Um(ns) autor(es) português(es) no British Medical Journal

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Esquema da comunicação

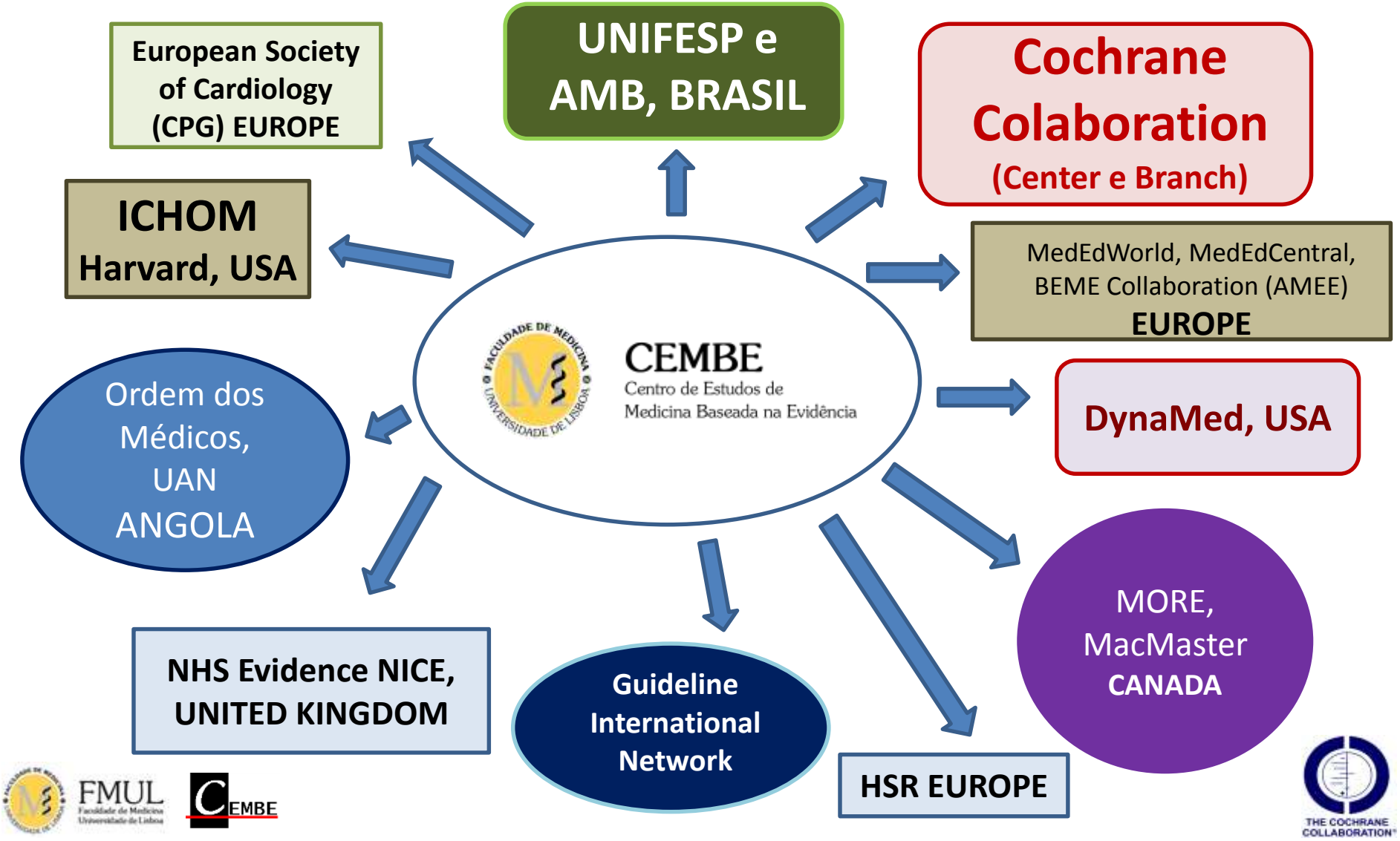
- O que é o Centro de Estudos de Medicina Baseada na Evidência da Faculdade de Medicina da Universidade de Lisboa
- Publicar numa revista de topo
- As revisões sistemáticas/meta-análises publicadas pelo CEMBE no British Medical Journal
- Discussão.

