

Haemodialysis works for reducing dabigatran levels: Implications for urgent use during bleeding or surgery

8 April 2013

Dabigatran is one of the new oral anticoagulants which are increasingly used to prevent thrombosis. In case of an emergency (e.g. bleeding or urgent surgery), there are - despite the lack of a specific antidote - effective ways to quickly lower plasma dabigatran concentrations, as now demonstrated by a study published in this month's issue of *Thrombosis and Haemostasis* by Prof. Harm Peters, MD, Professor of Internal Medicine, Department of Nephrology, Charité - Universitätsmedizin Berlin, Germany.

The absence of a clinically available fast-acting antidote or rapid-elimination procedure is a major drawback for all the new oral anticoagulants. However, as with every anticoagulant, it might become necessary to rapidly reverse its effects in emergency situations, for example, during serious bleeding or urgent surgery.

Dabigatran is a specific reversible oral direct thrombin inhibitor (i.e., the active moiety of the orally available pro-drug dabigatran etexilate) approved for prevention of venous thromboembolism and of stroke in patients with non-valvular [atrial fibrillation](#). Dabigatran is highly water soluble, has low [plasma protein](#) binding, and a half-life of 12 to 17 hours ([creatinine](#) clearance > 60 ml/min) which is roughly doubled in patients with severe [renal insufficiency](#) (creatinine clearance

Since a specific antidote to reverse dabigatran's effects on haemostasis is currently lacking, substantial clinical experience with non-specific reversal agents such as fresh frozen plasma or factor concentrates (e.g. PCC) are not available, and since haemodialysis data about removing dabigatran at therapeutic levels from the body are sparse, Peters and his team initiated an open-label trial to gather more in-depth information about

reductions of the anticoagulatory effects of dabigatran in human beings via haemodialysis. They investigated the pharmacokinetic, [pharmacodynamics](#) and safety profiles of dabigatran and the reduction of dabigatran plasma concentrations after 4-hour haemodialysis sessions in seven clinically stable end-stage renal disease patients without atrial fibrillation. The study was designed to determine the efficiency of a single optimized haemodialysis session in removing dabigatran from the circulation with dabigatran being administered for a period of three days to achieve peak plasma concentrations comparable to those observed in atrial fibrillation patients receiving 150 mg b.i.d. The results revealed that haemodialysis indeed is an effective method to remove dabigatran from the body. A single 4-hour dialysis session will rapidly eliminate at least 50% of dabigatran plasma levels, substantially reducing its anticoagulatory activity. There was a clinically negligible redistribution of dabigatran after haemodialysis.

These findings demonstrate that haemodialysis can be a suitable approach to eliminate dabigatran in emergency situations. The low [protein binding](#) of dabigatran allows dialysis to be effective for its removal from the body, differing from other new oral anticoagulants that have high amounts of protein binding. Thus patients taking and physicians prescribing dabigatran can probably fall back on a reliable method to reduce its anticoagulatory effects in critical situations.

The current study has some limitations as it only included a relatively small number of clinical stable male patients with relatively few co-morbidities and just 28 haemodialysis sessions. The therapeutic benefit of dialysis still requires confirmation in [patients](#) with bleeding complications or other [emergency situations](#).

More information: Khadzhynov D, Wagner F, Formella S, et al. Effective Elimination of Dabigatran by Haemodialysis: A Phase I Single Centre Study in Patients with End Stage Renal Disease. *Thromb Haemost* 2013; 109: 4.
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Provided by Thrombosis and Haemostasis

APA citation: Haemodialysis works for reducing dabigatran levels: Implications for urgent use during bleeding or surgery (2013, April 8) retrieved 17 June 2021 from

<https://medicalxpress.com/news/2013-04-haemodialysis-dabigatran-implications-urgent-surgery.html>

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