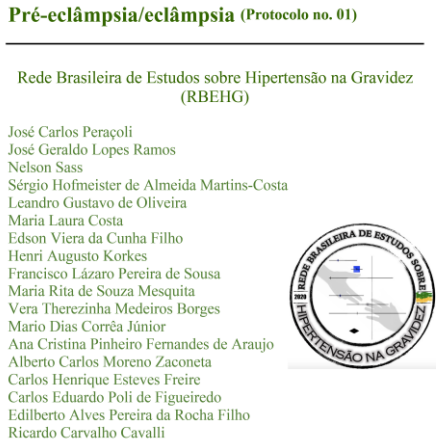
Prevention (AAS)

~~AntiOxidants~~

Anti HT

Antihipertensivos

Posição da RBEHG – PROTOCOLO 01


Pré-eclâmpsia/eclâmpsia (Protocolo no. 01)

Rede Brasileira de Estudos sobre Hipertensão na Gravidez (RBEHG)

José Carlos Peraçoli
José Geraldo Lopes Ramos
Nelson Sass
Sérgio Hofmeister de Almeida Martins-Costa
Leandro Gustavo de Oliveira
Maria Laura Costa
Edson Viera da Cunha Filho
Henri Augusto Korkes
Francisco Lázaro Pereira de Sousa
Maria Rita de Souza Mesquita
Vera Therezinha Medeiros Borges
Mario Dias Corrêa Júnior
Ana Cristina Pinheiro Fernandes de Araujo
Alberto Carlos Moreno Zaconeta
Carlos Henrique Esteves Freire
Carlos Eduardo Poli de Figueiredo
Edilberto Alves Pereira da Rocha Filho
Ricardo Carvalho Cavalli

Relação Risco *vs* Benefícios

Considerar Mãe e feto

Manifestações da hipertensão, dano em órgãos-alvo e condições fetais

Níveis de pressão arterial

- **Hipertensão arterial leve:** PA sistólica ≥ 140 e < 150 mmHg ou PA diastólica ≥ 90 e < 100 mmHg;
- **Hipertensão arterial moderada:** PA sistólica entre ≥ 150 e < 160 mmHg ou PA diastólica ≥ 100 e < 110 mmHg;
- ★ **Hipertensão arterial grave:** PA sistólica ≥ 160 mmHg ou PA diastólica ≥ 110 mmHg.

Carlos Eduardo Poli-de-Figueiredo, 2021

Antihipertensivos

Posição da RBEHG

Início de anti-hipertensivos:

Crise ou emergência hipertensiva

PAS $\geq$ 150 ou PAD $\geq$ 100 mmHg

PAS $\geq$ 140 ou PAD $\geq$ 90 mmHg persistentemente ou com sintomas

Alvo PAD 85 mmHg (ISSHP)

Antihipertensivos

Posição da RBEHG

Quadro 2. Agentes recomendados para o tratamento da crise ou emergência hipertensiva em gestantes

Agente	Dose inicial	Repetir, se necessário	Dose máxima
Hidralazina Ampola de 20 mg/mL	5 mg, Via intravenosa	5 mg, a cada 20 minutos	30 mg
A ampola de hidralazina contém 1 mL, na concentração de 20 mg/mL. Diluir uma ampola (1 mL) em 19 mL de água destilada, assim, obtém-se a concentração de 1 mg/mL.			
Nifedipino Comprimido de 10 mg	10 mg Via oral	10 mg, a cada 20-30 minutos (Via oral)	30 mg
Hidralazina em infusão contínua	5mg/hora Diluir 80 mg (4 mL de hidralazina) em 500 mL de soro fisiológico e manter infusão de 30 mL/hora		
Nitroprussiato de sódio Ampola 50 mg/2 mL	0,5 a 10 mcg/kg/min Infusão intravenosa contínua		#
A ampola de nitroprussiato de sódio contém 2 mL, na concentração de 50 mg/2 mL. Diluir uma ampola (2 mL) em 248 mL de soro glicosado 5%, assim teremos a concentração de 200 mcg/mL.			

Quadro 3. Esquema de infusão recomendado para o nitroprussiato de sódio

Dose desejada (mcg/kg/min)	0,5	1,0	2,0	3,0	4,0	5,0

HAS grave:

Reduzir PA 15-25%,

PAS 140-150 mmHg e

PAD 90-100 mmHg

e após medicação VO

Antihipertensivos

Posição da RBEHG

Quadro 1. Anti-hipertensivos recomendados para uso na gestação

Classe do agente	Agente	Posologia
Simpatolíticos de ação central, α2-agonistas	Metildopa Comprimidos de 250 e 500 mg	750 a 2.000 mg/dia 2 a 4x/dia
	Clonidina Comprimidos de 0,1 e 0,2 mg	0,2 a 0,6 mg/dia 2 a 3x/dia
Bloqueadores de canais de cálcio	Nifedipino retard Comprimidos de 10 e 20 mg	20 a 120 mg/dia 1 a 3x/dia
	Nifedipino de liberação rápida Comprimidos de 10 e 20 mg	20 a 60 mg/dia 2 a 3x/dia
	Anlodipino Comprimidos de 2,5, 5 e 10 mg	5 a 20 mg/dia 1 a 2x/dia
Vasodilatador periférico *	Hidralazina Drágeas de 25 e 50 mg	50-150 mg/dia 2 a 3x/dia
β-bloquedores *	Metoprolol Comprimidos de 25, 50 e 100 mg	100 a 200 mg/dia 1 a 2 x/dia
	Pindolol Comprimidos de 5 e 10 mg	10 a 30 mg/dia 2 a 3x/dia
	Carvedilol Comprimidos de 6,25 e 12,5 mg	12,5 a 50 mg/dia 1 a 2 x/dia Recomenda-se iniciar com 12,5 mg/dia por dois dias e a partir de então aumentar a dose

* Recomendamos essas medicações como terceira droga para associação de medicamentos para controle pressórico ou no caso de impossibilidade de uso das drogas de primeira escolha. Os β-bloqueadores de maior experiência clínica são o labetalol e o pindolol. Entretanto, o primeiro não está liberado para uso no Brasil e o segundo tem sido difícil de ser encontrado.

