Кафедра клинической фармакологии и доказательной медицины

Проект на тему:

«Какая из групп препаратов первой линии у больных с артериальной гипертензией достоверно снижает риск смерти: БРА или ингибиторы АПФ»

Подготовили:
Мусабаева А.
Тайтикенова Д.
Яковлева А.
Тойчиев Ш.
Проверила:
Калиева Ш.С.

Актуальность

Вопросы лечения артериальной гипертензии актуальны и по сей день, особенно для врача общей практики, встречающимся с этой проблемой ежедневно.

По эпидемиологическим данным артериальная гипертензия (АГ) является одним из широко распространенных заболеваний сердечно-сосудистой системы в Казахстане и за рубежом.

Распространенность артериальной гипертензии в Казахстане по данным различных исследователей варьируется от 15,2 до 27% (по данным Атырауской городской поликилиники №3).

Цель

Целью нашего проекта явилось выявить, какой из препаратов блокаторов ренин-ангиотензиновой системы рациональнее использовать как препарат выбора первой линии при лечении больных с артериальной гипертензией

Методы исследования

- PubMed
- Cochrane library
- National Institute for Health and Care Exellence
- The Journal of the American Medical Association
- The BMJ
- The Lancet

Abstract ▾ Send to: ▾

Eur Heart J. 2012 Aug;33(16):2088-97. doi: 10.1093/eurheartj/ehs075. Epub 2012 Apr 17.

Angiotensin-converting enzyme inhibitors reduce mortality in hypertension: a meta-analysis of randomized clinical trials of renin-angiotensin-aldosterone system inhibitors involving 158,998 patients.

van Vark LC[1], Bertrand M, Akkerhuis KM, Brugts JJ, Fox K, Mourad JJ, Boersma E.

⊕ **Author information**

Abstract

AIMS: Renin-angiotensin-aldosterone system (RAAS) inhibitors are well established for the reduction in cardiovascular morbidity, but their impact on all-cause mortality in hypertensive patients is uncertain. Our objective was to analyse the effects of RAAS inhibitors as a class of drugs, as well as of angiotensin-converting enzyme (ACE) inhibitors and AT1 receptor blockers (ARBs) separately, on all-cause mortality.

METHODS AND RESULTS: We performed a pooled analysis of 20 cardiovascular morbidity-mortality trials. In each trial at least two-thirds of the patients had to be diagnosed with hypertension, according to the trial-specific definition, and randomized to treatment with an RAAS inhibitor or control treatment. The cohort included 158 998 patients (71 401 RAAS inhibitor; 87 597 control). The incidence of all-cause death was 20.9 and 23.3 per 1000 patient-years in patients randomized to RAAS inhibition and controls, respectively. Overall, RAAS inhibition was associated with a 5% reduction in all-cause mortality (HR: 0.95, 95% CI: 0.91-1.00, P= 0.032), and a 7% reduction in cardiovascular mortality (HR: 0.93, 95% CI: 0.88-0.99, P= 0.018). The observed treatment effect resulted entirely from the class of ACE inhibitors, which were associated with a significant 10% reduction in all-cause mortality (HR: 0.90, 95% CI: 0.84-0.97, P= 0.004), whereas no mortality reduction could be demonstrated with ARB treatment (HR: 0.99, 95% CI: 0.94-1.04, P= 0.683). This difference in treatment effect between ACE inhibitors and ARBs on all-cause mortality was statistically significant (P-value for heterogeneity 0.036).

CONCLUSION: In patients with hypertension, treatment with an ACE inhibitor results in a significant further reduction in all-cause mortality. Because of the high prevalence of hypertension, the widespread use of ACE inhibitors may result in an important gain in lives saved.

У пациентов с артериальной гипертензией лечение ингибиторами АПФ приводит к значительному сокращению смертности. Таким образом, рекомендуется широкое распространение ингибиторов АПФ.

J Am Coll Cardiol. 2013 Jan 15;61(2):131-42. doi: 10.1016/j.jacc.2012.10.011. Epub 2012 Dec 5.

A meta-analysis reporting effects of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers in patients without heart failure.