O CEMBE no CAML

Origens do CEMBE

- Criado pelo Comité Científico da FMUL em 1999
- Unidade estrutural da FMUL
- A. Vaz Carneiro nomeado como Director
- Objectivos prioritários:
  - Promoção do conhecimento científico
  - Investigação clínica e epidemiológica
  - Formação a todos os níveis (pré, pós-graduada, CME e avançada – Mestrados/Doutoramentos)
  - Consultoria científica externa
  - Networking com Centros Internacionais.

A “rede” internacional do CEMBE



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Departamento de investigação

- Educação médica
  - BEME review ("OSCE for pre-med students")
- Medicina/saúde
  - Investigação secundária (revisões sistemáticas/meta-análises)
  - Estudos observacionais (prevalência e incidência)
  - Estudos de custo e carga da doença
  - Investigação em resultados em saúde (HOR) e em Serviços de Saúde (HSR)
  - Artigos científicos de metodologia MBE
  - Metodologia de Normas de Orientação Clínica (AGREE, ADAPTE, etc.)
- Gestão baseada na Evidência
- Políticas Baseadas na Evidência
- Registos de doentes.

Caffeine Exposure and the Risk of Parkinson's Disease: A Systematic Review and Meta-Analysis of Observational Studies

Efficacy of lipid lowering drug treatment for diabetic and non-diabetic patients: meta-analysis of randomised controlled trials

João Costa, Margarida Borges, Cláudio David, António Vaz Carneiro

British Medical Journal 2006;332:115-1124

Caffeine Intake and Dementia: Systematic Review and Meta-Analysis

JOURNAL OF PALLIATIVE MEDICINE
Volume 17, Number X, 2014
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DOI: 10.1089/jpm.2013.0567

Efficacy of Dignity Therapy on Depression and Anxiety in Portuguese Terminally Ill Patients: A Phase II Randomized Controlled Trial

Miguel Julião, MD,[1–4] Fátima Oliveira, RN,[5] Baltazar Nunes, PhD,[6] António Vaz Carneiro, MD, PhD,[2] and António Barbosa, MD, PhD[1,7]

The Burden of Disease and the Cost of Illness Attributable to Alcohol Drinking—Results of a National Study

Helena Cortez-Pinto, Miguel Gouveia, Luis dos Santos Pinheiro, João Costa, Margarida Borges and António Vaz Carneiro

BMJ

BMJ 2012;345:e4260 doi: 10.1136/bmj.e4260 (Published 11 July 2012) Page 1 of 20

RESEARCH

2009; 31: 112–124 MEDICAL TEACHER

A comprehensive checklist for reporting the use of OSCEs

MADALENA PATRÍCIO[1], MIGUEL JULIÃO[2], FILIPA FARELEIRA[3], MEREDITH YOUNG[4], GEOFFREY NORMAN[4] & ANTÓNIO VAZ CARNEIRO[1]

[1]Faculty of Medicine of the University of Lisbon, Portugal, [2]McMaster University, Canada

Risk of pneumonia associated with use of angiotensin converting enzyme inhibitors and angiotensin receptor blockers: systematic review and meta-analysis

OPEN ACCESS

Daniel Caldeira *cardiologist resident, assistant of clinical pharmacology*[1], Joana Alarcão *scientific consultant, assistant of clinical pharmacology*[2], António Vaz-Carneiro *clinical professor of medicine, director of the Center for Evidence-Based Medicine*[2,3], João Costa *professor of clinical pharmacology, coordinator of the Portuguese Cochrane Centre*[1,2,3]

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Como publicar numa revista de topo?

