

15 DE ABRIL — 6ª FEIRA

SESSÃO TELEVOTER HIPERTENSÃO

**ANTÓNIO PEDRO MACHADO
BRAZ NOGUEIRA,
CARLOS RABAÇAL
OLIVEIRA RAMOS**

Reappraisal of European guidelines on hypertension management: a European Society of Hypertension Task Force document

Giuseppe Mancia^a, Stéphane Laurent^b, Enrico Agabiti-Rosei^c, Ettore Ambrosioni^d, Michel Burnier^e, Mark J. Caulfield^f, Renata Cifkova^g, Denis Clément^h, Antonio Cocaⁱ, Anna Dominiczak^j, Serap Erdine^k, Robert Fagard^l, Csaba Farsang^m, Guido Grassiⁿ, Hermann Haller^o, Anthony Heagerty^p, Sverre E. Kjeldsen^q, Wolfgang Kiowski^r, Jean Michel Mallion^s, Athanasios Manolis^t, Krzysztof Narkiewicz^u, Peter Nilsson^v, Michael H. Olsen^w, Karl Heinz Rahn^x, Josep Redon^y, José Rodicio^z, Luis Ruilope^{a1}, Roland E. Schmieder^{a2}, Harry A.J. Struijker-Boudier^{a3}, Pieter A. van Zwieten^{a4}, Margus Viigimaa^{a5} and Alberto Zanchetti^{a6}

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Keywords: antihypertensive treatment, cardiovascular risk, guidelines, hypertension, organ damage

Abbreviations: ACE, angiotensin-converting enzyme; BP, blood pressure; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; ESC, European Society of Cardiology; ESH, European Society of Hypertension; ET, endothelin; IMT, carotid intima-media thickness; JNC, Joint National Committee; LVH, left ventricular hypertrophy; LVM, left ventricular mass; PDE-5, phosphodiesterase-5; PPAR-γ, peroxisome proliferator-activated receptor-γ; PWV, pulse wave velocity; SBP, systolic blood pressure; WHO, World Health Organization

^aClinica Medica, University of Milano-Bicocca, Ospedale San Gerardo, Monza, Milan, Italy, ^bPharmacology Department, Hôpital Européen Georges Pompidou, Paris, France, ^cDepartment of Medical and Surgical Sciences, Clinic of Internal Medicine, University of Brescia, Brescia, ^dUniversity of Bologna, Clinica Medica, Bologna, Italy, ^eDivision of Nephrology and Hypertension, Centre Hospitalier Universitaire, Vaudois, Lausanne, Switzerland, ^fWilliam Harvey Research Institute, Barts and The London School of Medicine, Queen Mary University of London, London, UK, ^gDepartment of Preventive Cardiology, Institute of Clinical and Experimental Medicine, Prague, Czech Republic, ^hDepartment of Cardiology and Angiology, University of Ghent, Ghent, Belgium, ⁱHypertension Unit, Department of Internal Medicine, Hospital Clinic, University of Barcelona, Barcelona, Spain, ^jBHF Glasgow Cardiovascular Research Centre, University of Glasgow, Glasgow, UK, ^kIstanbul University Cerrahpa, School of Medicine, Istanbul, Turkey, ^lHypertension and Cardiovascular Rehabilitation Unit, Department of Cardiovascular Diseases, University of Leuven, Leuven, Belgium, ^mCardiometabolic Centre, St. Imre Hospital, Budapest, Hungary, ⁿUniversity of Milano-Bicocca, Department of Clinical Medicine and Prevention, San Gerardo Hospital, Milan, Italy, ^oDepartment of Nephrology, Hannover Medical School, Hannover, Germany, ^pManchester Royal Infirmary, University of Manchester, Manchester, UK, ^qDepartment of Cardiology, Ullevål University Hospital, Oslo, Norway, ^rCardiovascular Center Zuerich, Zuerich, Switzerland, ^sCardiologie et Hypertension Artérielle, CHU de Grenoble, Grenoble, France, ^tCardiology, Asklepeion General Hospital, Athens, Greece, ^uDepartment of Hypertension and Diabetology, Medical University of Gdansk, Gdansk, Poland, ^vDepartment of Clinical Sciences Medicine, University Hospital, Malmö, Sweden, ^wClinical Physiology and Nuclear Medicine, Glostrup University Hospital, Glostrup, Denmark, ^xDivision of Nephrology and Hypertension, Department of Medicine, University of Münster, Münster, Germany, ^yInternal Medicine, Hospital Clínico, University of Valencia, Valencia, Spain, ^zDepartment of Medicine, University Complutense, ^{a1}Hospital 12 de Octubre, Madrid, Spain, ^{a2}Medizinische Klinik, University Erlangen-Nürnberg, Erlangen, Germany, ^{a3}Department of Pharmacology, University of Limburg in Maastricht, Maastricht, ^{a4}University of Amsterdam, Amsterdam, The Netherlands, ^{a5}Centre of Cardiology, North Estonia Medical Centre, Tallinn, Estonia and ^{a6}University of Milan and Istituto Auxologico Italiano, Milan, Italy

Correspondence to Professor Giuseppe Mancia, Clinica Medica, University of Milano-Bicocca, San Gerardo Hospital, Via Pergolesi 33, 20052 Monza, Milan, Italy
Tel: +39 039 2333357; fax: +39 039 322274; e-mail: giuseppe.mancia@unimib.it

Professor Stéphane Laurent, Department of Pharmacology and INSERM U970, European Hospital Georges Pompidou, Paris Descartes University, 20 rue Leblanc 75015 Paris, France
Tel: +33 1 56 09 39 91; fax: +33 1 56 09 39 92;
e-mail: stephane.laurent@egp.ap-hop-paris.fr

