ACEI vs ARBS
In Hypertension
( They Are The Same )
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Goals of Presentation:

- Understand the detrimental effects of ARB.
- Understand the beneficial effects of ARB blockade.
- Evaluate therapeutic options between ACEI and ARBS
Renin-Angiotensin-Aldosterone System (RAAS)

**Actions of RAAS**

**Circulating RAAS**
- Vasoconstriction
- Aldosterone release
- AVP release
- Stimulate thirst and sodium appetite
- Renal sodium and water reabsorption

**Tissue-based RAAS**
- Hypertrophy
- Hyperplasia
- Remodelling
- Cytokine activation
- Collagen deposition/ fibrosis
Renin-Angiotensin-Aldosterone System (RAAS)

In addition to ACE-mediated conversion of angiotensin I, several alternative pathways lead to production of angiotensin II (Ang II Escape).

* Angiotensin II can be formed directly from angiotensinogen by the actions of elastase, cathepsin G, and tissue plasminogen activator.

* Angiotensinogen can be converted to angiotensin II at the tissue level by chymase and cathepsin G.
Angiotensin II and The CV system -- HBP

I. Direct vasoconstriction
II. Enhancement of peripheral noradrenergic neurotransmission
III. Increased sympathetic discharge (CNS)
IV. Catecholamine release from adrenal medulla

I. Increased Na reabsorption by proximal tubule
II. Increased aldosterone release
III. Altered renal hemodynamics (vasoconstriction)

I. Stimulation of cell growth
II. Hemodynamic changes
   A. Increased cardiac afterload + preload
   B. Increased vascular wall tension

Rapid Pressor Response
Slow Pressor Response
Vascular + Cardiac Hypertrophy + Remodeling
Angiotensin II Receptors

* Angiotensin II exerts its effects through stimulation of receptors that are located in a variety of tissues.

The two angiotensin II receptor subtypes described best are designated:

\[ \text{AT}_1 \text{ and } \text{AT}_2 \]

The majority of the known effects of angiotensin II appear to be mediated through:

**The AT\(_1\) receptor.**
While the function of the AT$_2$ receptor subtype has not been proved entirely, evidence from several studies suggests that:

**Activation of this receptor subtype mediates:**

* Vasodilatation,
* Inhibition of cell proliferation, and apoptosis.

Thus, the actions of AT$_2$ receptor stimulation _counterbalance_ the actions of the AT$_1$ receptor.

**Medications that block the RAAS**

- Angiotensinogen
- Renin
- Angiotensin I
- Angiotensin Converting Enzyme (ACE)
- Angiotensin II
- AT$_1$ receptor
- Aldosterone

**Renin blockers** (Beta blockers)

**ACE-inhibitors**

**ARBs**

**Aldosterone blockers**
A II BLOCKADE

It is not coincidence that:
- beta-blockers (renin inhibitors)
- angiotensin converting enzyme--(ACE) inhibitors
- angiotensin receptor blockers (ARBs)
- Aldosterone blockade

—all A II antagonists

↓ CV risk and decrease mortality

….improve outcomes!

Therapies aimed at:

Modifying The Renin System

have been used extensively for treatment of ….

hypertension, heart failure, myocardial infarction, diabetes, and renal disease.
Currently, therapies fall into one of two classes of angiotensin antagonists:

* The angiotensin-converting enzyme inhibitors (ACEIs) … and

* The angiotensin II receptor antagonists (ARBs, or angiotensin receptor blockers), that selectively inhibit angiotensin II from activating the angiotensin-specific receptor (AT$_1$).

**RAAS: Pathways of ACE inhibition and angiotensin receptor blockade**

- Angiotensin I
  - ACE inhibitor
  - Angiotensin II
    - ARB
    - AT$_1$ receptor
    - AT$_2$ receptor
ACE Inhibitor: Mechanism of Action

Angiotensin II 

Kininase II

Vasoconstriction
Aldosterone
Vasopressin
Sympathetic
Angiotensinogen
Renin
Angiotensin I
ACE
Angiotensin II

ACE=Angiotensin converting enzyme

RAAS Blockers Have Been Studied Extensively in Outcomes Trials

Hypertension
- LIFE
- SCOPE
- STOP 2
- VALUE
- KYOTO HEART
- CAPPB
- ALLHAT
- ANBP2