Types of papers in medical science

- Research papers
  - Clinical trials
  - Diagnostic studies
  - Prognostic studies
  - Systematic reviews
  - Case reports
  - Case series
  - …
- Editorials
- Review articles
- Abstracts/posters
- Letters to the editor
- Thesis (master, PhD)
- Book reviews
- …

20 steps in publishing a paper…
(E. Huth 1990)

1. Decide on the scientific question of the paper
2. Decide whether the paper is worth writing
3. Decide on the importance of the paper (*so-what? question*)
4. Decide on the audience for the paper (*who cares? question*)
5. Select the journal
6. Search the literature
7. Decide on authorship
8. Assemble the materials needed to write the paper
9. Look up manuscript requirements for the journal
10. Consider the general structure of the text.

20 steps in publishing a paper…
(E. Huth 1990)

11. Develop a sketch or outline for the first draft
12. Write the first draft
13. Revise the first and subsequent drafts
14. Revise your prose for fluency, clarity, accuracy, economy…
15. Make sure that the details of the scientific style are correct
16. Prepare figures and tables
17. Revise the last completed draft of the final manuscript
18. Get into the journal website
19. Respond to the editors and reviewers questions
20. Get the PDF of the paper …

As revisões sistemáticas/meta-análises publicadas pelo CEMBE no BMJ

RS no BMJ

- Costa J, Borges M, David C, Vaz Carneiro A. Efficacy of lipid lowering drug treatment for diabetic and non-diabetic patients: meta-analysis of randomized controlled trials. **BMJ 2006;332:115-1124**
- Caldeira D, Alarcão J, Vaz-Carneiro A, Costa J. Risk of pneumonia associated with use of angiotensin converting enzyme inhibitors and angiotensin receptor blockers: systematic review and meta-analysis. **BMJ 2012;345:e4260**

Efficacy of lipid lowering drug treatment for diabetic and non-diabetic patients: meta-analysis of randomised controlled trials

João Costa, Margarida Borges, Cláudio David, António Vaz Carneiro

BMJ 2006;332:115-1124

Objective To evaluate the clinical benefit of lipid lowering drug treatment in patients with and without diabetes mellitus, for primary and secondary prevention.
Design Systematic review and meta-analysis.
Data sources Cochrane, Medline, Embase, and reference lists up to April 2004.
Study selection Randomised, placebo controlled, double blind trials with a follow-up of at least three years that evaluated lipid lowering drug treatment in patients with and without diabetes mellitus.
Data extraction Two independent reviewers extracted data. The primary outcome was major coronary events defined as coronary heart disease death, non-fatal myocardial infarction, or myocardial revascularisation procedures.
Results Twelve studies were included. Lipid lowering drug treatment was found to be at least as effective in diabetic patients as in non-diabetic patients. In primary prevention, the risk reduction for major coronary events was 21% (95% confidence interval 11% to 30%; $P < 0.0001$) in diabetic patients and 23% (12% to 33%; $P = 0.0003$) in non-diabetic patients. In secondary prevention, the corresponding risk reductions were 21% (10% to 31%; $P = 0.0005$) and 23% (19% to 26%; $P \leq 0.00001$). However, the absolute risk difference was three times higher in secondary prevention. When results were adjusted for baseline risk, diabetic patients benefited more in both primary and secondary prevention. Blood lipids were reduced to a similar degree in both groups.
Conclusions The evidence that lipid lowering drug treatment (especially statins) significantly reduce cardiovascular risk in diabetic and non-diabetic patients is strong and suggests that diabetic patients benefit more, in both primary and secondary prevention. Future research should define the threshold for treatment of these patients and the desired target lipid concentrations, especially for primary prevention.

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bmj.com

Diabetes and lipid lowering: where are we?