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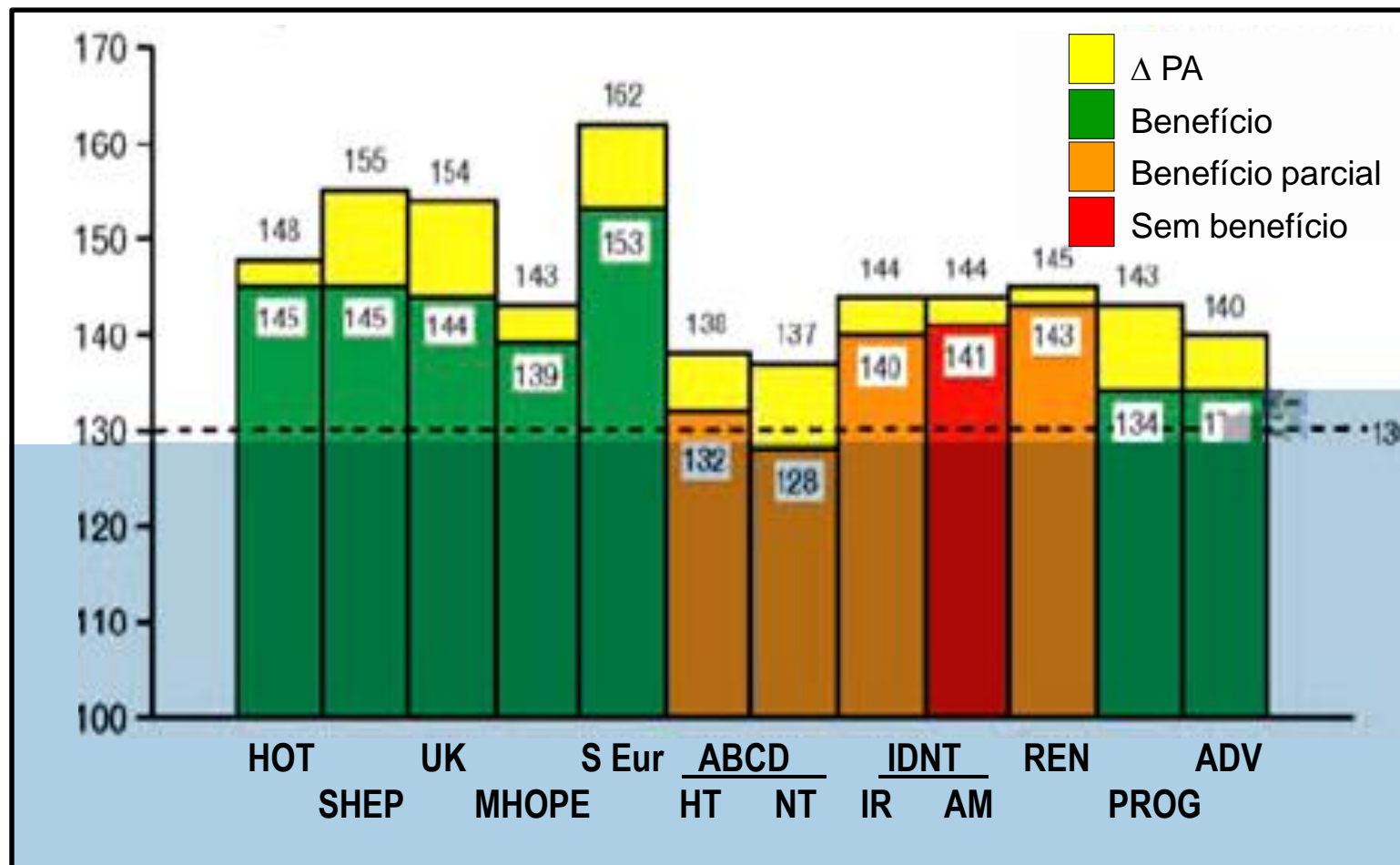
Introduction

In the 2 years since the publication of the 2007 guidelines for the management of arterial hypertension of the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC) [1], research on hypertension has actively been pursued and the results of new important studies (including several large randomized trials of antihypertensive therapy) have been published. Some of these studies have reinforced the evidence on which the recommendations of the 2007 ESH/ESC guidelines were based. However, other studies have widened the information available in 2007, modifying some of the previous concepts, and suggesting that new evidence-based recommendations could be appropriate.

The aim of this document of the ESH is to address a number of studies on hypertension published in the last 2 years in order to assess their contribution to our expanding knowledge of hypertension. Furthermore, some critical appraisal of the current recommendations of the ESH/ESC, as well as of other guidelines, might be a useful step toward the preparation of a third version of the European guidelines in the future.

The most important conclusions are summarized in boxes. The points that will be discussed are reported in Box 1.

Benefício do tratamento da HTA no diabético



ORIGINAL ARTICLE

Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus

The ACCORD Study Group*

ABSTRACT

BACKGROUND

There is no evidence from randomized trials to support a strategy of lowering systolic blood pressure below 135 to 140 mm Hg in persons with type 2 diabetes mellitus. We investigated whether therapy targeting normal systolic pressure (i.e., <120 mm Hg) reduces major cardiovascular events in participants with type 2 diabetes at high risk for cardiovascular events.

METHODS

A total of 4733 participants with type 2 diabetes were randomly assigned to intensive therapy, targeting a systolic pressure of less than 120 mm Hg, or standard therapy, targeting a systolic pressure of less than 140 mm Hg. The primary composite outcome was nonfatal myocardial infarction, nonfatal stroke, or death from cardiovascular causes. The mean follow-up was 4.7 years.

RESULTS

After 1 year, the mean systolic blood pressure was 119.3 mm Hg in the intensive-therapy group and 133.5 mm Hg in the standard-therapy group. The annual rate of the primary outcome was 1.87% in the intensive-therapy group and 2.09% in the standard-therapy group (hazard ratio with intensive therapy, 0.88; 95% confidence interval [CI], 0.73 to 1.06; $P=0.20$). The annual rates of death from any cause were 1.28% and 1.19% in the two groups, respectively (hazard ratio, 1.07; 95% CI 0.85 to 1.35; $P=0.55$). The annual rates of stroke, a prespecified secondary outcome, were 0.32% and 0.53% in the two groups, respectively (hazard ratio, 0.59; 95% CI, 0.39 to 0.89; $P=0.01$). Serious adverse events attributed to antihypertensive treatment occurred in 77 of the 2362 participants in the intensive-therapy group (3.3%) and 30 of the 2371 participants in the standard-therapy group (1.3%) ($P<0.001$).

CONCLUSIONS

In patients with type 2 diabetes at high risk for cardiovascular events, targeting a systolic blood pressure of less than 120 mm Hg, as compared with less than 140 mm Hg, did not reduce the rate of a composite outcome of fatal and nonfatal major cardiovascular events. (ClinicalTrials.gov number, NCT00000620.)

The members of the Writing Group (William C. Cushman, M.D., Gregory W. Evans, M.A., Robert P. Byington, Ph.D., David C. Goff, Jr., M.D., Ph.D., Richard H. Grimm, Jr., M.D., Ph.D., Jeffrey A. Cutler, M.D., M.P.H., Denise G. Simons-Morton, M.D., Ph.D., Jan N. Basile, M.D., Marshall A. Corson, M.D., Jeffrey L. Probstfield, M.D., Lois Katz, M.D., Kevin A. Peterson, M.D., William T. Friedewald, M.D., John B. Buse, M.D., Ph.D., J. Thomas Bigger, M.D., Hertz C. Gerstein, M.D., and Faramarz Ismail-Beigi, M.D., Ph.D.) assume responsibility for the integrity of the article. Address reprint requests to Dr. Cushman at the Preventive Medicine Section (111Q), Veterans Affairs Medical Center, 1030 Jefferson Ave., Memphis, TN 38104, or at william.cushman@va.gov.

