change in therapy should be approached cautiously if the diastolic blood pressure decreases <55-60 mm Hg.

Key Words: Hypertension, older persons, therapy

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Wednesday, May 16, 4:00 PM to 6:00 PM
Sympathetic Nervous System, II Imidazoline Receptors, Hypertension and Metabolic Disorders*

I1 RECEPTORS, CARDIOVASCULAR FUNCTION, AND METABOLISM

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Injected into the medullary site of the hypotensive action of clonidine, imidazolines and related compounds decrease blood pressure whereas no phenylethylamine compounds were capable of producing such an effect as the same site. There is much biochemical and pharmacological evidence to support the involvement of imidazoline receptors in the regulation of vasomotor tone as well as in the mechanism of action of some centrally acting antihypertensive drugs. Imidazoline specific binding sites (IBS), which do not recognize catecholamines, have been described in various tissues. Functional studies using selective antagonists have confirmed that the hypotensive effects of clonidine-like drugs are mediated, at least in part, by non-α-adrenergic imidazoline-specific receptors, while there sedative action clearly involves α₁-adrenergic receptors located in the locus coeruleus. Compared with clonidine, newer centrally acting antihypertensive drugs such as rilmenidine are more selective for imidazoline receptors than for α₂-adrenergic receptors. This selectivity may explain the reduced incidence of side effects of these drugs at therapeutic doses. Very recently, imidazoline-like compounds with no affinity and no activity at α₂-adrenergic receptors have become available. Some of these compounds lowered the blood pressure when injected centrally, indicating that an action on imidazoline I₁ receptors alone is sufficient to cause hypotension. Nevertheless, imidazoline receptors and α₂-adrenoceptors cooperate in the control of the vasomotor tone and in the hypotensive action of centrally acting hybrid drugs (ie, drugs which bind to both types of receptor). Additional non-cardiovascular effects of imidazoline-like drugs have also been described, such as insulin secretion stimulation and renal sodium reabsorption inhibition. These effects may account for long term benefits of imidazoline selective drugs, such as rilmenidine.

Key Words: Imidazoline receptors, α₂-adrenergic receptors, rilmenidine

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Sympathetic Nervous System, II Imidazoline Receptors, Hypertension and Metabolic Disorders*

DIABETES: THE BENEFITS OF BLOOD PRESSURE AND METABOLIC CONTROL IN HYPERTENSION

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Whereas individual research papers about antihypertensive treatment in diabetes might be somewhat confusing, the weight of the evidence strongly suggests that:

1. In patients with type 1 diabetes, it is advantageous to use angiotensin-converting enzyme (ACE) inhibitors as primary treatment.
2. In type 2 diabetes, aggressive blood pressure (BP) lowering is warranted and, the calcium antagonist controversy notwithstanding, all drugs appear to be similarly useful in reducing cardiovascular mortality. Specifically, in the SystEur study, compared with placebo, a calcium antagonist dramatically reduced cardiovascular (CV) events in elderly diabetics. The HOT study showed that, using a calcium antagonist-based regimen, the degree of BP lowering determines the degree of CV event reduction. Furthermore, the UKPDS did not find a difference in CV events reduction in patients treated with beta-blockers or with ACE inhibitors. In the UKPDS, the effect of BP lowering on reduction in CV events was more substantial than the degree of CV reduction by blood sugar lowering.
3. Both the CAPPP and the HOPE study found that treatment with an ACE inhibitor may be useful in reducing the incidence of new-onset type 2 diabetes mellitus.
4. Insulin resistance, a precursor of diabetes mellitus and a strong predictor of future CV disease, is differentially affected by antihypertensive treatment. Beta-blockers and diuretics worsen insulin resistance, whereas α₁-adrenergic blockers and central imidazoline agonists increase insulin sensitivity. The effect of ACE inhibitors and angiotensin blockers may also positively affect insulin resistance but the results are not uniformly positive.

It stands to reason that the differential effect of various drugs on insulin resistance and primary CV may be clinically relevant particularly in the course of the long-term prevention of mild hypertension. All current trials investigate the effect of the treatment on secondary prevention of