John P D Reckless

BMJ 2006;332;1103-1104
doi:10.1136/bmj.332.7550.1103

Editorial

Research p 1115

Premature morbidity and mortality is substantially due to cardiovascular disease, with tobacco use, hypertension, and abnormal lipids being the main modifiable causal factors. Glycaemia is directly related to cardiovascular risk,[1] and in people with diabetes the risk of cardiovascular disease approaches that in non-diabetic people with previous myocardial infarction.[2 3]

Because most people with type 2 diabetes have an absolute risk of cardiovascular disease of 20% or more over 10 years, guidelines suggest active intervention to reduce risk factors in patients with diabetes, including statin therapy to reduce the serum concentration of low density lipoprotein cholesterol (LDL-C) to <2 mmol/l.[3] In this week's *BMJ* Costa and colleagues report a meta-analysis of trials of lipid lowering drug therapy for primary and secondary coronary heart disease prevention in patients with and without diabetes.[4]

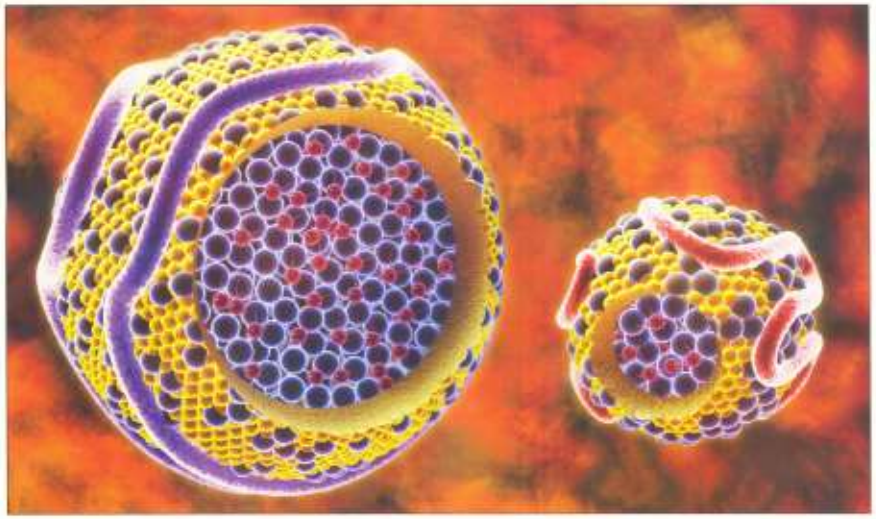
Review by the National Institute for Health and led trials (six primary prevention, eight secondary prevention) which fulfilled the criteria of having >500 patients per group treated for three years in whom cardiovascular outcome data for diabetes and non-diabetes subgroups could be identified separately. What did the meta-analysis find? In both primary and secondary prevention of major coronary events there were highly significant and similar relative risk reductions of 21% (diabetes) and 23% (non-diabetes), in the presence of similar lipid changes. In the analyses of secondary prevention the absolute risk was three times higher than in those for primary prevention.

Are there any difficulties with this study? This meta-analysis looked at lipid lowering drugs in general and not just statins (the agents of first choice to achieve target LDL cholesterol concentrations). Two studies used the fibrate gemfibrozil, which is less well tolerated and has more potential side effects than other agents,[3] but their omission would not materially affect the over-

13 May 2006

BMJ

332:1103–1162 No 7550 13 MAY 2006 Clinical research ISSN 0959 8138



Lipid lowering drugs in diabetes

They work, so use them p1105, p1115

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Risk of pneumonia associated with use of angiotensin converting enzyme inhibitors and angiotensin receptor blockers: systematic review and meta-analysis

Daniel Caldeira *cardiologist resident, assistant of clinical pharmacology*[1], Joana Alarcão *scientific consultant, assistant of clinical pharmacology*[2], António Vaz-Carneiro *clinical professor of medicine, director of the Center for Evidence-Based Medicine*[23], João Costa *professor of clinical pharmacology, coordinator of the Portuguese Cochrane Centre*[123]