Experiência do prescritor

Não usar iECA, BRA e IDR

Carlos Eduardo Poli-de-Figueiredo, 2021

Antihipertensivos

TRATAMENTO MEDICAMENTOSO

CAPÍTULO 11

HIPERTENSÃO ARTERIAL NA GESTAÇÃO

Coordenador: Carlos Eduardo Poli de Figueiredo
Coordenadora adjunto: Emilton Lima Júnior
Membros: Alexandre Jorge Gomes de Lucena, Fernanda Spadotto Baptista, Helius Carlos Finimundi

Posição das Diretrizes Brasileiras de Hipertensão Arterial 2020

O tratamento medicamentoso urgente é indicado em caso de hipertensão grave[674,675] e na presença de sinais premonitórios (GR: I, NE: B). Não existe consenso com relação ao valor de PA para indicar quando o tratamento medicamentoso deve ser iniciado. Sugere-se iniciar o tratamento medicamentoso quando a PA estiver acima de 150-160/100-110 mmHg[665,674,676] com o objetivo de manter a PA entre 120-160/80-100 mmHg (GR: IIb, NE: B).

Barroso WKS, Rodrigues CIS, Bortolotto LA, Mota-Gomes MA, Brandão AA, Feitosa ADM, et al. Diretrizes Brasileiras de Hipertensão Arterial – 2020. Arq. Bras. Cardiol. 2021;116(3):516-658.

QUADRO 11.7

TRATAMENTO MEDICAMENTOSO

A escolha do medicamento anti-hipertensivo depende da experiência do médico assistente e da familiaridade com o medicamento escolhido e dos efeitos colaterais[683] (GR: IIb, NE: B). O uso de IECA, BRA e IDR é contraindicado na gestação (GR: I, NE: B), e atenolol e prazosin devem ser evitados se possível[683,684] (GR: IIa, NE: B).

Barroso WKS, Rodrigues CIS, Bortolotto LA, Mota-Gomes MA, Brandão AA, Feitosa ADM, et al. Diretrizes Brasileiras de Hipertensão Arterial – 2020. Arq. Bras. Cardiol. 2021;116(3):516-658.

QUADRO 11.7

TRATAMENTO MEDICAMENTOSO

Inicio com PA< 160/110 mmHg :
Controverso, exceto se lesão em órgão alvo

Reduz HAS grave
Reduz desfechos fetais desfavoráveis
(CHIPS PAD <86 mmHg vs <101 mmHg

Meta
PAS > 120 e < 160 mmHg
PAD > 80 e < 110 mmHg

Monoterapia
Primeira linha – metildopa, nifedipina de ação prolongada, betabloqueadores

Associar
Outro medicamento de primeira linha
Ou
Diurético tiazídico, clonidina, hidralazina

Nunca IECA, BRA

Barroso WKS, Rodrigues CIS, Bortolotto LA, Mota-Gomes MA, Brandão AA, Feitosa ADM, et al. Diretrizes Brasileiras de Hipertensão Arterial – 2020. Arq. Bras. Cardiol. 2021;116(3):516-658.

ELSEVIER
Check for updates
Canadian Journal of Cardiology 34 (2018) 526–531

Guidelines

Hypertension Canada's 2018 Guidelines for the Management of Hypertension in Pregnancy

Sonia Butalia, BSc, MD, MSc,[a,b,c] Francois Audibert, MD, MSc,[d] Anne-Marie Côté, MD, MHSc,[e] Tabassum Firoz, MD, MSc,[f] Alexander G. Logan, MD,[g] Laura A. Magee, MD, MSc,[h,i] William Mundle, MD,[j] Evelyne Rey, MD, MSc,[k] Doreen M. Rabi, MD, MSc,[a,b,c] Stella S. Daskalopoulou, MD, PhD,[l] and Kara A. Nerenberg, MD, MSc;[b,c,m] for Hypertension Canada