Savarese G[1], Costanzo P, Cleland JG, Vassallo E, Ruggiero D, Rosano G, Perrone-Filardi P.

Author information

Abstract

OBJECTIVES: The goal of the study was to assess the effects of angiotensin-converting enzyme inhibitors (ACE-Is) and angiotensin receptor blockers (ARBs) on the composite of cardiovascular (CV) death, myocardial infarction (MI), and stroke, and on all-cause death, new-onset heart failure (HF), and new-onset diabetes mellitus (DM) in high-risk patients without HF.

BACKGROUND: ACE-Is reduce CV events in high-risk patients without HF whereas the effects of ARBs are less certain.

METHODS: Twenty-six randomized trials comparing ARBs or ACE-Is versus placebo in 108,212 patients without HF were collected in a meta-analysis and analyzed for the risk of the composite outcome, all-cause death, new-onset HF, and new-onset DM.

RESULTS: ACE-Is significantly reduced the risk of the composite outcome (odds ratio [OR]: 0.830 [95% confidence interval (CI): 0.744 to 0.927]; p = 0.001), MI (OR: 0.811 [95% CI: 0.748 to 0.879]; p < 0.001), stroke (OR: 0.796 [95% CI: 0.682 to 0.928]; p < 0.004), all-cause death (OR: 0.908 [95% CI: 0.845 to 0.975]; p = 0.008), new-onset HF (OR: 0.789 [95% CI: 0.686 to 0.908]; p = 0.001), and new-onset DM (OR: 0.851 [95% CI: 0.749 to 0.965]; p < 0.012). ARBs significantly reduced the risk of the composite outcome (OR: 0.920 [95% CI: 0.869 to 0.975], p = 0.005), stroke (OR: 0.900 [95% CI: 0.830 to 0.977], p = 0.011), and new-onset DM (OR: 0.855 [95% CI: 0.798 to 0.915]; p < 0.001).

CONCLUSIONS: In patients at high CV risk without HF, ACE-Is and ARBs reduced the risk of the composite outcome of CV death, MI, and stroke. ACE-Is also reduced the risk of all-cause death, new-onset HF, and new-onset DM. Thus, ARBs represent a valuable option to reduce CV mortality and morbidity in patients in whom ACE-Is cannot be used.

У пациентов с высоким кардиоваскулярным риском без СН , ИАПФ и БРА снижают риск сердечно-сосудистой смерти , инфаркта миокарда и инсульта. При приёме ИАПФ также снижается риск смерти, включая начальные стадии СН, и впервые выявленный СД. Таким образом, БРА представляют собой ценный вариант , чтобы уменьшить кардиоваскулярную смертность и заболеваемость у пациентов , у которых не может быть использованы ИАПФ.

ORIGINAL ARTICLE

Telmisartan, Ramipril, or Both in Patients at High Vascular Events

The ONTARGET Investigators

N Engl J Med 2008; 358:1547-1559 | April 10, 2008 | DOI: 10.1056/NEJMoa0801317

BACKGROUND

In patients who have vascular disease or high-risk diabetes without heart failure, angiotensin-converting–enzyme (ACE) inhibitors reduce mortality and morbidity from cardiovascular causes, but the role of angiotensin-receptor blockers (ARBs) in such patients is unknown. We compared the ACE inhibitor ramipril, the ARB telmisartan, and the combination of the two drugs in patients with vascular disease or high-risk diabetes.

Full Text of Background...

METHODS

After a 3-week, single-blind run-in period, patients underwent double-blind randomization, with 8576 assigned to receive 10 mg of ramipril per day, 8542 assigned to receive 80 mg of telmisartan per day, and 8502 assigned to receive both drugs (combination therapy). The primary composite outcome was death from cardiovascular causes, myocardial infarction, stroke, or hospitalization for heart failure.

CONCLUSIONS

Telmisartan was equivalent to ramipril in patients with vascular disease or high-risk diabetes and was associated with less angioedema. The combination of the two drugs was associated with more adverse events without an increase in benefit. (ClinicalTrials.gov number, NCT00153101.)