*The members of the Action to Control Cardiovascular Risk in Diabetes (ACCORD) Study Group are listed in Section 1 in Supplementary Appendix 1, available with the full text of this article at NEJM.org. The affiliations of the members of the Writing Group are listed in the Appendix.

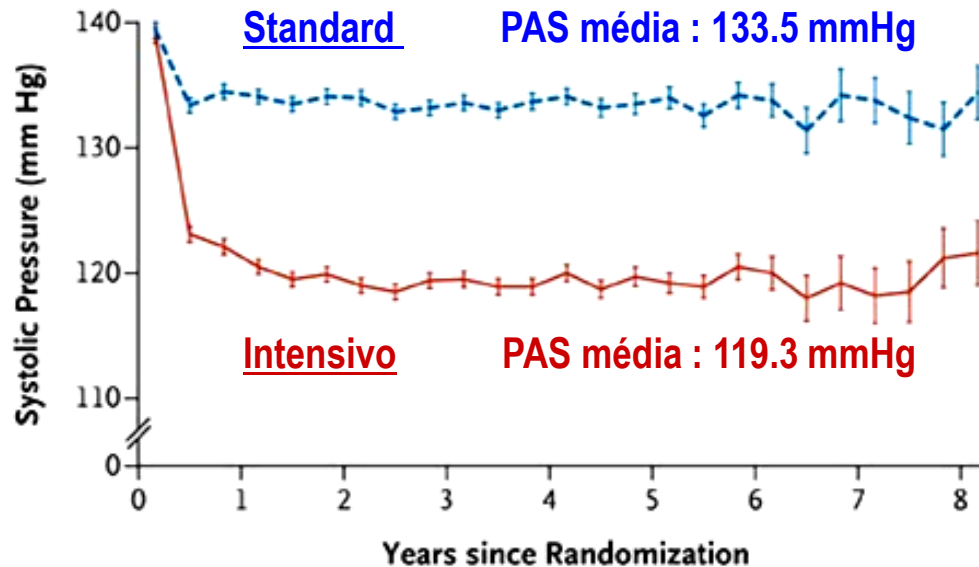
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Estudo ACCORD

Em diabéticos tipo 2 com risco cardiovascular elevado, o tratamento intensivo da PA para valores de PAS < 120 mmHg, em comparação com a redução para valores < 140 mmHg, não reduziu a taxa de eventos cardiovasculares major, fatais e não fatais.



The ACCORD Study Group. N Engl J Med 2010;10.1056/NEJMoa1001286



The NEW ENGLAND
JOURNAL of MEDICINE

The J-Curve Phenomenon and the Treatment of Hypertension

Is There a Point Beyond Which Pressure Reduction Is Dangerous?

Lisa Farnett, PharmD; Cynthia D. Mulrow, MD, MSc; William D. Linn, PharmD; Catherine R. Lucey, MD; Michael R. Tuley, PhD

We critically appraised the medical literature to evaluate whether there is a point beyond which blood pressure reduction in hypertensive subjects is no longer beneficial and possibly even deleterious. Thirteen studies that stratified cardiovascular outcomes by level of achieved blood pressure in treated hypertensive subjects who had been followed up for at least 1 year were critiqued by four independent reviewers. Data addressing population, protocol, and methodological characteristics were evaluated. Studies did not show a consistent J-shaped relationship between treated blood pressure and stroke, but they did demonstrate a consistent J-shaped relationship for cardiac events and diastolic blood pressure. The beneficial therapeutic threshold point was 85 mm Hg. We conclude that low treated diastolic blood pressure levels, ie, below 85 mm Hg, are associated with increased risk of cardiac events.

(JAMA. 1991;265:489-496)

THERE is ample scientific evidence to conclude that uncontrolled hypertension increases cardiovascular morbidity and mortality, and clinical trial data have shown that lowering elevated blood pressure levels decreases morbidity and mortality. The question that remains is: "To what level should blood pressure be lowered to optimize treatment?" Recently, some authors have focused on the dangers of lowering blood

pressure below certain levels and have suggested that excessive reductions in blood pressure may explain why major clinical trials have not shown greater effects in reducing coronary artery disease.^{1,2} These authors have proposed a "J-shaped curve" relationship between blood pressure and cardiac morbidity and mortality, whereby lowering blood pressure below a critical point is no longer beneficial and possibly even deleterious. Other authors have maintained the traditional premise of "the lower the blood pressure the better."³

Support for the traditional therapeutic goal of "the lower the better" is based largely on the results of large observational studies and actuarial data. Although these studies often included normotensive subjects and stratified cardiovascular outcomes based on baseline rather than treated levels of blood

pressure, they illustrate the controversy addressed in this review. For example, data from the massive Build and Blood Pressure Study,⁴ the mortality surveillance study of the Multiple Risk Factor Intervention Trial screeners,⁵ subsets of the Pooling Project,⁶ the Framingham study,⁷ and the Coronary Drug Project study,⁸ as well as data from several lesser known studies,⁹⁻¹⁸ have shown positive linear relationships without threshold points between baseline blood pressure levels and cardiovascular events. In general, these studies have analyzed data using best fit smooth curves between the points that relate blood pressure and cardiovascular events. These methods do not allow detection of a J-curve as to reveal a J-shaped curve individual points must be connected. Regardless of these limitations, the magnitude and consistency of these data have prompted many authorities to accept low blood pressure targets for hypertensive patients.

In fact, in a recent meta-analysis, MacMahon et al¹ combined nine observational studies and concluded that "there is no evidence of any threshold below which lower levels of blood pressure were not associated with lower levels of stroke and coronary heart disease." Their methods of analysis and results have been criticized.^{19,20} The analysis was based on baseline rather than treated blood pressure levels, and five observational studies that did not support a continuous linear relationship were excluded.^{19,20} Moreover, at

From the College of Pharmacy, The University of Texas at Austin (Drs Farnett and Linn); the Division of General Internal Medicine, the Department of Medicine, The University of Texas Health Science Center at San Antonio (Drs Mulrow and Lucey); and the Geriatric Research, Education, and Clinical Center at the Audie L. Murphy Memorial Veterans Hospital at San Antonio (Tex) (Drs Mulrow and Tuley).

Reprint requests to Ambulatory Care (11C), Audie L. Murphy Memorial Veterans Hospital, 7400 Merton Mintner Blvd, San Antonio, TX 78248 (Dr Mulrow).

The lower is not always the better



1ª Consulta



Amália, 67 anos com **hipertensão** e **diabetes** desde há 10 anos. Assintomática.

Medicada com 1 anti-hipertensor cujo nome desconhece (no fim da embalagem) e 2 ADO's.

Obesa, sedentária. Não fuma.

Portadora de análises de há 3 meses: Col:185, HbA1C:7.9%, Creat:1.0, K+:4.0, microalbuminúria. **ECG**: ritmo sinusal e HVE .