Heart failure
- ELITE II
- Val-HeFT
- CHARM
- CONSENSUS I
- SOLVD
- V-HeFT II
- PEP-CHF

High Risk
- HOPE
- ONTARGET
- TRANSCEND
- JIKEI HEART
- KYOTO HEART

Diabetes – Renal
- RENAAAL
- IDNT
- ABCD

Pre-diabetes
- NAVIGATOR
- DREAM

Myocardial infarction
- OPTIMAAL
- VALIANT
- CONSENSUS II
- ISIS-4
- GISSI-3
- SMILE
- SAVE
- AIRE
- TRACE

Coronary Artery Disease
- EUROPA
- PEACE
- IMAGINE
While ACEIs and ARBs both target the renin system and are regarded by clinicians as effectively equivalent

The Question?

Is an angiotensin receptor blocker (ARB) better than an ACEI because theoretically it would more completely block the effects of All?
Evaluation of Therapeutic Options - Criteria for Choice of Agent:

- Should reduce BP over 24 hours (i.e. be long-acting) in order to reduce end-organ damage
- Should have proven CV morbidity and mortality benefits.
- Quality of life.
- Safety, adverse events
- Tolerability, persistence, and adherence
- Risk factor reduction and other intermediate outcomes

Evidence on Comparative Long-term Benefits and Harms of ACEIs vs. ARBs for Essential Hypertension

(How do they differ?)
ACEIs and ARBs appear to have similar long-term effects on blood pressure among individuals with essential hypertension. This conclusion is based on evidence from 50 studies) in which 13,532 patients receiving an ACEI or an ARB were followed for periods from 12 weeks to 5 years (median 16.5 weeks).
Mortality and major cardiovascular events

( STRENGTH OF EVIDENCE : MODERATE)

A Meta analysis of randomized controlled trials between ARBs and ACEi, that includes 6 trials on about 50,000 patients. Results suggested that:

• ARBs are as effective as ACEi on the risk of MI, CV morbidity and total mortality.

• ARBs may be slightly more protective than ACEi on the risk of stroke.
No differences were found in measures of general quality of life; this is based on 4 studies, 2 of which did not provide quantitative data.
Rate of use of a single antihypertensive

(STRENGTH OF EVIDENCE: HIGH)

* There was no statistically evident difference in the rate of treatment success based on use of a single antihypertensive for ARBs compared to ACEIs.
Risk factor reduction and other intermediate outcomes

(STRNGTH OF EVIDENCE: Moderate (lipid levels, markers of carbohydrate metabolism/diabetes control, progression of renal disease) to Low (progression to type 2 diabetes and LV mass/function)

* There were no consistent differential effects of ACEIs vs. ARBs on several potentially important clinical outcomes, including lipid levels, progression to type 2 diabetes mellitus, markers of carbohydrate metabolism/diabetes control, measures of LV mass or function, and progression of renal disease (either based on creatinine, GFR, or proteinuria).
Safety, adverse events, tolerability, persistence, and adherence

(Strength of evidence: High (cough, withdrawals due to adverse events) to Low (angioedema))

* ACEIs have been consistently shown to be associated with greater risk of cough than ARBs

* Angioedema was reported only in patients treated with ACEIs.
Persistence and Adherence

(Strength of evidence: Moderate)

* ACEIs and ARBs have similar rates of adherence based on pill counts; this result may not be applicable outside the clinical trial setting.

* Rates of continuation with therapy appear to be somewhat better with ARBs than with ACEIs.
Remaining Issues

* Despite the relative importance of both ACEIs and ARBs for treatment of essential hypertension, there is a paucity of comparative evidence for

* With the exception of rates of cough, the hypothesis that ACEIs and ARBs have clinically meaningful differences in long-term outcomes in individuals with essential hypertension:

is not strongly supported by the available evidence.
* Given the importance of these issues, it is notable how few large, long-term, head-to-head studies have been published.

Further research in this area should considered

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**Conclusions**

- No Evidence of superiority of ARBs Over ACEI.
- Both drugs have the same therapeutic option criteria (BP control and reducing CV morbidity and mortality ...).
- Cost should always be part of the equation.
- ACEI are still first choice but use ARBs in all situations where ACEI cannot be tolerated…

...and maybe as an add-on or in combination in patients T2DM/microalbuminuria.
So the answer to the question should ARBs replace ACEIs in Hypertension management?

is NO . . .

THEY ARE THE SAME

THANK U