- Эффект от приёма телмисартана был равнозначен эффекту рамиприла у пациентов с кардиоваскулярными заболеваниями или с высоким риском СД и было связано с уменьшением отека Квинке. Сочетание же этих двух препаратов не эффективно, т.к. ведёт к увеличению количества побочных эффектов

Effects of the angiotensin-receptor blocker telmisartan on cardiovascular events in high-risk patients intolerant to angiotensin-converting enzyme inhibitors: a randomised controlled trial

The Telmisartan Randomised AssessmeNt Study in ACE iNtolerant subjects with cardiovascular Disease (TRANSCEND) Investigators[‡]

Summary

Background

Angiotensin-converting enzyme (ACE) inhibitors reduce major cardiovascular events, but are not tolerated by about 20% of patients. We therefore assessed whether the angiotensin-receptor blocker telmisartan would be effective in patients intolerant to ACE inhibitors with cardiovascular disease or diabetes with end-organ damage.

Methods

After a 3-week run-in period, 5926 patients, many of whom were receiving concomitant proven therapies, were randomised to receive telmisartan 80 mg/day (n=2954) or placebo (n=2972) by use of a central automated randomisation system. Randomisation was stratified by hospital. The primary outcome was the composite of cardiovascular death, myocardial infarction, stroke, or hospitalisation for heart failure. Analyses were done by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT00153101.

Findings

The median duration of follow-up was 56 (IQR 51–64) months. All randomised patients were included in the efficacy analyses. Mean blood pressure was lower in the telmisartan group than in the placebo group throughout the study (weighted mean difference between groups 4·0/2·2 [SD 19·6/12·0] mm Hg). 465 (15·7%) patients experienced the primary outcome in the telmisartan group compared with 504 (17·0%) in the placebo group (hazard ratio 0·92, 95% CI 0·81–1·05, p=0·216). One of the secondary outcomes—a composite of cardiovascular death, myocardial infarction, or stroke—occurred in 384 (13·0%) patients on telmisartan compared with 440 (14·8%) on placebo (0·87, 0·76–1·00, p=0·048 unadjusted; p=0·068 after adjustment for multiplicity of comparisons and overlap with primary outcome). 894 (30·3%) patients receiving telmisartan were hospitalised for a cardiovascular reason, compared with 980 (33·0%) on placebo (relative risk 0·92, 95% CI 0·85–0·99; p=0·025). Fewer patients permanently discontinued study medication in the telmisartan group than in the placebo group (639 [21·6%] *vs* 705 [23·8%]; p=0·055); the most common reason for permanent discontinuation was hypotensive symptoms (29 [0·98%] in the telmisartan group *vs* 16 [0·54%] in the placebo group).

Interpretation

Telmisartan was well tolerated in patients unable to tolerate ACE inhibitors. Although the drug had no significant effect on the primary outcome of this study, which included hospitalisations for heart failure, it modestly reduced the risk of the composite outcome of cardiovascular death, myocardial infarction, or stroke.

Телмисартан хорошо переносится пациентами, которым не подходят ингибиторы АПФ. Препарат не оказывает существенного влияния на снижение случаев госпитализации пациентов по поводу сердечной недостаточности, но немного уменьшает риск сердечно-сосудистой смерти, инфаркта миокарда или инсульта.

J Hypertens. 2007 May;25(5):951-8.

Blood pressure-dependent and independent effects of agents that inhibit the renin-angiotensin system.

Blood Pressure Lowering Treatment Trialists' Collaboration[1], Turnbull F, Neal B, Pfeffer M, Kostis J, Algert C, Woodward M, Chalmers J, Zanchetti A, MacMahon S.

⊕ Author information

Erratum in
J Hypertens. 2007 Jul;25(7):1524.

Abstract

OBJECTIVES: To evaluate the blood pressure-dependent and independent effects of angiotensin-converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB) on major cardiovascular events.

METHODS: Using data from 26 large-scale trials comparing an ACEI or an ARB with placebo or another drug class, meta-regression analyses were conducted in which treatment-specific relative risks for major cause-specific outcomes [stroke, major coronary heart disease (CHD) events and heart failure] were regressed against follow-up blood pressure differences.

