Pharmacological Properties of the Central Antihypertensive Agent, Moxonidine

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SUMMARY

The sympathetic nervous system plays a central role in the pathophysiology not only of hypertension and other cardiovascular diseases but also metabolic disorders including disturbances of glucose and lipid homeostasis. A centrally acting sympathetic agent is therefore attractive not only for lowering blood pressure, but also intervening with multiple disease processes. Older agents such as clonidine and guanabenz have numerous side effects, including sedation and dry mouth that limit their acceptability to patients. Moxonidine and the related agent rilmenidine have greatly reduced side effects, because they have reduced activity at the α₂-adrenergic receptors that mediate these undesirable actions. Instead, moxonidine and rilmenidine act primarily through a novel cellular site, termed the I₁-imidazoline receptor. The molecular biology of the I₁-imidazoline receptor protein has recently been described, and the cell signaling pathways linked to this protein have been characterized. Moxonidine has unique effects on a number of cell types through this unusual cellular site of action. There are multiple therapeutic implications of these cellular actions, especially for metabolic syndrome and its associated derangements in glucose and lipid metabolism. Finally, the clinical trials that seemed to identify an unfavorable outcome in severe heart failure are dissected and
critiqued. We conclude that moxonidine and future successors to this agent could be of great value in treating multiple chronic diseases.