Hypertension Canada 2018 Guidelines
Hypertension in Pregnancy

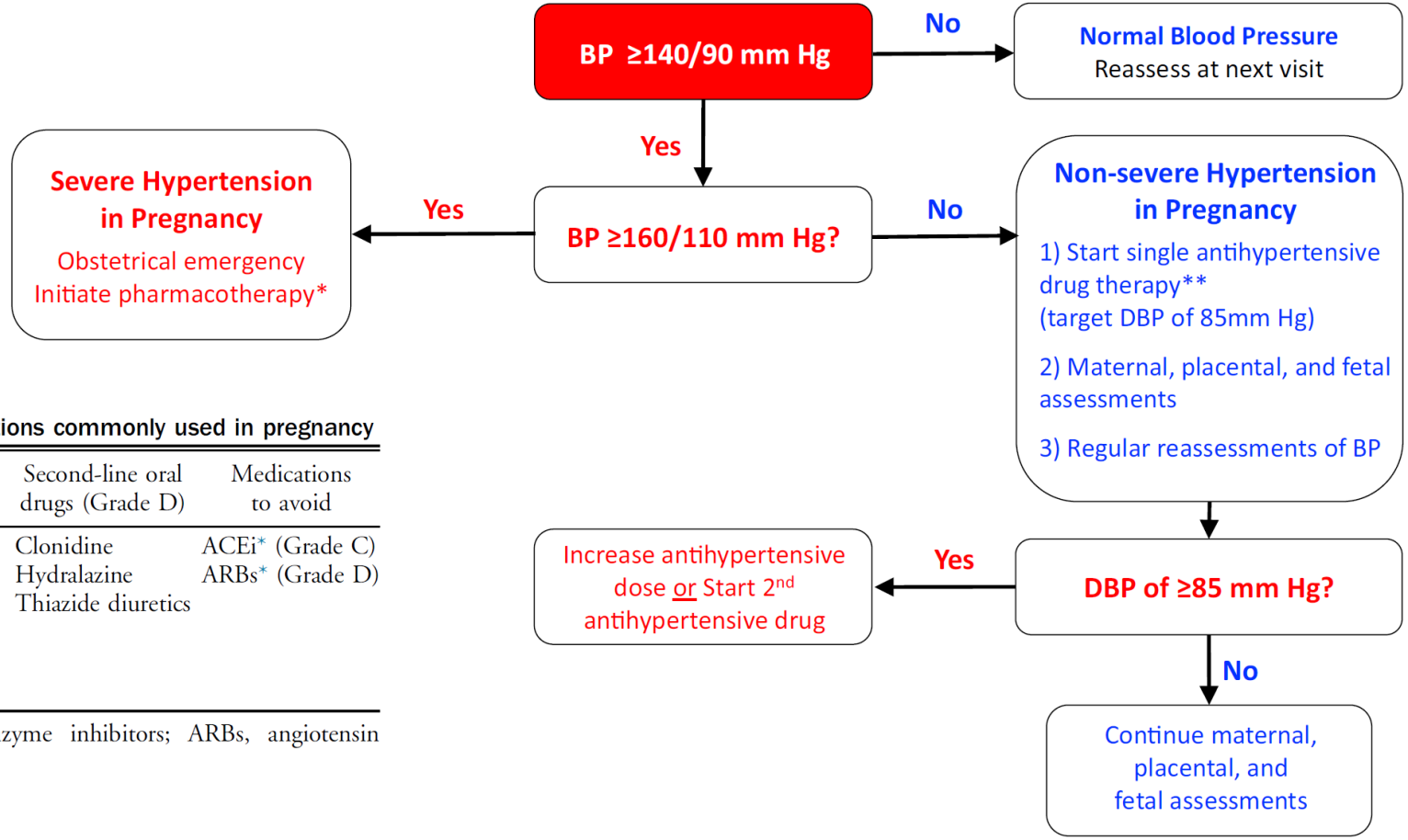


Table 2. Antihypertensive medications commonly used in pregnancy

First-line oral drugs (Grade C)	Second-line oral drugs (Grade D)	Medications to avoid
Labetalol	Clonidine	ACEi* (Grade C)
Methyldopa	Hydralazine	ARBs* (Grade D)
Long-acting oral nifedipine	Thiazide diuretics	
Other β-blockers (acebutolol, metoprolol, pindolol, and propranolol)		

ACEi, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers.

* Fetotoxicity of renal system.

Figure 2. Management of hypertension in pregnancy. BP, blood pressure; DBP, diastolic blood pressure. * See Magee et al.[2] ** See Table 2.

Pregnancy Hypertension xxx (xxxx) xxx–xxx
Contents lists available at ScienceDirect
Pregnancy Hypertension
journal homepage: www.elsevier.com/locate/preghy

ISSHP 2018

The hypertensive disorders of pregnancy: ISSHP classification, diagnosis & management recommendations for international practice

Mark A. Brown[a,b,*], Laura A. Magee[c], Louise C. Kenny[d], S. Ananth Karumanchi[e], Fergus P McCarthy[f], Shigeru Saito[g], David R. Hall[h], Charlotte E. Warren[i], Gloria Adoyi[j], Salisu Ishaku[j], on behalf of the International Society for the Study of Hypertension in Pregnancy (ISSHP)

6. Management principles for the hypertensive disorders of pregnancy

6.1. Chronic essential hypertension

- Use antihypertensives to maintain blood pressure in the range 110–140/80–85 mmHg.
- Acceptable initial anti-hypertensives include labetalol, oxprenolol, methyldopa, nifedipine, diltiazem; prazosin and hydralazine are usually used as 2nd or 3rd line agents [76].

PA 110-140/80-85 mmHg

Tto urgente >160/110 mmHg

Alvo: PAD 85 mmHg e PAS < 160 mmHg

Parar se PAD < 80 mmHg

6.5. Pre-eclampsia

6.5.1. Ante-natal

ISSHP endorses the following key management points:

1. Regardless of the hypertensive disorder of pregnancy, blood pressure requires urgent treatment in a monitored setting when ≥160/110 mmHg; acceptable agents for this include oral nifedipine or intravenous labetalol or hydralazine.
2. Regardless of the hypertensive disorder of pregnancy, we recommend that blood pressures consistently at or above 140/90 mmHg be treated aiming for a target diastolic blood pressure of 85 mmHg (and systolic blood pressure at least below 160 mmHg; some Units target 110–140 mmHg) to reduce the likelihood of developing severe maternal hypertension and possibly other complications such as low platelets and elevated liver enzymes with symptoms. Antihypertensive drugs should be reduced or ceased if diastolic BP falls below 80 mmHg Acceptable agents include oral methyldopa, labetalol, oxprenolol, nifedipine, with 2nd or 3rd line agents hydralazine and prazosin.

Manejo da hipertensão crônica na gestação

Tratamento da hipertensão crônica

NICE guideline
Published: 25 June 2019
www.nice.org.uk/guidance/ng133

- Continuar tratamento anti-hipertensivo em uso, se seguro na gestação, **a menos que:**
  - PAS sustentada < 110 mmHg ou
  - PAD sustentada < 70 mmHg ou
  - Hipotensão sintomática
- **Oferecer** tratamento anti-hipertensivo a mulheres gestantes que tem HAS crônica e ainda não estão em tratamento se tiverem:
  - PAS sustentada ≥ 140 mmHg ou
  - PAD sustentada ≥ 90 mmHg.

Manejo da hipertensão crônica na gestação

Tratamento da hipertensão crônica e da hipertensão gestacional

NICE guideline
Published: 25 June 2019
www.nice.org.uk/guidance/ng133

NICE guideline

- PA alvo na hipertensão na gestação: 135/85 mmHg.
- Considerar labetalol (não tem no Brasil) para tratar HAS crônica na mulher gestante.
- **Considerar nifedipina quando labetalol não for apropriado.**
- **Considerar metildopa quando labetalol ou nifedipina não forem apropriados.**
- Basear a escolha em perfil de eventos adversos e risco e as preferencias da mulher.