RESULTS: From a total of 146 838 individuals with high blood pressure or an elevated risk of cardiovascular disease, 22 666 major cardiovascular events were documented during follow-up. The analyses showed comparable blood pressure-dependent reductions in risk with ACEI and ARB (P >or= 0.3 for all three outcomes). The analyses also showed that ACEI produced a blood pressure-independent reduction in the relative risk of CHD of approximately 9% (95% confidence interval 3-14%). No similar effect was detected for ARB, and there was some evidence of a difference between ACEI and ARB in this regard (P = 0.002). For both stroke and heart failure there was no evidence of any blood pressure-independent effects of either ACEI or ARB.

CONCLUSION: There are similar blood pressure-dependent effects of ACEI and ARB for the risks of stroke, CHD and heart failure. For ACEI, but not ARB, there is evidence of blood pressure-independent effects on the risk of major coronary disease events.

БРА и ИАПФ оказывают схожее влияние на риск инсульта, ИБС и сердечной недостаточности. Однако есть свидетельства, доказывающие роль ИАПФ (но не БРА) при снижении риска крупных коронарных событий.

Blood pressure lowering efficacy of angiotensin receptor blockers for primary hypertension

Balraj S Heran[1,*], Michelle MY Wong[2], Inderjit K Heran[3], James M Wright[4]

Database Title
The Cochrane Library

Editorial Group: Cochrane Hypertension Group

Published Online: 8 OCT 2008

Abstract

Jump to...

Background

Angiotensin receptor blockers (ARBs) are widely prescribed for hypertension so it is essential to determine and compare their effects on blood pressure (BP), heart rate and withdrawals due to adverse effects (WDAE).

Objectives

To quantify the dose-related systolic and/or diastolic BP lowering efficacy of ARBs versus placebo in the treatment of primary hypertension.

Search methods

We searched CENTRAL (The Cochrane Library 2007, Issue 1), MEDLINE (1966 to February 2007), EMBASE (1988 to February 2007) and reference lists of articles.

Selection criteria

Double-blind, randomized, controlled trials evaluating the BP lowering efficacy of fixed-dose monotherapy with an ARB compared with placebo for a duration of 3 to 12 weeks in patients with primary hypertension.

Data collection and analysis

Two authors independently assessed trial quality and extracted data. We contacted study authors for additional information. WDAE information was collected from the trials.

Main results

Forty six RCTs evaluated the dose-related trough BP lowering efficacy of 9 ARBs in 13 451 participants with a baseline BP of 156/101 mm Hg. The data do not suggest that any one ARB is better or worse at lowering BP. A dose of 1/8 or 1/4 of the manufacturers' maximum recommended daily dose (Max) achieved a BP lowering effect that was 60 to 70% of the BP lowering effect of Max. A dose of 1/2 Max achieved a BP lowering effect that was 80% of Max. ARB doses above Max did not significantly lower BP more than Max. Due to evidence of publication bias, the largest trials provide the best estimate of the trough BP lowering efficacy for ARBs as a class of drugs: -8 mm Hg for SBP and -5 mm Hg for DBP. ARBs reduced BP measured 1 to 12 hours after the dose by about 12/7 mm Hg.

Authors' conclusions

The evidence from this review suggests that there are no clinically meaningful BP lowering differences between available ARBs. The BP lowering effect of ARBs is modest and similar to ACE inhibitors as a class; the magnitude of average trough BP lowering for ARBs at maximum recommended doses and above is -8/-5 mmHg. Furthermore, 60 to 70% of this trough BP lowering effect occurs with recommended starting doses. The review did not provide a good estimate of the incidence of harms associated with ARBs because of the short duration of the trials and the lack of reporting of adverse effects in many of the trials.

- Данные этого обзора показывают, что нет клинически значимых различий между доступными БРА. В общем эффект снижения БРА похож на ингибиторы АПФ, как класса.
- Данный обзоре не обеспечивают хорошую оценку вреда, связанного с БРА, из-за короткой продолжительности испытаний.

