

Editorial



Potential of Grape Seed Extract to Prevent Calcification of Bioprosthetic Heart Valve

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► See the article “Entelon150® (*Vitis vinifera* Seed Extract) Attenuates Degenerative Changes in Intravascular Valve Prostheses in Rabbits” in volume 54 on page 43.

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Valvular heart disease is one of the major causes of heart failure, the prevalence of which is expected to increase given the life expectancy is getting longer. The standard treatment is replacement of the dysfunctional valves with artificial valves. The application of bioprosthetic heart valves (BHV) is spreading, especially along with transcatheter aortic valve replacement (TAVR) nowadays.¹⁾ BHV has less risk of thromboembolism but it eventually becomes incompetent by degeneration and calcification, compared to mechanical heart valve. BHV calcification is pathophysiologically related to cytotoxic effect of pretreatment of glutaraldehyde, extracellular matrix damage, host immune/inflammatory response, oxidative stress, and metabolic disorders.²⁾ As drugs preventing or delaying calcification of BHV, statins³⁾ and immunosuppressive therapy such as steroid and antithymocyte globulin,²⁾⁴⁾ have been reported; however, more evidence is required to confirm the efficacy of those drugs with a concern to their side effects after long-term use.

In this current issue, Lee et al.⁵⁾ reported their data to compare the effects of Entelon150® on calcification and inflammation of BHV tissue with those of other prescribed drugs (losartan and rosuvastatin). Entelon150® is an herbal product of grape seed extracts which have been known to have anti-inflammatory, antioxidant, and anti-angiogenic activity.⁶⁾ The authors showed its significant effect to reduce calcification in the rabbit model implanted with BHV tissue in the external jugular veins. The amount of Ca⁺² in the implanted BHV was significantly lower in Entelon150® treated group than in control group, to the similar degree to other treatment groups. It was supported with less expression of bone morphogenic protein 2 protein in the vascular tissue implanted with BHV tissue of Entelon150® group. The results of comparison between Entelon150® group and control group were basically compatible with those of the previous study using a dog model.⁷⁾ The effect of Entelon150® on calcification of BHV tissue is worthy of notice, as Entelon150® is an extract of natural product without any particular side effects, in contrast to other drugs such as losartan and rosuvastatin with long term side effects. Inflammation around the vessel implanted with BHV tissue seemed to decrease with treatment of Entelon150®, but it did not reach statistical significance in this study, which was probably related to the limited number of cases. Either site- or cell-specific analysis might provide meaningful differences in inflammation.

The authors suggested the promising possibility of Entelon150® as an adjuvant drug to attenuate calcification of BHV using an animal model. In order to obtain more high-level

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evidence for clinical application, further studies would be required to expand animal experiments with more numbers of cases, longer administration of the drug, and intra-arterial BHV implantation methods, which are more comparable to human status, followed by appropriately-designed clinical studies in humans.

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