ACOG 2019

The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

ACOG PRACTICE BULLETIN

Clinical Management Guidelines for Obstetrician–Gynecologists

NUMBER 203

Committee on Practice Bulletins—Obstetrics. This Practice Bulletin was developed by the American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics in collaboration with Alex Vidaeff, MD, MPH; Jimmy Espinoza, MD, MSc; Hyagriv Simhan, MD; and Christian M. Pettker, MD.

Chronic Hypertension in Pregnancy

The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

ACOG PRACTICE BULLETIN

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Gestational Hypertension and Preeclampsia

Table 3. Antihypertensive Agents Used for Ur

Drug	Dose
Labetalol	10–20 mg IV, then 20–80 mg every 10–30 minutes to a maximum cumulative dosage of 300 mg; or constant infusion 1–2 mg/min IV
Hydralazine	5 mg IV or IM, then 5–10 mg IV every 20–40 minutes to a maximum cumulative dosage of 20 mg; or constant infusion of 0.5–10 mg/hr
Nifedipine (immediate release)	10–20 mg orally, repeat in 20 minutes if needed; then 10–20 mg every 2–6 hours; maximum daily dose is 180 mg

Abbreviations: IM, intramuscularly; IV, intravenously.

Table 2. Common Oral Antihypertensive Agents in Preg

Drug	Dosage
Labetalol	200–2,400 mg/d orally in two to three divided doses. Commonly initiated at 100–200 mg twice daily
Nifedipine	30–120 mg/d orally of an extended-release preparation. Commonly initiated at 30–60 mg once daily (extended-release)
Methyldopa	500–3,000 mg/d orally in two to four divided doses. Commonly initiated at 250 mg twice or three times daily
Hydrochlorothiazide	12.5–50 mg daily

Carlos Eduardo Poli-de-Figueiredo

HAS grave - AVC

Stroke and Severe Preeclampsia and Eclampsia: A Paradigm Shift Focusing on Systolic Blood Pressure

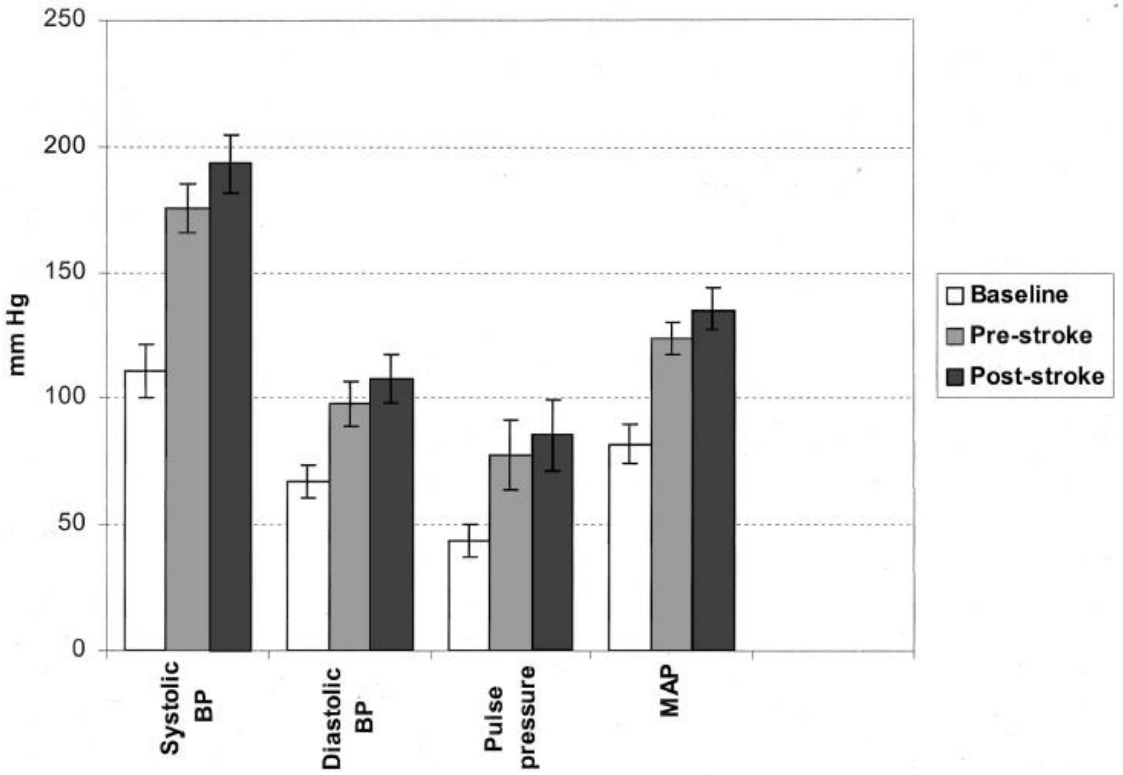
VOL. 105, NO. 2, FEBRUARY 2005
© 2005 by The American College of Obstetricians and Gynecologists.

James N. Martin Jr, MD, Brad D. Thigpen, DO, Robert C. Moore, MD, Carl H. Rose, MD, Julie Cushman, RN, and Warren May, PhD

PAS Pré AVC:

