PHARMACOTHERAPY

VASCULAR EHLERS-DANLOS SYNDROME

Celiprolol, a β_1 -adrenoceptor blocker with β_2 -adrenoceptor agonist vasodilatory properties, might become the cardioprotective therapy of choice for patients with vascular Ehlers–Danlos syndrome (vEDS)—an inherited disorder characterized by defective collagen synthesis—suggests the results of a trial published in *The Lancet*.

Aiming to reduce the incidence of arterial events that characterize this rare, but severe, disease, Pierre Boutouyrie and colleagues have conducted a multicenter, prospective trial in which 53 patients with vEDS were randomly assigned to receive celiprolol or no β -blocker treatment. The trial was open, but the evaluation of clinical events was blinded. The primary end point was a composite of fatal or nonfatal arterial rupture or dissection.

After 5 years of follow-up, the trial was ended prematurely owing to significant differences observed between the two studied groups: a 64% reduction in risk of the primary end point was noted in the group receiving celiprolol (20% of celiprolol-treated patients experienced arterial events, compared with 50% of patients in the control group). “[This reduction] could be translated into a 15-year gain in life expectancy,” says Boutouyrie.

A mutation in the collagen 3A1 gene is associated with vEDS and can be used to identify patients who should be treated.

“We have to work with Sanofi-Aventis, the developer of the original molecule, on how to provide celiprolol to patients who need it,” says Boutouyrie. The mechanisms by which celiprolol protects against arterial damage are not clear. “We found no significant change in blood pressure and heart rate,” comments Boutouyrie. Arterial stiffness, however, was increased. The researchers now plan to further study the effects of celiprolol and other drugs, such as angiotensin-receptor antagonists, in a mouse knock-out model of collagen III.

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Original article Ong, K.-T. *et al.* Effect of celiprolol on prevention of cardiovascular events in vascular Ehlers–Danlos syndrome: a prospective randomised, open, blinded-endpoints trial. *Lancet* doi:10.1016/S0140-6736(10)60960-9