Letter to the Editor

Comment on "The Enhancing Effect of Focused Ultrasound on TNK-Tissue Plasminogen Activator-Induced Thrombolysis using an In Vitro Circulating Flow Model"

Dear Editor,

We recently read the article by Papadopoulos et al published in the *Journal of Stroke and Cerebrovascular Diseases*.[1] However, we have some concerns about the methodology and their potential consequences on the interpretation of results.

In this in vitro study, Papadopoulos et al, assessed different combinations of acoustic parameters with or without microbubbles in order to improve the therapeutic efficacy of Tenecteplase.[1] Surprisingly, the authors reported a clot weight loss of 1200 mg in the control condition (without ultrasound, microbubbles, or Tenecteplase) and they did not provide a clear explanation of this result. After a careful reading of the article, we think that the presence of degassed water in the circulating flow system might explain this astonished result. Indeed, degassed water induces an osmotic hemolysis of the clot, thus resulting in a decrease in clot weight. In addition, Tenecteplase is a plasminogen activator which mainly cleaves the plasminogen into plasmin in the plasma.[2] The plasmin degrades then the fibrin network.[2] The use of degassed water therefore impairs the efficacy of Tenecteplase. This experimental bias is also found in 2 publications from the same research group in the *Journal of Stroke and Cerebrovascular Diseases*.[3,4]

We appreciate the authors for their valuable work; however, we think that this experimental bias should compromise the interpretation of these results. Our comments do not in any way diminish the interest and the originality of this in vitro study, but further experiments in physiological conditions (using an iso-osmotic solution such as plasma) are required to confirm these results.

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