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Letter to the Editor

Angiotensin receptor blockers = angiotensin converting enzyme inhibitors minus dry cough?

Sir,

Blockade of the renin angiotensin aldosterone system (RAAS) is an important pharmacological intervention in cardiovascular (CV) diseases. Hypertension, heart failure (HF) and myocardial infarction are important indications for use of angiotensin converting enzyme inhibitors (ACEIs), which potentially decrease morbidity and prolong survival. Dry cough is an important adverse effect seen in about 20% of the patients which might require discontinuation of the drug.[1] In such situations, angiotensin receptor blockers (ARBs) serve as replacement drugs in all the indications, as they are largely devoid of this limiting adverse effect.

The eighth joint national committee recommends the use of ACEIs or ARBs, as one of the first line antihypertensives.[2] American College of Cardiology Foundation guidelines for HF recommend the use of ACEIs for HF with reduced ejection fraction.[3] ARBs are recommended in those intolerant to ACEIs. However, they can be used as alternatives if the patient is already on ARBs (like hypertensives). American College of Cardiology Foundation guidelines for non-ST-elevation myocardial infarction recommends ARBs in those intolerant to ACEIs with similar survival benefits.[4] Similar guideline also holds good for ST-elevation myocardial infarction.[5] However, are ARBs as efficacious as ACEIs? Are they interchangeable? Can a patient be started directly on ARBs rather than risking dry cough with ACEIs? A theoretical overview would suggest that the two are largely interchangeable although there are difference in terms of generation of angiotensin peptides, receptor activation, and effect on bradykinin metabolism. However, clinically the questions are yet to be answered comprehensively.

A meta-analysis which included 20 randomized clinical trials to detect any significant effect of RAAS inhibition on all-cause and CV mortality in different populations in which the absolute majority of the patients had hypertension showed 5% and 7% reduction respectively in the RAAS inhibition group which was almost entirely attributable to ACEIs and not ARBs.[6] A meta-analysis of 26 randomized trials comparing ARBs or ACEIs versus placebo in high-risk patients without HF showed that while both ACEIs and ARBs reduced the risk of the composite outcome of CV death, myocardial infarction and stroke, ACEIs also reduced the risk of all-cause death, new-onset HF, and new-onset diabetes mellitus.[7] The authors thus concluded that ARBs represent a valuable option in those who cannot use ACEIs. A meta-analysis of thirty-five randomized controlled trials to evaluate the effects of ACEIs and ARBs on all-cause mortality, CV deaths, and major CV events in patients with diabetes mellitus found ACEIs to be beneficial in all the outcomes while ARBs did not show any benefit.[8] However, a meta-analysis in patients with primary hypertension to compare the effects of ACEIs and ARBs on total mortality and CV events did not show any significant difference between the two groups.[9] The lack of efficacy data with placebo-controlled trials for ARBs were mentioned, as a factor to be considered before choosing ARBs over ACEIs by the study authors. This effect of RAAS inhibition in hypertension also needs to be considered in relation to other first line antihypertensives. While individual drug groups might have more survival benefits in specific population, overall, the guidelines for management of hypertension emphasize on reduction of blood pressure rather than the specific first line drug used to achieve the reduction, as being more meaningful with regard to the clinical outcome.[2] In this regard, a more recent meta-analysis evaluated the benefits and harms of first-line renin-angiotensin system (RAS) inhibitors compared with other first-line antihypertensive drugs in patients with hypertension. The study found that all-cause mortality was similar among the first-line antihypertensive drugs.[10] Thiazides caused less HF and stroke than RAS inhibitors. Compared with calcium channel blockers, RAS inhibitors reduced HF, but increased stroke with the benefit on the former being more. Complicating matters further are the fact that most of the trials have considered the different drugs within individual groups (ACEIs or ARBs) to be similar in their benefits/harm. However, this might not necessarily be true.

Until, there is more clinical evidence and clarity with regard to the equivalence of benefits between the two drug groups, it would be prudent to adhere to the clinical guidelines considering ARBs, as replacement alternative in patients intolerant of ACEIs unless specifically mentioned otherwise.

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