> 160 mmHg – 95,8%

> 155 mmHg – 100%



Journal of the American Heart Association

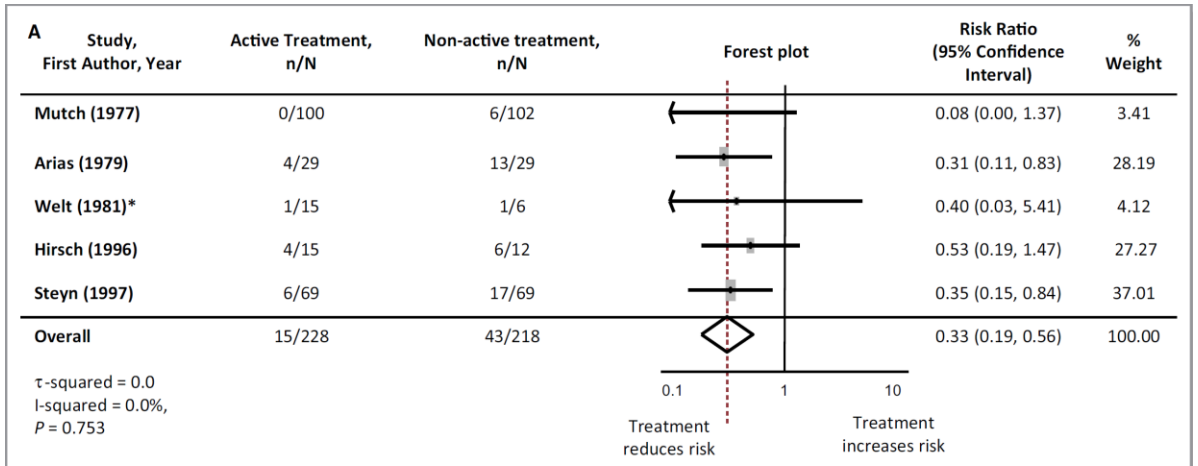
SYSTEMATIC REVIEW AND META-ANALYSIS

Impacto antihipertensivos

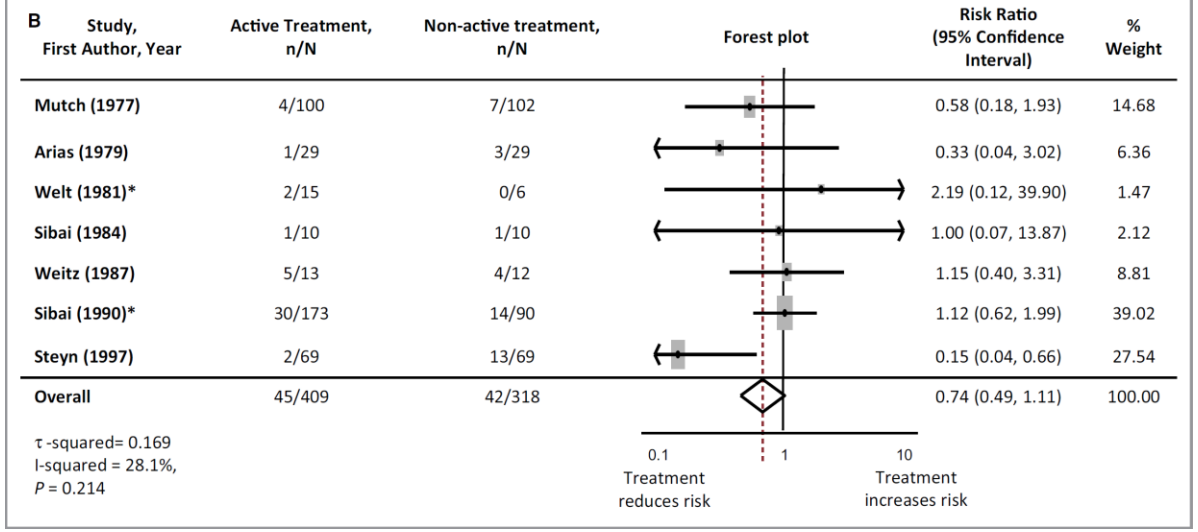
Impact of Antihypertensive Treatment on Maternal and Perinatal Outcomes in Pregnancy Complicated by Chronic Hypertension: A Systematic Review and Meta-Analysis

Louise M. Webster, BMBS, BMedSci; Frances Conti-Ramsden, MA, MBBS; Paul T. Seed, CStat; Andrew J. Webb, MBBS, PhD, FRCP; Catherine Nelson-Piercy, MBBS, MA; Lucy C. Chappell, BMBCh, PhD

HAS grave



Pré-eclâmpsia



- N = 15 ECR (1166 mulheres)
- **Tratamento antihipertensivo versus placebo/sem tratamento antihipertensivo**
- **Redução significativa da incidência de hipertensão severa (5 estudos, 446 mulheres, risk ratio 0,33, IC95%CI 0,19-0,56).**
- **Sem diferença**:
  - **Incidência pré-eclâmpsia sobreposta**
  - **Morte fetal ou neonatal**
  - **Peso do nascimento**
  - **PIG**

Cochrane Library

Cochrane Database of Systematic Reviews

Abalos E, Duley L, Steyn DW, Gialdini C.
Antihypertensive drug therapy for mild to moderate hypertension during pregnancy.
Cochrane Database of Systematic Reviews 2018, Issue 10. Art. No.: CD002252.
DOI: 10.1002/14651858.CD002252.pub4.

Antihypertensive drug therapy for mild to moderate hypertension during pregnancy (Review)

Abalos E, Duley L, Steyn DW, Gialdini C

- **Antihypertensive drug therapy for mild to moderate hypertension during pregnancy reduces the risk of severe hypertension. The effect on other clinically important outcomes remains unclear.**
- **If antihypertensive drugs are used, beta blockers and calcium channel blockers appear to be more effective than the alternatives for preventing severe hypertension.**
- **High-quality large sample-sized randomised controlled trials are required in order to provide reliable estimates of the benefits and adverse effects of antihypertensive treatment for mild to moderate hypertension for both mother and baby, as well as costs to the health services, women and their families.**