PA:190/110 mmHg com pulso rítmico 80 ppm. Obs CP negativa

Televoter: Quantos factores de resistência ao tratamento identifica na sua doente?

1. Dois
2. Três
3. Quatro
4. Cinco
5. Seis
6. Tenho dúvidas

0% 0% 0% 0% 0% 0%



Factores de resistência ao tratamento

Idade avançada (≥ 75 anos)

Pressão sistólica basal muito elevada

Hipertrofia ventricular esquerda

Sexo feminino

Obesidade

Diabetes

Doença renal crónica

Ingestão elevada de sal

Raça negra

Expansão da volémia

Factores de resistência ao tratamento

Idade avançada (≥ 75 anos)

Pressão sistólica basal muito elevada

Hipertrofia ventricular esquerda

Sexo feminino

Obesidade

Diabetes

Doença renal crónica

Ingestão elevada de sal ?

Raça negra

Factores de resistência ao tratamento que cursam com maior expansão da volémia

Idade avançada (≥ 75 anos)

Pressão sistólica basal muito elevada

Hipertrofia ventricular esquerda

Sexo feminino

Obesidade

Diabetes

Doença renal crónica

Ingestão elevada de sal ?

Raça negra

A diminuição do potássio induzida pelas tiazidas é responsável pelo aparecimento de diabetes de novo

Epidemiology/Population Studies

Changes in Serum Potassium Mediate Thiazide-Induced Diabetes

Tariq Shafi, Lawrence J. Appel, Edgar R. Miller, III, Michael J. Klag, Rulan S. Parekh

Abstract—Thiazides, recommended as first-line antihypertensive therapy, are associated with an increased risk of diabetes. Thiazides also lower serum potassium. To determine whether thiazide-induced diabetes is mediated by changes in potassium, we analyzed data from 3790 nondiabetic participants in the Systolic Hypertension in Elderly Program, a randomized clinical trial of isolated systolic hypertension in individuals aged ≥ 60 years treated with chlorthalidone or placebo. Incident diabetes was defined by self-report, antidiabetic medication use, fasting glucose ≥ 126 mg/dL, or random glucose ≥ 200 mg/dL. The mediating variable was change in serum potassium during year 1. Of the 459 incident cases of diabetes during follow-up, 42% occurred during year 1. In year 1, the unadjusted incidence rates of diabetes per 100 person-years were 6.1 and 3.0 in the chlorthalidone and placebo groups, respectively. In year 1, the adjusted diabetes risk (hazard ratio) with chlorthalidone was 2.07 (95% CI: 1.51 to 2.83; $P < 0.001$). After adjustment for change in serum potassium, the risk was significantly reduced (hazard ratio: 1.54; 95% CI: 1.09 to 2.17; $P = 0.01$); the extent of risk attenuation (41%; 95% CI: 34% to 49%) was consistent with a mediating effect. Each 0.5-mEq/L decrease in serum potassium was independently associated with a 45% higher adjusted diabetes risk (95% CI: 24% to 70%; $P < 0.001$). After year 1, chlorthalidone use was not associated with increased diabetes risk. In conclusion, thiazide-induced diabetes occurs early after initiating treatment and appears to be mediated by changes in serum potassium. Potassium supplementation might prevent thiazide-induced diabetes. This hypothesis can and should be tested in a randomized trial. (*Hypertension*. 2008;52:1022-1029.)

Key Words: hypertension ■ diabetes mellitus ■ thiazide diuretics ■ chlorthalidone ■ hypokalemia ■ potassium

A hipocaliemia induzida pelos diuréticos associa-se ao aumento do risco de eventos cardiovasculares em hipertensos idosos

Scientific Contributions

Hypokalemia Associated With Diuretic Use and Cardiovascular Events in the Systolic Hypertension in the Elderly Program

Lonneke V. Franse, Marco Pahor, Mauro Di Bari, Grant W. Somes,
William C. Cushman, William B. Applegate

Abstract—The treatment of hypertension with high-dose thiazide diuretics results in potassium depletion and a limited benefit for preventing coronary events. The clinical relevance of hypokalemia associated with low-dose diuretics has not been assessed. To determine whether hypokalemia that occurs with low-dose diuretics is associated with a reduced benefit on cardiovascular events, we analyzed data of 4126 participants in the Systolic Hypertension in the Elderly Program (SHEP), a 5-year randomized, placebo-controlled clinical trial of chlorthalidone-based treatment of isolated systolic hypertension in older persons. After 1 year of treatment, 7.2% of the participants randomized to active treatment had a serum potassium <3.5 mmol/L compared with 1% of the participants randomized to placebo ($P<0.001$). During the 4 years after the first annual visit, 451 participants experienced a cardiovascular event, 215 experienced a coronary event, 177 experienced stroke, and 323 died. After adjustment for known risk factors and study drug dose, the participants who received active treatment and who experienced hypokalemia had a similar risk of cardiovascular events, coronary events, and stroke as those randomized to placebo. Within the active treatment group, the risk of these events was 51%, 55%, and 72% lower, respectively, among those who had normal serum potassium levels compared with those who experienced hypokalemia ($P<0.05$). The participants who had hypokalemia after 1 year of treatment with a low-dose diuretic did not experience the reduction in cardiovascular events achieved among those who did not have hypokalemia. (*Hypertension*. 2000;35:1025-1030.)

Key Words: hypokalemia ■ diuretics ■ myocardial infarction ■ stroke ■ clinical trials

