NEW HORIZON

Angiotensin-Converting Enzyme (ACE) Inhibitors and Sarcopenia

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Sarcopenia is the age-associated complex syndrome that is associated with muscle mass & function loss alone or in conjunction with increased fat mass. The causes of sarcopenia are multifactorial and can include disuse, changing endocrine function, chronic diseases, inflammation, insulin resistance, and nutritional deficiencies (1). There has been a slow but consistent rise in elderly population since 1960's. Aging is associated with a natural decline in physiological functions, including loss of bone mass density (BMD), muscle mass and strength (2). Sarcopenia is associated with increased morbidity and mortality. Till now most efforts to counteract sarcopenia have met with limited success except resistance exercises and good nutrition (3).

ACE is an important component of the renin-angiotensin system, the central hormonal regulator of blood pressure. Angiotensin-converting enzyme (ACE) inhibitors have long been used as a treatment in primary and secondary prevention in cardiovascular disease as well as secondary stroke prevention. ACE inhibitors may exert their beneficial effects on skeletal muscles through a number of different mechanisms (3,4) (*Fig 1*). Recent evidence suggests that ACEIs may improve physical function by means of direct effects on body composition in older persons, rather than through its blood-pressure-lowering effects. Clinical and genetic studies in humans and experimental evidence in animals suggest that modulation of the renin-angiotensin system is associated with metabolic and biochemical changes in skeletal muscle and fat, changes that are associated with declining physical function. ACEIs may modulate this process through a variety of molecular mechanisms including their influence on oxidative stress and on metabolic and inflammation pathway, through improvements in endothelial function, and angiogenesis thereby improving skeletal muscle blood flow (3,4). ACE inhibitors can increase mitochondrial numbers and IGF-I levels thereby helping to counter sarcopenia (5,6). One of the recent study confirmed that enalapril to blunt angiotensin-II dependent activation of pro-inflammatory and pro-oxidant pathways which may be earlier events with respect to the pro-fibrotic ones, and may in part account for both functional impairment and muscle necrosis (7).

Similaraly , captopril treatment reduced food intake and body weight, improved insulin sensitivity and decreased the mRNA expression of markers of inflammation in one of the recent research (8).

Observational studies have shown that the long-term use of ACE inhibitors was associated with a lower decline in muscle strength and walking speed in older hypertensive people and a greater lower limb lean muscle mass when compared with users of other antihypertensive agents (9,10).Several studies have shown that ACE inhibitors improved exercise capacity in younger people with heart failure and this was also confirmed in older people with heart failure,Although this could be largely attributed to improvements in cardiac function (10,11).

Functionally impaired older people without heart failure has shown that ACE inhibitors increase 6-minute walking distance to a degree comparable to that achieved after 6 months of exercise training (12).However, a study comparing the effects of nifedipine with ACE inhibitors in older people found no difference between treatments in muscle strength, walking distance, or functional performance (13).

Sarcopenia is an ever increasing global health concern that needs to be urgently addressed.These studies may have major public health implications for older adults, as

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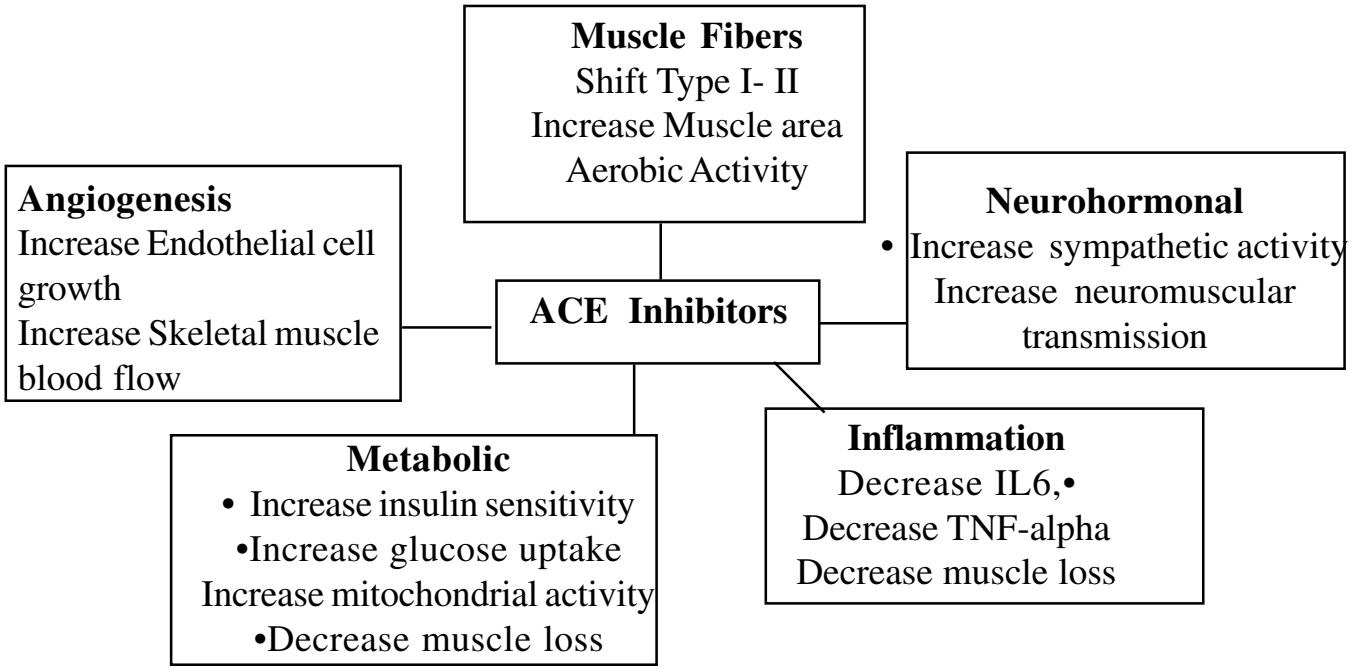

consequence of the fact that, in this population, gradual loss of muscle mass and muscle strength can play a key role in the onset and progression of disability. Therefore, if findings of observational studies will be later confirmed in randomized controlled trials, ACE inhibitors could represent an effective intervention to prevent physical decline in the elderly, leading to greater autonomy in this growing population.However, further evidence is required before recommending ACE inhibitors to counter the effects of sarcopenia

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