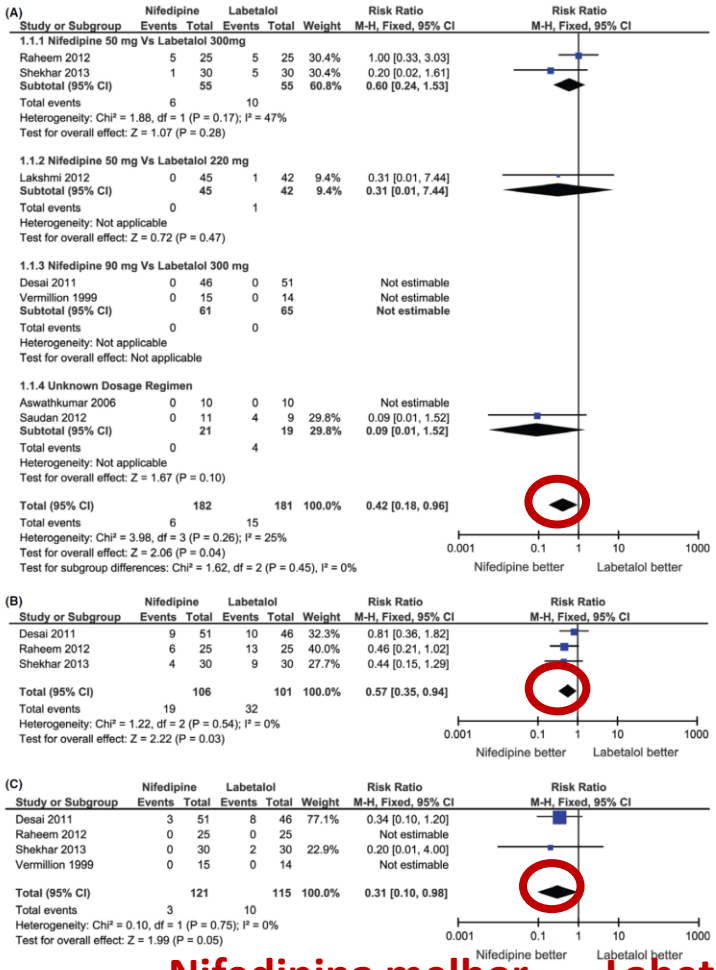
Nifedipina

Oral nifedipine versus intravenous labetalol for severe hypertension during pregnancy: a systematic review and meta-analysis

S Shekhar,[a] N Gupta,[b] R Kirubakaran,[c] P Pareek[d]

BJOG 2016;123:40–47.

Morte neonatal - Efeitos maternos- HAS persistente



Nifedipina melhor **Labetalol melhor**

DOI: 10.1111/1471-0528.12737
www.bjog.org

Systematic review

Oral antihypertensive therapy for severe hypertension in pregnancy and postpartum: a systematic review

T Firoz,[a,b] LA Magee,[c,d] K MacDonell,[e] BA Payne,[b,c] R Gordon,[c] M Vidler,[b,c] P von Dadelszen,[b,c]
for the Community Level Interventions for Pre-eclampsia (CLIP) Working Group

- Nifedipina
- Labetalol
- Metildopa

- Nifedipina ação prolongada melhor que capsula★
- Nifedipina ~ Hidralazina EV
- Nifedipina ~Labetalol EV

Study or subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk difference M-H, Random, 95% CI
4.5.1 Nifedipine capsule vs. Nifedipine PA tablet						
Australia 2002	11	31	3	33	9.4%	0.26 [0.07, 0.46]
Subtotal (95% CI)		**31**		**33**	**9.4%**	**0.26 [0.07, 0.46]**
Total events	11		3			
Heterogeneity: Not applicable						
Test for overall effect: $Z = 2.65$ ($P = 0.008$)						
4.5.2 Nifedipine po/sl vs. Hydralazine IV						
Brazil 1992	0	20	0	17	16.8%	0.00 [−0.10, 0.10]
Iran 2002	0	65	0	61	22.6%	0.00 [−0.03, 0.03]
Iran 2011	1	25	0	25	16.4%	0.04 [−0.06, 0.14]
South Africa 1989	1	17	0	16	12.3%	0.06 [−0.09, 0.21]
Subtotal (95% CI)		**127**		**119**	**68.2%**	**0.00 [−0.02, 0.03]**
Total events	2		0			
Heterogeneity: Tau² = 0.00; Chi² = 1.67, df = 3 ($P = 0.64$); $I^2 = 0\%$						
Test for overall effect: $Z = 0.34$ ($P = 0.73$)						
4.5.3 Nifedipine po/sl vs. Labetalol IV						
Malaysia 2011	1	25	0	25	16.4%	0.04 [−0.06, 0.14]
USA 1999	0	6	0	6	6.0%	0.00 [−0.27, 0.27]
Subtotal (95% CI)		**31**		**31**	**22.5%**	**0.03 [−0.06, 0.13]**
Total events	1		0			
Heterogeneity: Tau² = 0.00; Chi² = 0.08, df = 1 ($P = 0.78$); $I^2 = 0\%$						
Test for overall effect: $Z = 0.70$ ($P = 0.48$)						
Total (95% CI)		**189**		**183**	**100.0%**	**0.05 [−0.03, 0.12]**
Total events	14		3			
Heterogeneity: Tau² = 0.01; Chi² = 21.64, df = 6 ($P = 0.001$); $I^2 = 72\%$						
Test for overall effect: $Z = 1.15$ ($P = 0.25$)						
Test for subgroup differences: Chi² = 6.89, df = 2 ($P = 0.03$), $I^2 = 71.0\%$						

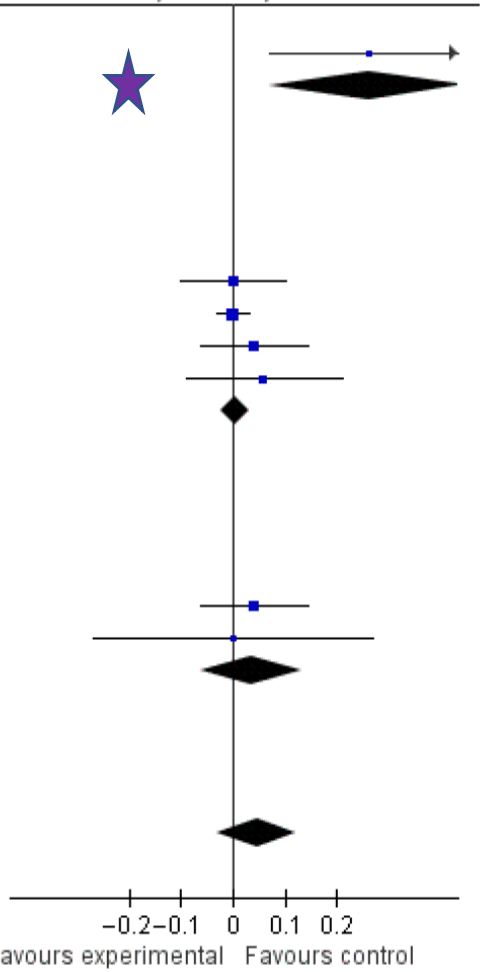


Figure 2. Maternal hypotension.