NORMA

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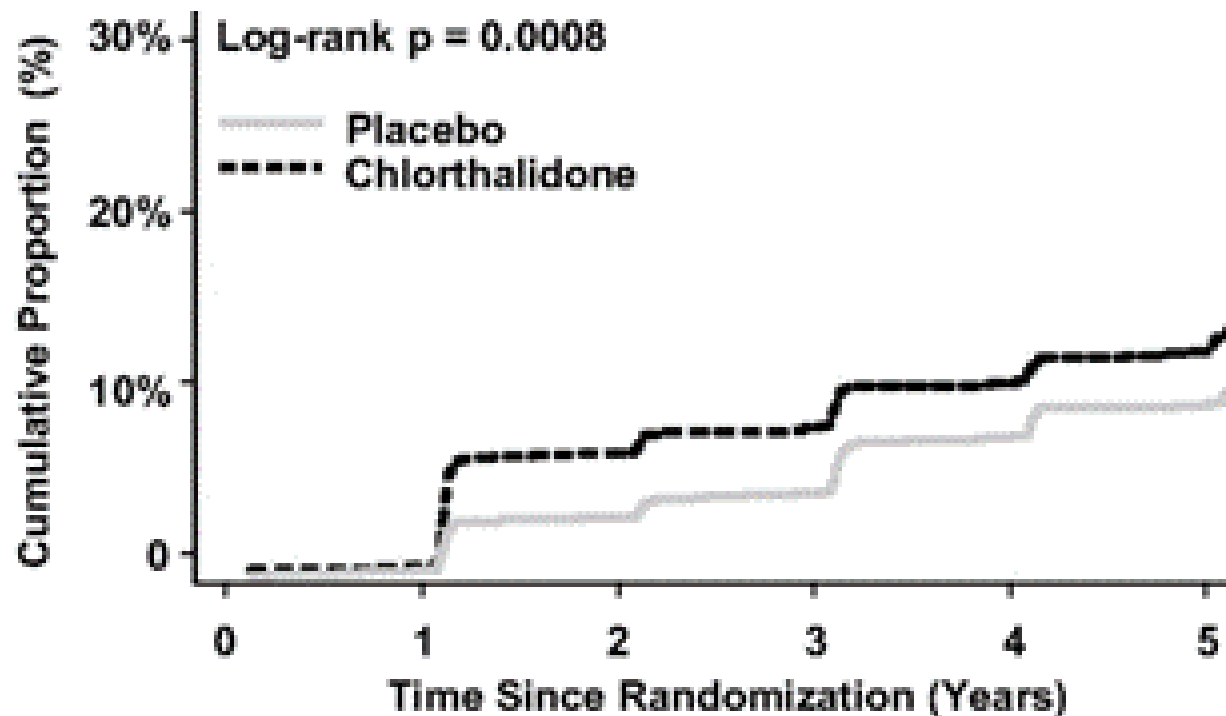
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ASSUNTO:	Terapêutica na Hipertensão Arterial: diuréticos
PALAVRAS-CHAVE:	Diuréticos
PARA:	Médicos do Serviço Nacional de Saúde
CONTACTOS:	Departamento da Qualidade na Saúde - Programa Nacional de Prevenção e Controlo das Doenças Cardiovasculares (espigamacedo@dgs.pt)

Nos termos da alínea c) do n.º 2 do artigo 2.º do Decreto Regulamentar n.º 66/2007, de 29 de Maio, na redacção dada pelo Decreto Regulamentar n.º 21/2008, de 2 de Dezembro, emite-se a Norma seguinte:

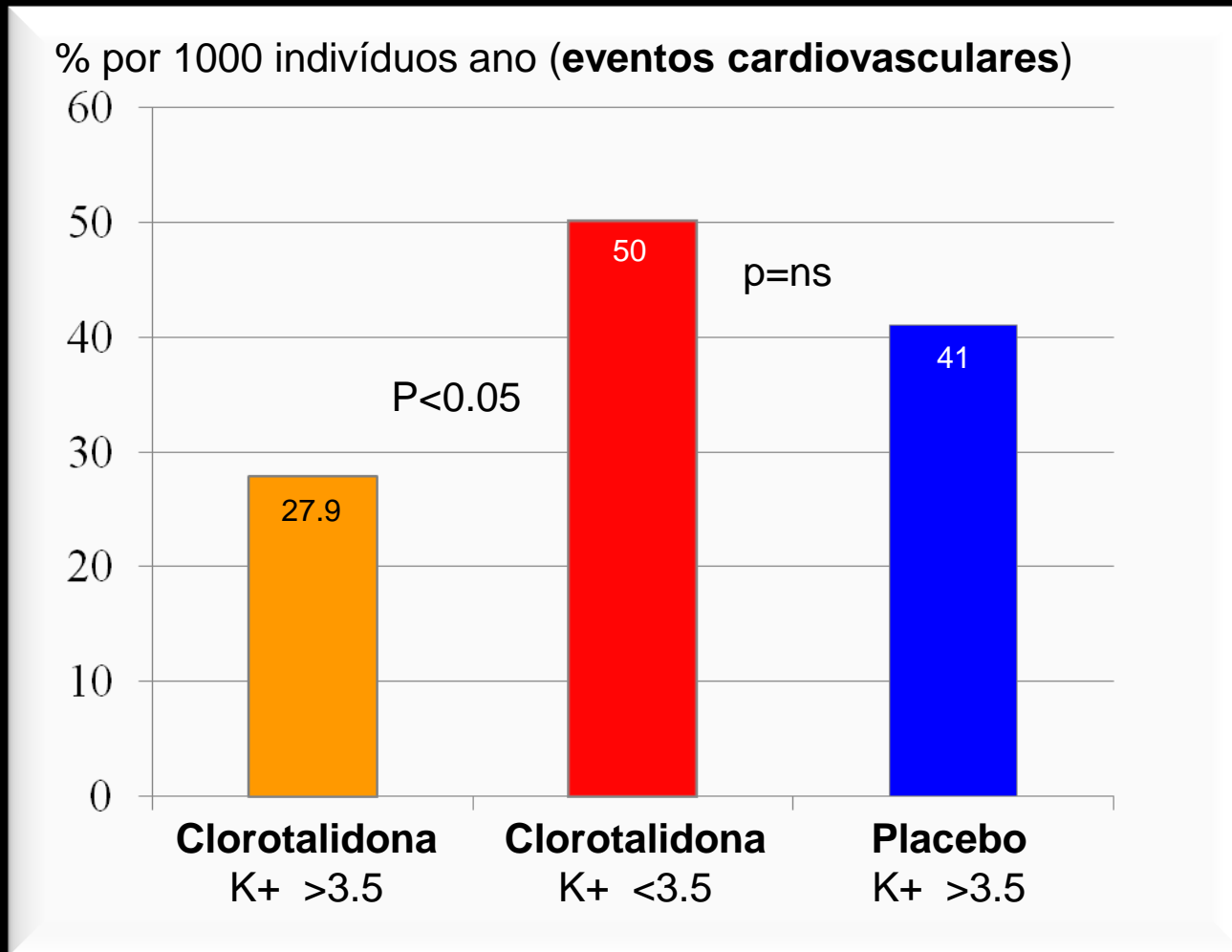
1. Os diuréticos tiazídicos¹ em doses baixas (12,5 – 25 mg/dia de hidroclorotiazida, clortalidona e a indapamida), são usados como agentes de primeira linha no tratamento da hipertensão arterial.
2. A medicação anti-hipertensora é iniciada nos doentes com pressão arterial sistólica ≥ 140 mmHg e/ou pressão arterial diastólica > 90 mmHg, com ajuste de dose, de forma a ser obtido um resultado terapêutico inferior a estes valores.
3. Os diuréticos tiazídicos estão contra-indicados em casos de gota.
4. Excepções à presente Norma são fundamentadas no processo clínico de doente com hipertensão arterial essencial.