[1]Laboratory of Clinical Pharmacology and Therapeutics, Faculty of Medicine, University of Lisbon; [2]Center for Evidence-Based Medicine, Faculty of Medicine, University of Lisbon, Avenue Professor Egas Moniz, 1649-028, Lisbon, Portugal; [3]Cochrane Coordinating Center Portugal, Faculty of Medicine, University of Lisbon

BMJ 2012;345:e4260

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Caldeira D, Alarcão J, Vaz-Carneiro A, Costa J. Risk of pneumonia associated with use of angiotensin converting enzyme inhibitors and angiotensin receptor blockers: systematic review and meta-analysis. BMJ 2012;345:e4260

Abstract

Objective To systematically review longitudinal studies evaluating use of angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) and risk of pneumonia.

Design Systematic review and meta-analysis.

Data sources Medline through PubMed, Web of Science with conference proceedings (inception to June 2011), and US Food and Drug Administration website (June 2011). Systematic reviews and references of retrieved articles were also searched.

Study selection Two reviewers independently selected randomised controlled trials and cohort and case-control studies evaluating the use of ACE inhibitors or ARBs and risk of pneumonia and retrieved characteristics of the studies and data estimates.

Data synthesis The primary outcome was incidence of pneumonia and the secondary outcome was pneumonia related mortality. Subgroup analyses were carried according to baseline morbidities (stroke, heart failure, and chronic kidney disease) and patients' characteristics (Asian and non-Asian). Pooled estimates of odds ratios and 95% confidence intervals were derived by random effects meta-analysis. Adjusted frequentist indirect comparisons between ACE inhibitors and ARBs were estimated and combined with direct evidence whenever available. Heterogeneity was assessed using the I^2 test.

Results 37 eligible studies were included. ACE inhibitors were associated with a significantly reduced risk of pneumonia compared with control treatment (19 studies: odds ratio 0.66, 95% confidence interval 0.55 to 0.80; I^2=79%) and ARBs (combined direct and indirect odds ratio estimate 0.69, 0.56 to 0.85). In patients with stroke, the risk of pneumonia was also lower in those treated with ACE inhibitors compared with control treatment (odds ratio 0.46, 0.34 to 0.62) and ARBs (0.42, 0.22 to 0.80). ACE inhibitors were associated with a significantly reduced risk of pneumonia among Asian patients (0.43, 0.34 to 0.54) compared with non-Asian patients (0.82, 0.67 to 1.00; P<0.001). Compared with control treatments, both ACE inhibitors (seven studies: odds ratio 0.73, 0.58 to 0.92; I^2=51%) and ARBs (one randomised controlled trial: 0.63, 0.40 to 1.00) were associated with a decrease in pneumonia related mortality, without differences between interventions.

Conclusions The best evidence available points towards a putative protective role of ACE inhibitors but not ARBs in risk of pneumonia. Patient populations that may benefit most are those with previous stroke and Asian patients. ACE inhibitors were also associated with a decrease in pneumonia related mortality, but the data lacked strength.

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Table of Contents

Review

Coronary Revascularization in Diabetic Patients

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Review: ACE inhibitors reduce risk for pneumonia

Caldeira D, Alarcão J, Vaz-Carneiro A, Costa J. Risk of pneumonia associated with use of angiotensin converting enzyme inhibitors and angiotensin receptor blockers: systematic review and meta-analysis. BMJ. 2012;345:e4260.

Clinical impact ratings: ★★★★★☆☆ ★★★★★★☆ ★★★★★★☆ ★★★★★★☆

Question

Do angiotensin-converting enzyme (ACE) inhibitors and angiotensin-receptor blockers (ARBs) affect risk for pneumonia?

Review scope

Included studies compared ACE inhibitors or ARBs with placebo, each other, or any other active drug in patients with any baseline disease or risk factors, and had predefined outcomes. Outcomes were pneumonia (pneumonia, lower respiratory tract infection, or hospitalization due to lower respiratory tract infection) and pneumonia-related mortality (death directly related to pneumonia, or in-hospital death or death within 30 d of pneumonia onset). Data on upper respiratory tract infections were excluded.