The NEW ENGLAND JOURNAL of MEDICINE

CHIPS trial

Less-Tight versus Tight Control of Hypertension in Pregnancy

Laura A. Magee, M.D., Peter von Dadelszen, M.B., Ch.B., D.Phil., Evelyne Rey, M.D., Susan Ross, M.B.A., Ph.D., Elizabeth Asztalos, M.D., Kellie E. Murphy, M.D., Jennifer Menzies, M.Sc., Johanna Sanchez, M.I.P.H., Joel Singer, Ph.D., Amiram Gafni, D.Sc., Andrée Gruslin, M.D.,* Michael Helewa, M.D., Eileen Hutton, Ph.D., Shoo K. Lee, M.D., Ph.D., Terry Lee, Ph.D., Alexander G. Logan, M.D., Wessel Ganzevoort, M.D., Ph.D., Ross Welch, M.B., B.S., D.A., M.D., Jim G. Thornton, M.B., Ch.B., M.D., and Jean-Marie Moutquin, M.D.

N ENGL J MED 372;5 NEJM.ORG JANUARY 29, 2015

- **HAS crônica ou HAS gestacional NÃO GRAVE E SEM PROTEINÚRIA.**
- PAD 90 a 105 mmHg (ou 85 a 105 mmHg se anti-hipertensivos)

- **MENOS RIGOROSO: Alvo PAD 100 mmHg (*less tight*).**
- **RIGOROSO: Alvo PAD 85 mmHg (*tight*).**

- **N:** 987 (HAS prévia 74,6%) - *Less tight* 493 vs *Tight* 488

- **PAD 4,6 mmHg maior no *LESS TIGHT* (95%CI 3,7-5,4)**

- **Desfechos semelhantes entre *TIGHT* e *LESS TIGHT***

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Desfechos Semelhantes, exceto

Table 3. Secondary and Other Maternal Outcomes.*

Variable	Less-Tight Control (N=493)	Tight Control (N=488)	Adjusted Odds Ratio (95% CI)†
Placental abruption — no. (%)	11 (2.2)	11 (2.3)	0.94 (0.40–2.21)
Severe hypertension — no. (%)	200 (40.6)	134 (27.5)	1.80 (1.34–2.38)
Preeclampsia — no./total no. (%)	241/493 (48.9)	223/488 (45.7)	1.14 (0.88–1.47)
Defined only by new proteinuria¶	148/493 (30.0)	132/488 (27.0)	1.08 (0.74–1.59)
At least one symptom of preeclampsia‖	171/493 (34.7)	156/488 (32.0)	1.11 (0.84–1.46)
Abnormal laboratory test results			
Platelet count <100×10⁹/liter	21/493 (4.3)	8/488 (1.6)	2.63 (1.15–6.05)
Elevated AST or ALT level, with symptoms	21/492 (4.3)	9/488 (1.8)	2.33 (1.05–5.16)
HELLP syndrome**	9/493 (1.8)	2/488 (0.4)	4.35 (0.93–20.35)
Serum creatinine level >2.3 mg/dl	0	1/488 (0.2)	

CHIPS Labetalol vs Metildopa
BJOG 2016 a

DOI: 10.1111/1471-0528.13569
www.bjog.org
BJOG. 2016 Jun;123(7):1143-51. doi: 10.1111/1471-0528.13569

Do labetalol and methyldopa have different effects on pregnancy outcome? Analysis of data from the Control of Hypertension In Pregnancy Study (CHIPS) trial

LA Magee,[a,b,c] for the CHIPS Study Group* P von Dadelszen,[b,c] J Singer,[c,d] T Lee,[d] E Rey,[e] S Ross,[f] E Asztalos,[g,h,i] KE Murphy,[h,i] J Menzies,[b] J Sanchez,[i] A Gafni,[j] A Gruslin,[k,†] M Helewa,[l] E Hutton,[m] G Koren,[n] SK Lee,[g] AG Logan,[o] JW Ganzevoort,[p] R Welch,[q] JG Thornton,[r] J-M Moutquin[s]

- Metildopa (24,6%) vs Labetalol (24,6%) na **randomização**

METILDOPA com resultados favoráveis:

- Menor n° RN com peso ao nascer <P10: aOR 0,48 (95%CI 0,2-0,87)

- Metildopa (22,8%) vs Labetalol (44,1%) **após randomização**
- Menor n° de desfechos primário: aOR 0,64 (95%CI 0,4-1,0)
- Peso ao nascer <P10: aOR 0,54 (95%CI 0,32-0,92)
- HAS materna grave: aOR 0,51 (95%CI 0,31-0,83)
- PE: aOR 0,55 (95%CI 0,36-0,85)
- Parto com < 34 semanas: aOR 0,53 (95%CI 0,29-0,96)
- Parto com < 37 semanas: aOR 0,55 (95%CI 0,35-0,85)

Cochrane Library

Cochrane Database of Systematic Reviews

Duley L, Meher S, Jones L.

Drugs for treatment of very high blood pressure during pregnancy.

Cochrane Database of Systematic Reviews 2013, Issue 7. Art. No.: CD001449.

DOI: 10.1002/14651858.CD001449.pub3.

Drugs for treatment of very high blood pressure during pregnancy (Review)

Duley L, Meher S, Jones L

- N 35 trials. 3573 women
- CCB < persistente high blood pressure than hydralazine
- Hydralazine < than ketanserin, but more side effects and HELLP
- Labetalol less hypotension than diazoxide
- Nimodipine high incidence of high blood pressure
- ...

Authors' conclusions

Until better evidence is available the choice of antihypertensive should depend on the clinician's experience and familiarity with a particular drug; on what is known about adverse effects; and on women's preferences. Exceptions are nimodipine, magnesium sulphate (although this is indicated for women who require an anticonvulsant for prevention or treatment of eclampsia), diazoxide and ketanserin, which are probably best avoided.

