New Evidence: Rat Poison Not Best Solution for Cardiovascular Patients

Kidney Interational study highlights negative effects of vitamin K antagonists, potential of vitamin K2

OSLO, NORWAY and METUCHEN, NJ (October 15th 2015) – *Kidney International*, a journal of the International Society of Nephrology, has approved for publication in October 2015 a new paper showing the protective effect vitamin K2 as MK-7 (menaquinone-7; MenaQ7® provided by NattoPharma) on arteriovenous fistula failure, a common complication suffered by chronic kidney disease (CKD) patients requiring hemodialysis.

The study, "Vitamin K- antagonist aggravate CKD induced neointimal hyperplasia and calcification in arterialized veins: potential role for vitamin K2 to prevent AVF failure", is significant because it adds to the growing body of evidence demonstrating the dangers of vitamin K antagonists (i.e., oral anticoagulants), a common traditional cardiovascular therapy, and how Vitamin K2 provides an alternative impactful therapy to combat cardiovascular damage.

"Arteriovenous fistula (AVFs) is a frequently used vascular access type for chronic kidney disease patients requiring hemodialysis. AVF failure is a complication leading to high hospitalization rates and morbidity. Whereas early AVF failure is caused by thrombosis or the veins' inability to dilate, later-course AVF failure is induced by stenosis and thrombosis resulting from neointimal hyperplasia (NIH) and calcification," says Dr. Leon Schurgers, associate professor and senior scientist at the department of biochemistry, the Cardiovascular Research Institute CARIM of University of Maastricht (The Netherlands), and researcher on the study. "Vascular calcification is a frequent complication in CKD patients; diagnosed as arterial calcification and calcification of arterialized veins. Recent work indicates that AVF calcification contributes to AVF failure."

Dr. Schurgers notes that CKD patients have significantly lower circulating vitamin K concentrations compared to the general population and hemodialysis patients have a poor overall vitamin K status due to low vitamin K intake. In addition, a high number of CKD patients at risk of arterial and venous thrombosis receive oral anticoagulants (vitamin K-antagonists; VKA). VKAs interact with carboxylation of coagulation factors but also impair the carboxylation, or activation, of Matrix Gla Protein (MGP), a vitamin K-dependent protein produced by vascular smooth muscle cells that is a powerful vascular calcification inhibitor in media and of intimal atherosclerotic plaques calcification.

"These constellations make CKD patients and patients undergoing VKA therapy, such as warfarin, prone to vascular calcification," he explains. "Treatment of CKD patients with vitamin K2 has been a suggested option to inhibit vascular calcification by counteracting the vitamin K deficiency."

To that end, AVF was generated in 190 rats. CKD was induced using adenine-enriched diet. Effects of CKD, VKA and K2 on AVF remodeling were evaluated using histology, morphometric analysis and immunohistochemistry. Examination of native and arterialized human veins was performed.

Results showed that arterialization, CKD ($p<.001$) and VKA ($p<.0001$) significantly enhanced venous NIH. K2 supplementation additional to VKA reduced NIH in arterialized veins ($p<.05$) in healthy but not in CKD animals. Arterialization, CKD ($p<.005$) and VKA treatment ($p<.002$) increased calcification while K2 supplementation attenuated calcification in healthy and CKD animals.

According to researchers, K2 enhanced matrix Gla protein (MGP) carboxylation in control ($p<.05$) and CKD ($p<.002$) animals. Human vein samples contained inactive MGP at calcification and NIH sites, indicating local vitamin K-deficiency. “We show that VKA treatment has detrimental effects on AVF remodeling,” says Dr. Schurgers. “K2 supplementation reduced NIH and calcification indicating vasoprotective effects. In arterialized veins, K2 should be considered as therapeutic approach to prevent NIH and calcification.”

“Clearly oral anticoagulant vitamin K antagonists thin blood at the expense of other essential metabolic functions, such as proper calcium utilization for bone support and cardiovascular protection,” says Hogne Vik, NattoPharma CEO. “It is time the medical community change the standard of care away from ‘poison.’”

To view the new study in *Kidney International,* visit:
http://www.nature.com/ki/journal/vaop/ncurrent/full/ki2015298a.html.

# # #

About MenaQ7®
MenaQ7® is the best documented, commercially available vitamin K2 as MK-7 with guaranteed actives and stability, clinical substantiation, and international patents granted and pending. MenaQ7® is available in two varieties: natural vitamin K2 as MK-7 Crystals and nature-identical synthetic vitamin K2 as MK-7 PURE. For more information on the health benefits of MenaQ7, visit menaq7.com.

About NattoPharma
NattoPharma ASA, based in Norway, is the world’s leader in vitamin K2 research and development. NattoPharma is the exclusive international supplier of MenaQ7® Vitamin K2 as MK-7, and has a multi-year research and development program to substantiate and discover the health benefits of vitamin K2 for applications in the marketplace for functional food and dietary supplements. With a global presence, the company established its North American subsidiary, NattoPahrma USA, Inc., in Meuchen, NJ. For more information, visit nattopharma.com.

For more information, please contact:

Hogne Vik, CEO NattoPharma
Cell phone: +47 97 53 53 26
E-mail: hogne.vik@nattopharma.com

Kate Quackenbush, Director of Communications
NattoPharma USA, Inc.
Phone: 609-643-0749
E-mail: kate.quackenbush@nattopharma.com