Review methods

MEDLINE, Web of Science with conference proceedings, reference lists, reviews, and the US Food and Drug Administration (FDA) Web site were searched to June 2011 for randomized controlled trials (RCTs), cohort studies, and case–control studies. 37 studies met selection criteria: 18 RCTs (n = 74 097, mean age range 45 to 78 y, mean follow-up range 0.2 to 4.8 y), 11 cohort studies, and 8 case–control studies. 7 RCTs compared ACE inhibitors with controls, 9 compared ARBs with controls, and 2 compared ACE inhibitors with ARBs. 17 RCTs had adequate randomization, 8 had concealed allocation, 14 had blinding of outcome assessors, and 16 described withdrawals; 2 reported pneumonia as a prespecified outcome. Only results from RCTs are presented in this abstract.

Main results

ACE inhibitors had a lower risk for pneumonia than control treatment and did not differ from ARBs (Table); ARBs did not differ from control. ACE inhibitors and ARBs did not differ from control treatment or each other for pneumonia-related mortality (Table).

Angiotensin–converting enzyme (ACE) inhibitors and angiotensin–receptor blockers (ARBs) and risk for pneumonia*

Outcomes	Comparisons	Number of trials (n)	Odds ratio (95% CI)
Pneumonia	ACE inhibitors vs control	5 (17 565)	0.69 (0.56 to 0.85)†
	ARBs vs control	9 (38 877)	0.90 (0.79 to 1.01)
	ACE inhibitors vs ARBs	1 (17 118)	0.89 (0.75 to 1.05)
Pneumonia-related mortality	ACE inhibitors vs control	3 (6501)	0.61 (0.20 to 1.90)
	ARBs vs control	1 (7599)	0.63 (0.40 to 1.00)
	ACE inhibitors vs ARBs	1 (141)	7.29 (0.14 to 367)

**Abbreviations defined in Glossary. Odds ratios reported in article based on a random-effects model. Control groups included placebo or any other active drug.*

†Statistically significant.

Conclusion

Angiotensin-converting enzyme inhibitors reduce risk for pneumonia; the effect for angiotensin-receptor blockers is not clear.

Source of funding: No external funding.

For correspondence: Dr. J. Costa, University of Lisbon, Lisbon, Portugal. E-mail jncosta@fm.ul.pt.

Commentary

For several years, it has been suggested that ACE inhibitors may decrease the risk for pneumonia. The Perindopril Protection Against Recurrent Stroke Study, an RCT done in Australasia, Europe, and Asia, found that patients of Asian ethnicity who had a previous stroke or transient ischemic attack and were treated with an ACE inhibitor had a reduced risk for pneumonia (1). A Japanese study of patients with stroke had similar findings (2). Caldeira and colleagues did a meta-analysis, including RCTs and observational studies, to examine the potential effect of both ACE inhibitors and ARBs on development of pneumonia. The results suggest that patients receiving ACE inhibitors, but not ARBs, had reduced risk for pneumonia that was pronounced in Asian patients. Caldeira and colleagues suggest that ACE inhibitors might be continued in patients at high risk for pneumonia, even if ACE inhibitor–induced cough develops.

Several concerns limit the conclusions of the study, the most important being that pneumonia was not a primary outcome in most of the studies. Pneumonia incidents were compiled from reported adverse events in several studies, and others were obtained from FDA regulatory documents. Analyses had significant heterogeneity because multiple study types were included, and reporting bias was a possibility.

At this time, evidence is insufficient to select an ACE inhibitor over an ARB for patients with hypertension, diabetes, or left ventricular systolic dysfunction. For patients of Asian descent with stroke, one might be tempted to use an ACE inhibitor based on this and previous studies. However, further research using pneumonia as a specified outcome is needed. It would be interesting to see if the protective effect in patients of Asian descent persists in Asian patients living in Europe or North America.

Randolph J. Lipchik, MD
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