Incidência de Diabetes de novo no Estudo SHEP

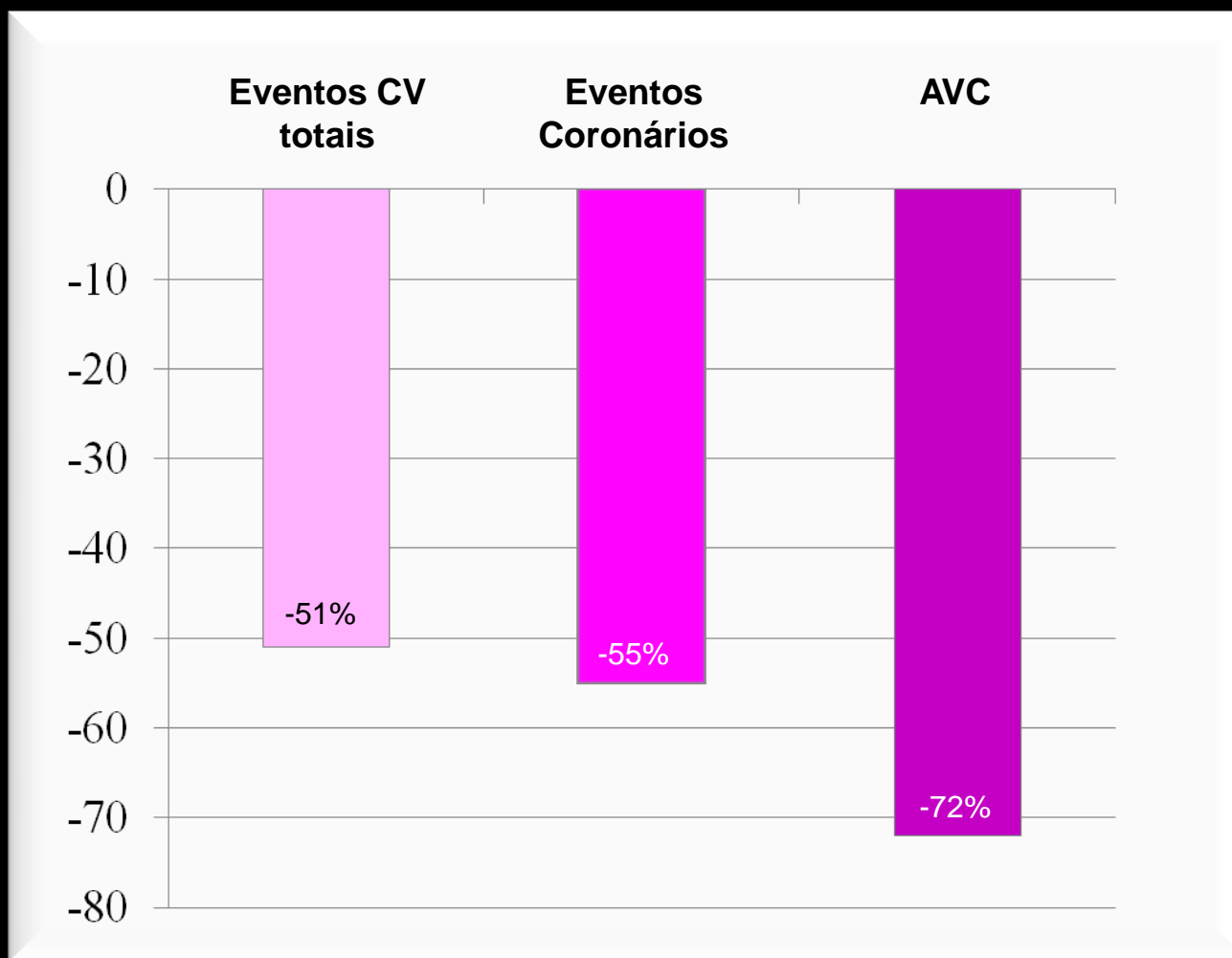


ALLHAT Study

Os doentes tratados com Clorotalidona que desenvolveram hipocaliemia tiveram um risco de eventos cardiovasculares semelhante aos aleatorizados para placebo.



% Redução dos eventos cardiovasculares nos hipertensos com K⁺ normal (versus ↓K⁺)



Diur

+

BERA

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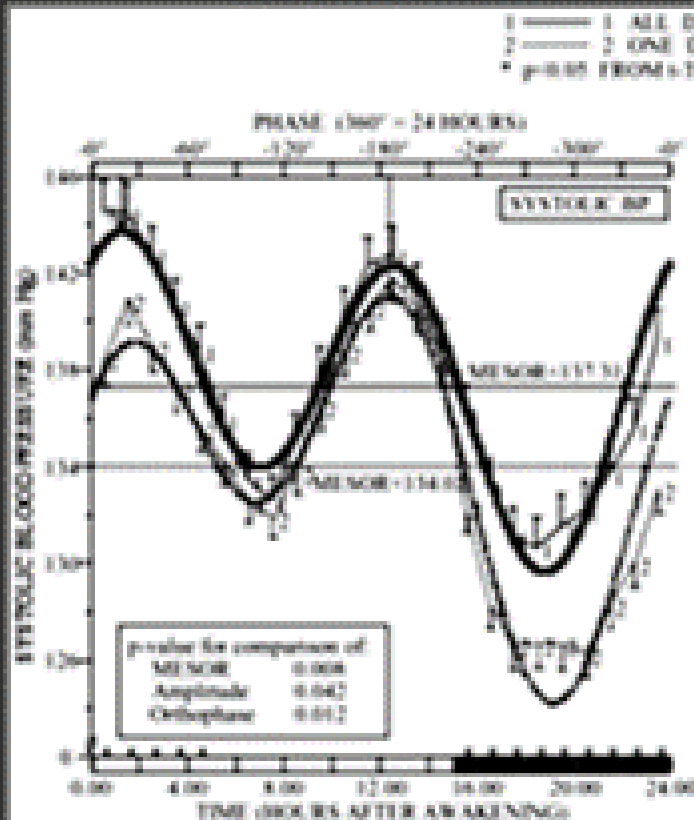
Amlodipina
Felodipina
Lercanidipina
Nifedipina

A detailed illustration of a man with a distressed expression, wide eyes, and an open mouth, trapped inside the upper bulb of a large, ornate hourglass. He is reaching out with both hands against the glass. The hourglass is made of clear glass with a wooden frame and stands on a wooden base. A large pile of sand has accumulated in the lower bulb, while the upper bulb is mostly empty. The background is dark, and the lighting highlights the man and the hourglass. The text "Cronoterapia da Hipertensão" is overlaid in the center in a bold, yellow font.

