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The possible effect of colchicine on arteriovenous fistula maturation via neointimal hyperplasia blockage

To the Editor: In a recent issue of *Kidney International* Janardhanan *et al.*[1] reported the role of simvastatin on venous neointimal hyperplasia (VNH) in a murine hemodialysis vascular access model. They concluded that simvastatin causes a significant reduction in VNH, with an increase in mean lumen vessel area. It is plausible to find an available agent that increases the rate of arteriovenous fistula maturation (AVF) by preventing VNH. Clinical availability of simvastatin in patients with chronic kidney disease remains under debate due to possible side effects such as rhabdomyolysis or liver toxicity. Thus, we have a proposition for the authors to address this issue on the basis of recent findings of the study about colchicine treatment for the prevention of stent restenosis in diabetic patients with coronary artery disease.[2]

Neointimal hyperplasia has been well established in arteriovenous fistula failure.[3] Furthermore, preventing neointimal hyperplasia has recently become a target in maintaining an intact vascular access. However, there are no clinically available drugs that affect neointima formation in native AVF in the hemodialysis population. Colchicine inhibits microtubule polymerization by binding to tubulin, thus affecting the process that requires cytoskeletal changes including cell mitosis and neutrophil motility. This anti-inflammatory and anti-mitotic drug is associated with the prevention of neointimal hyperplasia in bare-metal stent restenosis in patients with coronary artery disease.[2] In line with this study, we suggest that colchicine may increase AVF maturation rate, hence both experimental and clinical studies are needed to clarify this temporal relationship.

1. Janardhanan R, Yang B, Vohra P *et al.* Simvastatin reduces venous stenosis formation in a murine hemodialysis vascular access model. *Kidney Int* 2013; **84**: 338–352.
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Eray Eroglu[1] and Ismail Kocyigit[2]

[1]Department of Internal Medicine, Erciyes University Medical Faculty, Kayseri, Turkey and [2]Department of Nephrology, Erciyes University Medical Faculty, Kayseri, Turkey

Correspondence: *Eray Eroglu, Department of Internal Medicine, Erciyes University Medical Faculty, 38039 Kayseri, Turkey.*
E-mail: drerayeroglu@hotmail.com

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The Authors Reply: We would like to thank Drs Eroglu and Kocyigit[1] for their comment on the possible use of colchicine on arteriovenous fistula maturation via neointimal hyperplasia blockage. We used simvastatin because it is a pleiotropic molecule capable of modulating the gene expression of vascular endothelial growth factor-A and matrix metalloproteinase-9. In our studies, simvastatin-treated vessels had improved vascular remodeling in an experimental murine model of arteriovenous fistula (AVF) with chronic kidney disease using a clinical dose.[2] As pointed out by Eroglu and Kocyigit,[1] simvastatin is associated with rhabdomyolysis, hepatotoxicity, and uremia-induced cardiomyopathy.[3] Taking this into consideration, we have begun to consider local delivery of simvastatin to the vessel wall using nanoparticles or alginate gel wraps to decrease these side effects.

Colchicine treatment for 6 months has been shown recently to decrease stent restenosis in patients with coronary disease treated with bare-metal stents.[4] This is felt to be because of its ability to inhibit microtubule formation as well as its anti-inflammatory component.[5] Furthermore, it is interesting that a trial using colchicine was negative in patients undergoing angioplasty of coronary arteries, whereas a separate trial in patients undergoing stent placement was positive.[4,6] The mechanism for this observation may be due to elastic recoil, which occurs in the artery after angioplasty and also in the vein. In conclusion, we think colchicine is a plausible therapy, which may reduce venous neointimal hyperplasia in patients with hemodialysis vascular access, and further studies using this molecule need to be performed to determine its efficacy.

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Rajiv Janardhanan[1] and Sanjay Misra[2]

[1]Amity Centre for Vascular Biology and Amity Institute of Biotechnology, Amity University Uttar Pradesh, Noida, Uttar Pradesh, India and [2]Vascular and Interventional Radiology Translational Laboratory, Department of Radiology, Mayo Clinic, Rochester, Minnesota, USA

Correspondence: *Sanjay Misra, FAHA Mayo Clinic, Vascular and Interventional Radiology Translational Laboratory, Department of Radiology, 200 First Street SW, Rochester, Minnesota 55905, USA.*
Email: misra.sanjay@mayo.edu

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