First-line drugs inhibiting the renin angiotensin system versus other first-line antihypertensive drug classes for hypertension

Hao Xue[1], Zhuang Lu[1], Wen Lu Tang[1,*], Lu Wei Pang[2], Gan Mi Wang[1], Gavin WK Wong[3], James M Wright[3]

Editorial Group: Cochrane Hypertension Group

Published Online: 11 JAN 2015

Assessed as up-to-date: 10 DEC 2014

Database Title

The Cochrane Library

Abstract

Jump to...

Background

Renin-angiotensin system (RAS) inhibitors are widely prescribed for treatment of hypertension, especially for diabetic patients on the basis of postulated advantages for the reduction of diabetic nephropathy and cardiovascular morbidity and mortality. Despite widespread use of angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) for hypertension in both diabetic and non-diabetic patients, the efficacy and safety of RAS inhibitors compared to other antihypertensive drug classes remains unclear.

Objectives

To evaluate the benefits and harms of first-line RAS inhibitors compared to other first-line antihypertensive drugs in patients with hypertension.

Search methods

We searched the Cochrane Hypertension Group's Specialised Register, MEDLINE, MEDLINE In-Process, EMBASE and ClinicalTrials.gov for randomized controlled trials up to November 19, 2014 and the Cochrane Central Register of Controlled Trials (CENTRAL) up to October 19, 2014. The WHO International Clinical Trials Registry Platform (ICTRP) is searched for inclusion in the Cochrane Hypertension Group's Specialised Register.

Selection criteria

We included randomized, active-controlled, double-blinded studies with at least six months follow-up in people with primary elevated blood pressure (≥130/85 mmHg), which compared first-line RAS inhibitors with other first-line antihypertensive drug classes and reported morbidity and mortality or blood pressure outcomes. Patients with proven secondary hypertension were excluded.

Data collection and analysis

Two authors independently selected the included trials, evaluated the risk of bias and entered the data for analysis.

Authors' conclusions

We found predominantly moderate quality evidence that all-cause mortality is similar when first-line RAS inhibitors are compared to other first-line antihypertensive agents. First-line thiazides caused less HF and stroke than first-line RAS inhibitors. The quality of the evidence comparing first-line beta-blockers and first-line RAS inhibitors was low and the lower risk of total CV events and stroke seen with RAS inhibitors may change with the publication of additional trials. Compared with first-line CCBs, first-line RAS inhibitors reduced HF but increased stroke. The magnitude of the reduction in HF exceeded the increase in stroke. The small differences in effect on blood pressure between the different classes of drugs did not correlate with the differences in the primary outcomes.

- В данном исследовании доказывается сравнительно высокий риск смерти при использовании в антигипертензивной терапии ингибиторов РААС, по сравнению с другими группами препаратов.
- Например, использование в терапии первой линии тиазидов отразило меньшее количество СН и инсультов, чем при применении ингибиторов РААС.

Intervention Review

Angiotensin converting enzyme (ACE) inhibitors versus angiotensin receptor blockers for primary hypertension

Edmond CK Li[1,*], Balraj S Heran[2], James M Wright[2]

Database Title
The Cochrane Library

Editorial Group: Cochrane Hypertension Group

Published Online: 22 AUG 2014

Abstract

Jump to...

Background

Angiotensin converting enzyme inhibitors (ACE inhibitors) and angiotensin receptor blockers (ARBs) are widely prescribed for primary hypertension (systolic blood pressure > 140 mmHg or diastolic blood pressure > 90 mmHg). However, while ACE inhibitors have been shown to reduce mortality and morbidity in placebo-controlled trials, ARBs have not. Therefore, a comparison of the efficacies of these two drug classes in primary hypertension for preventing total mortality and cardiovascular events is important.

Objectives

To compare the effects of ACE inhibitors and ARBs on total mortality and cardiovascular events, and their rates of withdrawals due to adverse effects (WDAEs), in people with primary hypertension.

Search methods

We searched the Cochrane Hypertension Group Specialized Register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, the World Health Organization (WHO) International Clinical Trials Registry Platform, and the ISI Web of Science up to July 2014. We contacted study authors for missing and unpublished information, and also searched the reference lists of relevant reviews for eligible studies.

Selection criteria

We included randomized controlled trials enrolling people with uncontrolled or controlled primary hypertension with or without other risk factors. Included trials must have compared an ACE inhibitor and an ARB in a head-to-head manner, and lasted for a duration of at least one year. If background blood pressure lowering agents were continued or added during the study, the protocol to do so must have been the same in both study arms.