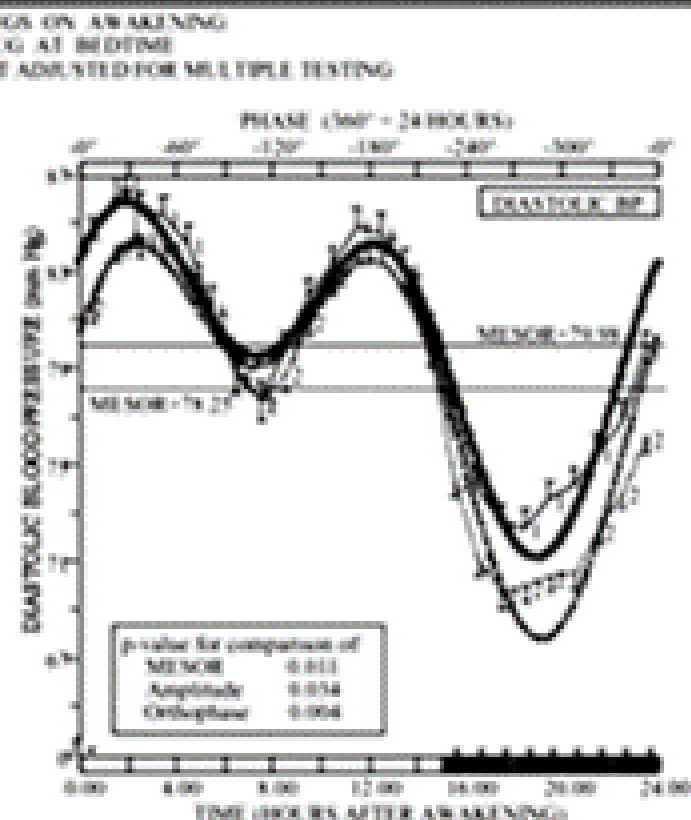
Cronoterapia da Hipertensão

Redução acrescida da PA com a administração de ≥ 1 anti-hipertensor à noite

PA Sistólica



PA Diastólica



Cronoterapia da Hipertensão



Hipertensão Resistente

Definição

Toda a hipertensão não controlada apesar do tratamento com três anti-hipertensores, sendo um deles (idealmente) um diurético.

Resistant Hypertension: Diagnosis, Evaluation, and Treatment

A Scientific Statement From the American Heart Association Professional Education Committee of the Council for High Blood Pressure Research

David A. Calhoun, MD, FAHA, Chair; Daniel Jones, MD, FAHA; Stephen Textor, MD, FAHA;
David C. Goff, MD, FAHA; Timothy P. Murphy, MD, FAHA; Robert D. Toto, MD, FAHA;
Anthony White, PhD; William C.ushman, MD, FAHA; William White, MD;
Domenic Sica, MD, FAHA; Keith Ferdinand, MD; Thomas D. Giles, MD;
Bonita Falkner, MD, FAHA; Robert M. Carey, MD, MACP, FAHA

Abstract—Resistant hypertension is a common clinical problem faced by both primary care clinicians and specialists. While the exact prevalence of resistant hypertension is unknown, clinical trials suggest that it is not rare, involving perhaps 20% to 30% of study participants. As older age and obesity are 2 of the strongest risk factors for uncontrolled hypertension, the incidence of resistant hypertension will likely increase as the population becomes more elderly and heavier. The prognosis of resistant hypertension is unknown, but cardiovascular risk is undoubtedly increased as patients often have a history of long-standing, severe hypertension complicated by multiple other cardiovascular risk factors such as obesity, sleep apnea, diabetes, and chronic kidney disease. The diagnosis of resistant hypertension requires use of good blood pressure technique to confirm persistently elevated blood pressure levels. Pseudoresistance, including lack of blood pressure control secondary to poor medication adherence or white coat hypertension, must be excluded. Resistant hypertension is almost always multifactorial in etiology. Successful treatment requires identification and reversal of lifestyle factors contributing to treatment resistance; diagnosis and appropriate treatment of secondary causes of hypertension; and use of effective multidrug regimens. As a subgroup, patients with resistant hypertension have not been widely studied. Observational assessments have allowed for identification of demographic and lifestyle characteristics associated with resistant hypertension, and the role of secondary causes of hypertension in promoting treatment resistance is well documented; however, identification of broader mechanisms of treatment resistance is lacking. In particular, attempts to elucidate potential genetic causes of resistant hypertension have been limited. Recommendations for the pharmacological treatment of resistant hypertension remain largely empiric due to the lack of systematic assessments of 3 or 4 drug combinations. Studies of resistant hypertension are limited by the high cardiovascular risk of patients within this subgroup, which generally precludes safe withdrawal of medications; the presence of multiple disease processes (eg, sleep apnea, diabetes, chronic kidney disease, atherosclerotic disease) and their associated medical therapies, which confound interpretation of study results; and the difficulty in enrolling large numbers of study participants. Expanding our understanding of the causes of resistant hypertension and thereby potentially allowing for more effective prevention and/or treatment will be essential to improve the long-term clinical management of this disorder. (*Hypertension*. 2008;51:1403-1419.)

Key Words: AHA Scientific Statements ■ hypertension ■ blood pressure

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

This statement was approved by the American Heart Association Science Advisory and Coordinating Committee on January 3, 2008. A single reprint is available by calling 800-242-8721 (US only) or by writing the American Heart Association, Public Information, 7272 Greenville Ave, Dallas, TX 75231-4596. Ask for reprint No. 71-0439. A copy of the statement is also available at <http://www.americanheart.org/presenter.jhtml?identifier=3003999> by selecting either the "topic list" link or the "chronological list" link. To purchase additional reprints, call 843-216-2533 or e-mail kelle.ramsay@wolterskluwer.com.