Drogas HAS grave

Semelhantes:

- Nifedipina
- Hidralazina
- Labetalol

Evidência insuficiente:

- Demais

British Journal of Clinical Pharmacology

Br J Clin Pharmacol (2018) **84** 1906–1916 1906

SYSTEMATIC REVIEW AND META-ANALYSIS

Drugs for treating severe hypertension in pregnancy: a network meta-analysis and trial sequential analysis of randomized clinical trials

Correspondence Dr. Kannan Sridharan, Associate Professor, Department of Pharmacology and Therapeutics, College of Medicine and Medical Sciences, Arabian Gulf University, Manama, Bahrain. Tel.: +973 3345 3123; E-mail: skannandr@gmail.com

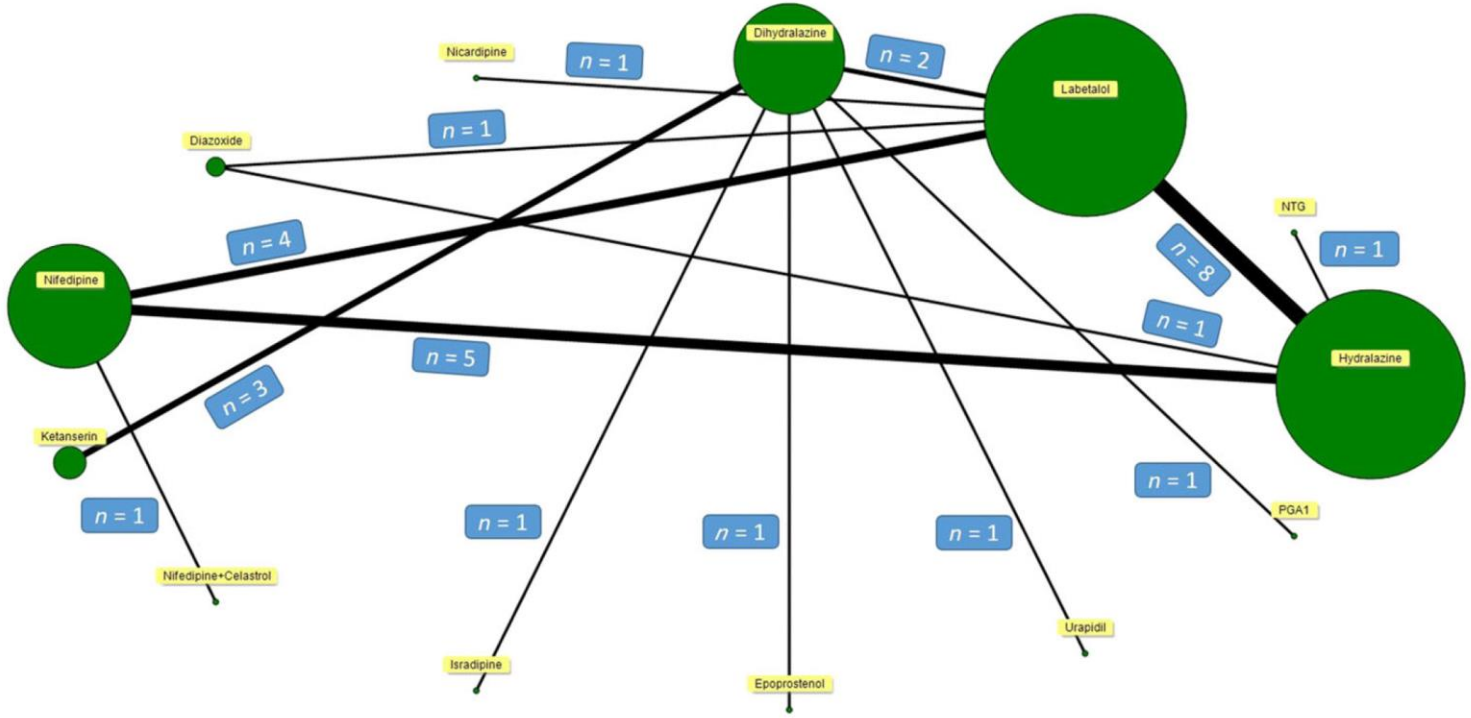

Figure 2

Network plot for primary outcome. The majority of the studies compared hydralazine with labetalol followed by nifedipine and labetalol

Conclusions

Oral antihypertensive regimens (nifedipine retard, labetalol, and methyldopa) for management of severe hypertension in pregnancy: an open-label, randomised controlled trial

Thomas Easterling, Shuchita Mundle, Hillary Bracken, Seema Parvekar, Sulabha Mool, Laura A Magee, Peter von Dadelszen, Tara Shochet, Beverly Winikoff

Lancet 2019; 394: 1011–21

Severe hypertension in pregancy

- Nifedipine retard more effective than labetalol/methyldopa
- Nidfedipine retard and labetalol more effective than methyldopa

- High frequency of achieving primary outcomes (all)

- Low adverse events, but more ICU admitions with nifedipine

- **All three drugs are viable options in low-resource settings**

Easterling T et al. Oral antihipertensive regimens (nifedipine retard, labetalol and methyldopa) for the management of severe hypertension in pregnancy: an open-label, randomised controlled trial. Lancet 2019; 394:1011-21

Antihipertensivos na gestação

- **COMO USAR:**
  - Com cuidado e com monitoramento da PA, do bem estar materno e do bem estar fetal
  - Via oral e/ou via parenteral (emergência)
  - Nifedipina (BCC), Metildopa, Beta-bloqueadores, Hidralazina ou conforme a sua experiencia
  - Hidralazina, NPS
- **QUANDO USAR:**
  - Hipertensão grave
  - Hipertensão com lesões em órgãos alvo
  - Risco materno
  - Fora de alvo desejado
- **PRÓS:**
  - Reduz o risco de hipertensão grave, AVC e de lesão em órgão alvo
  - Pode viabilizar o feto no manejo expectante
- **CONTRA:**
  - Pode induzir baixa perfusão placentária e eventos adversos
  - Risco materno

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