Data collection and analysis

We used standard methodological procedures expected by The Cochrane Collaboration.

Main results

Nine studies with 11,007 participants were included. Of the included studies, five reported data on total mortality, three reported data on total cardiovascular events, and four reported data on cardiovascular mortality. No study separately reported cardiovascular morbidity. In contrast, eight studies contributed data on WDAE. Included studies were of good to moderate quality. There was no evidence of a difference between ACE inhibitors and ARBs for total mortality (risk ratio (RR) 0.98; 95% confidence interval (CI) 0.88 to 1.10), total cardiovascular events (RR 1.07; 95% CI 0.96 to 1.19), or cardiovascular mortality (RR 0.98; 95% CI 0.85 to 1.13). Conversely, a high level of evidence indicated a slightly lower incidence of WDAE for ARBs as compared with ACE inhibitors (RR 0.83; 95% CI 0.74 to 0.93; absolute risk reduction (ARR) 1.8%, number needed to treat for an additional beneficial outcome (NNTB) 55 over 4.1 years), mainly attributable to a higher incidence of dry cough with ACE inhibitors. The quality of the evidence for mortality and cardiovascular outcomes was limited by possible publication bias, in that several studies were initially eligible for inclusion in this review, but had no extractable data available for the hypertension subgroup. To this end, the evidence for total mortality was judged to be moderate, while the evidence for total cardiovascular events was judged to be low by the GRADE approach.

Authors' conclusions

Our analyses found no evidence of a difference in total mortality or cardiovascular outcomes for ARBs as compared with ACE inhibitors, while ARBs caused slightly fewer WDAEs than ACE inhibitors. Although ACE inhibitors have shown efficacy in these outcomes over placebo, our results cannot be used to extrapolate the same conclusion for ARBs directly, which have not been studied in placebo-controlled trials for hypertension. Thus, the substitution of an ARB for an ACE inhibitor, while supported by evidence on grounds of tolerability, must be made in consideration of the weaker evidence for the efficacy of ARBs regarding mortality and morbidity outcomes compared with ACE inhibitors. Additionally, our data mostly derives from participants with existing clinical sequelae of hypertension, and it would be useful to have data from asymptomatic people to increase the generalizability of this review. Unpublished subgroup data of hypertensive participants in existing trials comparing ACE inhibitors and ARBs needs to be made available for this purpose.

- Результаты данных исследований не обнаружили разницы в общей смертности или сердечно-сосудистых исходов между БРА и ИАПФ
- Замещение ИАПФ на БРА при непереносимости пациентом из-за побочных эффектов (например, сухой кашель), должны учитывать низкий доказательный уровень эффективности БРА в отношении снижения смертности и заболеваемости по сравнению с ингибиторами АПФ.

Hypertension in adults: diagnosis and management

NICE guidelines [CG127] Published date: August 2011

Step 1 treatment

1.6.6 Offer people aged under 55 years step 1 antihypertensive treatment with an angiotensin-converting enzyme (ACE) inhibitor or a low-cost angiotensin-II receptor blocker (ARB). If an ACE inhibitor is prescribed and is not tolerated (for example, because of cough), offer a low-cost ARB. **[new 2011]**

1.6.7 Do not combine an ACE inhibitor with an ARB to treat hypertension. **[new 2011]**

- Пациентам в возрасте до 55 лет на первой ступени антигипертензивной терапии назначают ИАПФ или БРА. Если имеется непереносимость ИАПФ (например, из-за кашля), предлагают БРА.
- Не рекомендуется сочетать ИАПФ с БРА

Общий вывод

Результаты крупных клинических исследований БРА II показали, что они не снижают риск ССО и смертность при широком спектре клинических состояний. И мы считаем, что роль БРА II в профилактике сердечно-сосудистых осложнений требует переоценки. Различия во влиянии на смертность больных АГ свидетельствуют о том, что ИАПФ следует отдавать предпочтение, а назначение БРА II должно быть ограничено пациентами с непереносимостью ИАПФ.