

ロサルタンのマルファン症候群における有効性は有望なようである

COMPARE：アンジオテンシン受容体拮抗薬はマルファン症候群患者の大動脈根部拡大を軽減する

COMPARE: Angiotensin-receptor blocker reduces aortic root enlargement in patients with Marfan syndrome

一般の人々に用いられる高血圧治療薬が、マルファン症候群患者における危険でしばしば致命的な循環器系の問題を有意に軽減することが示されたと2013年European Society of Cardiology学会で発表された。COMPARE (COzaar in Marfan Patients Reduces aortic Enlargement) スタディでは、ロサルタン (Cozaar) で治療された患者において3年後の大動脈拡大発現率がこの治療を受けなかった患者と比較し有意に低かったことを明らかにした。研究者らはマルファン症候群患者233人 (平均年齢41歳、女性47%) を組み入れた。これらの患者のうち27%が過去に予防的大動脈根部置換術を施行されており、多く(73%)がβ遮断薬による治療を受けていた。計117人が追加治療を受けない群に、116人が1日50mgのロサルタンを内服し副作用がなければ14日後に倍量を内服する群に無作為に割り付けられた。大動脈拡大は磁気共鳴画像を用いてモニターされた。3年後に大動脈拡大はコントロール群よりもロサルタン群で有意に少なく(0.77mm対1.35mm, $P=0.014$)、ロサルタン群の患者の50%は大動脈根部の拡大を示さなかったのに対しコントロール群におけるその割合は31%であった($P=0.022$)。

Full Text

A common drug that is used to treat high blood pressure in the general population has been found to significantly reduce a dangerous and frequently fatal cardiac problem in patients with Marfan syndrome according to researchers at the European Society of Cardiology 2013 Congress.

Results of the COMPARE (COzaar in Marfan Patients Reduces aortic Enlargement) study reveal that patients treated with losartan (Cozaar) had a significantly reduced rate of aortic enlargement after 3 years compared to patients who did not receive the treatment.

"Our study is the first large, prospective randomized study to assess the effects of losartan on aortic enlargement in adults with Marfan syndrome, and confirms previous findings in a mouse model," said lead investigator Maarten Groenink M.D., PhD from the Departments of Cardiology and Radiology at Academic Medical Centre in Amsterdam, The Netherlands.

"We're very excited to see that such a commonly used drug that is not expensive and has a familiar side-effect profile could have a significant effect on this very serious and frightening risk factor for these patients. These findings may change standard clinical management."

Marfan syndrome, a heritable connective tissue disorder, affects 2-3 in 10,000 people. It causes progressive enlargement of the aorta, making it prone to rupture, which can be fatal in more than 50% of cases. Currently, the only effective treatment is prophylactic surgical aortic root replacement.

In addition to lowering blood pressure, the main benefit of losartan is believed to be its interference with the biochemical process that causes aortic enlargement.

To assess this, the COMPARE study included 233 participants (47% female) with Marfan syndrome from all four academic Marfan screening centers in the Netherlands.

Subjects were a mean age of 41 years, 27% had previously undergone prophylactic aortic root replacement, and the majority (73%) were being treated with beta blockers.

A total of 117 subjects were randomized to receive no further treatment, while 116 were randomized to receive losartan 50 mg daily, doubling after 14 days if there were no side effects. Aortic enlargement was monitored with magnetic resonance imaging (MRI) for three years of follow-up.

During the study period, if patients in either arm required prophylactic aortic root replacement the decision was left to the discretion of the attending cardiologists based on existing guidelines and anticoagulation therapy was initiated when appropriate.

The study showed that after 3 years aortic root enlargement was significantly less in the losartan group than in controls (0.77 mm vs. 1.35 mm, $P=0.014$), and 50% of losartan patients showed no growth of the aortic root compared to 31% of controls ($P=0.022$).

In Marfan syndrome aortic enlargement is usually confined to the 'aortic root', but may also extend beyond it. The study showed that aortic enlargement beyond the root was not significantly reduced by losartan. However, among the subset of patients who had already received aortic root replacement, dilation in the aortic arch was significantly lower in patients treated with losartan compared to controls (0.50 mm vs. 1.01 mm; $P=0.033$). "This result should be interpreted with some caution as baseline aortic dimensions of patients with prior aortic root replacement were not completely comparable between the groups," said Dr. Groenink.

Although the reduced rate of aortic enlargement in the losartan group suggests this drug may postpone or even prevent aortic rupture as well as the need for prophylactic surgery in Marfan patients, the study did not actually demonstrate this result.

There were no differences in the rate of aortic dissections (0 in the losartan group and 2 controls) or elective aortic surgery (10 in the losartan group and 9 in controls) and no cardiovascular deaths occurred.

"The incidence of clinical events was low in our study and therefore the clinical relevance of losartan treatment on aortic surgery and aortic dissection could not be determined," said Dr. Groenink, adding that only a larger prospective trial with longer follow-up can ultimately determine this outcome.

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