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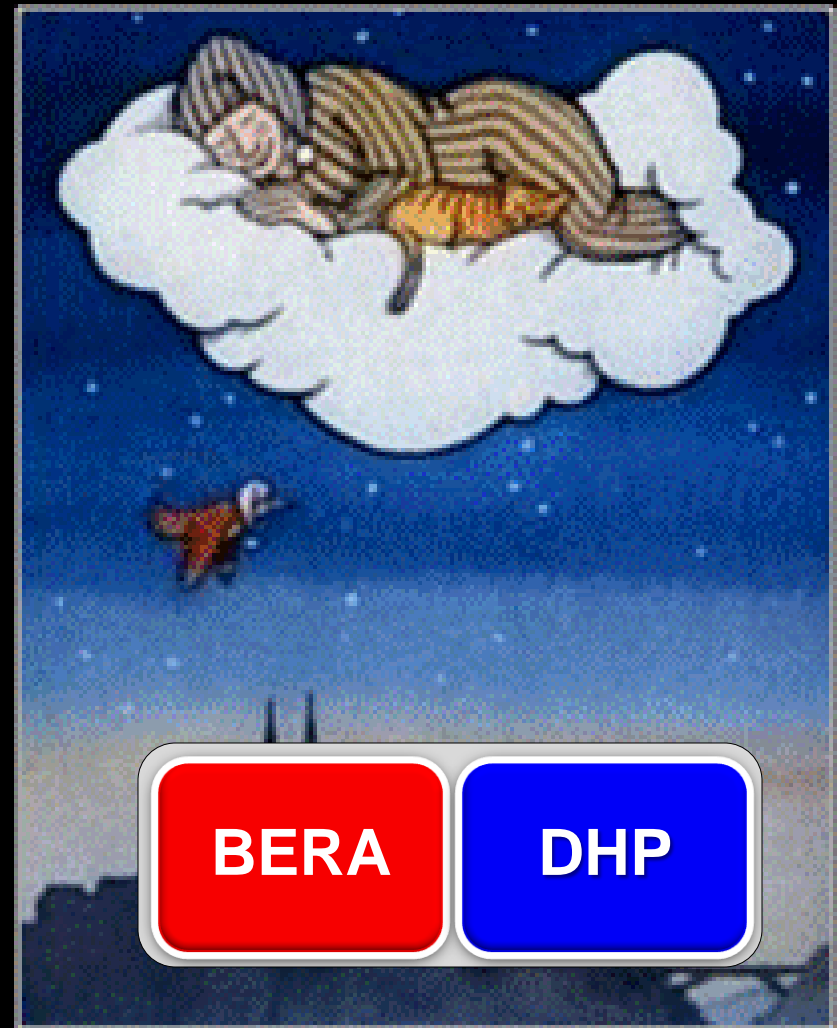
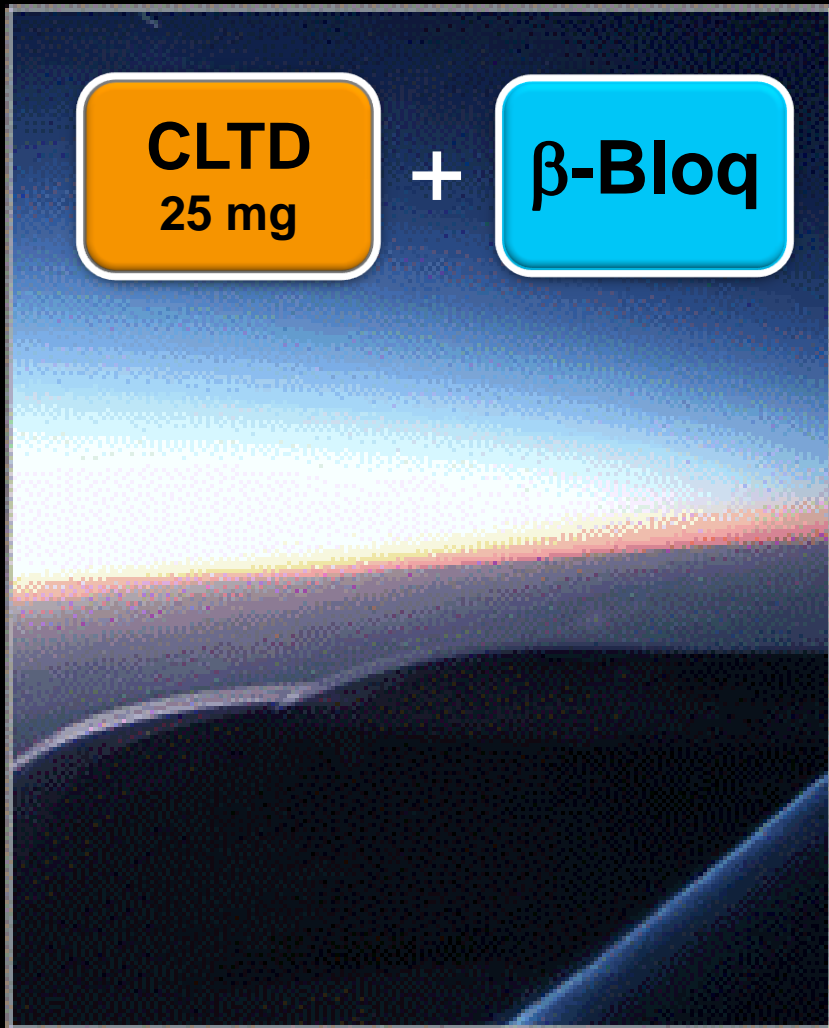
HTA Ligeira / moderada
↓ Factores de resistência
ao tratamento



HTA moderada / grave
↑ Factores de resistência
ao tratamento



Cronoterapia da Hipertensão



Tratamento da Hipertensão Resistente

CLTD
25 mg

+

Espiro
12.5 - 25 mg

+

β -Bloq

BERA

DHP

HTA ligeira
↓ Factores de resistência
ao tratamento

BERA

BERA

HCTZ
12.5-25 mg

HTA moderada
↓ Factores de resistência
ao tratamento

BERA

HCTZ

BERA

DHP

DHP

+

BERA

HCTZ

BERA

DHP

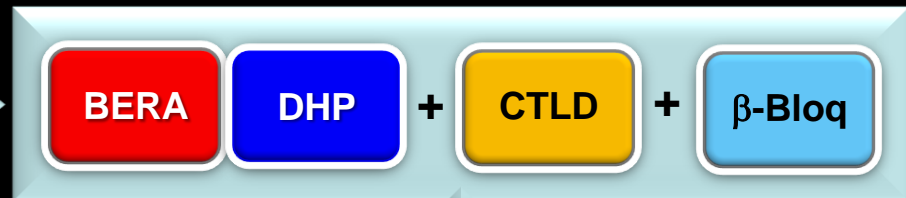
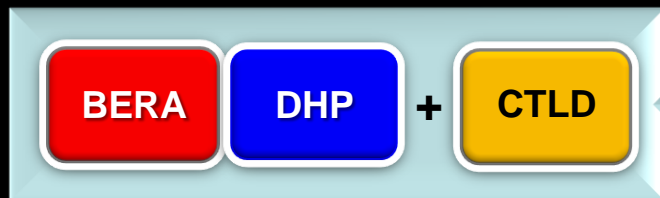
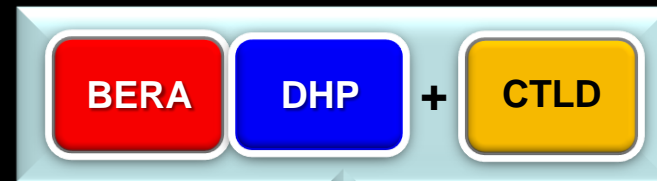
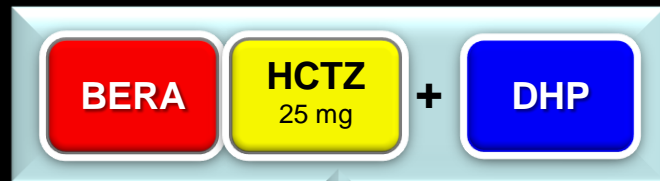
+

CTLD

HTA Resistente

HTA Resistente

HTA Resistente



Tratamento da Hipertensão Resistente

CLTD
25 mg

+

Espiro
12.5 - 25 mg

+

β -Bloq

BERA

DHP