

## Stroke Note

# Reversal of Vitamin K Antagonist Therapy by Prothrombin Complex Concentrate before Thrombolysis for Acute Stroke

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Vitamin K antagonist (VKA) frequently fails to prevent cerebral infarction, with 30% of VKA-treated patients experiencing ischemic stroke despite an international normalized ratio (INR) of  $\geq 2$  [1]. Intravenous (IV) thrombolysis is only recommended for patients with an INR of  $< 1.7$  [2]. Indeed, experimental results confirmed the high risk of post-thrombolytic hemorrhages at therapeutic INR levels [3]. However, administration of prothrombin complex concentrate (PCC) and vitamin K can obtain rapid and sustained reversal of VKA-induced coagulopathy with a very low ( $< 1.7\%$ ) thrombotic risk [4]. This reversal strategy was effective in two rodent models of ischemic stroke with prior effective anticoagulation (INR range: 2–3.5) [3, 5]. Only a few isolated human cases of VKA antagonized by recombinant factor VIIa, fresh frozen plasma or PCC preceding IV [6] or intra-arterial thrombolysis have been reported.

Our group is conducting a prospective pilot study to determine whether IV thrombolysis immediately after a 15-min infusion of PCC (and vitamin K) is safe and effective in ischemic stroke patients with magnetic resonance angiography-proven arterial occlusion and an INR of  $> 1.7$ . The mean  $\pm$  SD values of the 4 patients included to date are the following: age  $82 \pm 1.3$  years, National Institute of Health Stroke Scale (NIHSS) score of  $14 \pm 2.7$ , initial INR of 2.1 (range: 1.8–2.4), and stroke onset-to-needle time of  $187 \pm 23$  min. The mean post-reversal INR declined to 1.23 (range: 1.2–1.3), and no thrombotic complications occurred. The mean 24-hour NIHSS score was  $6.5 \pm 3.8$ . Of the 4 included patients, 3 were fully recanalized on 24-hour control magnetic resonance imaging, and 1 had an asymptomatic thrombolysis-related type 1 intracerebral hemorrhage. These preliminary observations are very encouraging. The real therapeutic challenge might be not only extending IV thrombolysis to ischemic stroke patients on VKA, regardless of their INR value, but also using a similar strategy in patients receiving new oral anticoagulants if effective antidotes become available.

## Disclosure Statement

The authors have no conflicts of interest to declare.

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