Reviewer's report

Title: Early recovery of microvascular perfusion induced by t-PA in combination with abciximab or eptifibatide during postischemic reperfusion

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Reviewer: Dr. Sorin Brener

Level of interest: A paper whose findings are important to those with closely related research interests

Advice on publication: Unable to decide on acceptance or rejection until the authors have responded to the compulsory revisions

This is an experimental model of ischemia-reperfusion designed to test the hypothesis that fibrinolysis and platelet inhibition is superior to each component alone with respect to immediate extent of reperfusion injury. Numerous other models have examined this issue in depth, both in experimental animals and in humans.

Compulsory revisions (Important comments):
1. The aim should be clarified to state that in both phases the same paramters were measured, thus the combination of t-PA with GP IIb/IIIa inhibitor was tested against each component alone (P.4, 1st paragraph)
2. The extent of I/R injury is not measured; it is inferred from various markers of reperfusion. The best way to prove the hypothesis is to perform histology at the end of the experiment in addition to these measurements.
3. Most importantly, nowhere in the manusrcript is there a comparison between t-PA with abciximab/eptifibatide vs. abciximab or eptifibatide alone. In most figures it appears that there is no significant difference between groups 3 or 4 and 5 or 6. If that is correct, it would mean that the main contribution to improved reperfusion stems from platelet aggregation inhibition alone. In the current manuscript, there is no clear evidence for an additive role of fibrinolysis in this model. Obviously, this is very different from AMI patients in whom the thrombus needs to be lysed before reperfusion can occur.
4. The authors fluctuate in the Discussion between assigning greater importance to platelet inhibition (P 6-7) vs. leukocyte adhesion and other mechanisms (P 8). This should be reconciled by recognizing the dependence of reperfusion injury on a multitude of factors, many of whom can not be fully expressed within 30 minutes.
5. There needs to be considerable improvement in the writing style (language) to improve the quality of the manuscript.

Discretionary Revisions (Suggestions):
1. P. 2, 1st para: add .platelet aggregation inhibition... Also consider clarifying the protocol with respect to combination therapy.
2. P. 2, 3rd para: the conclusion that combination therapy is superior to platelet inhibition alone is not
supported by the analyses presented.
3. P. 4-5 You may chose to present for each parameter of I/R a comparison beteen the different groups rather than the present format. Again comparisons between combination therpay and platelet inhibition alone are missing.
4. P. 7, 3rd para: add ...is also related to inhibition of leokocyte...
5. P. 7, 4th para: reference [11] is mistaken. Also the statement that ..."abciximab or eptifibatide has no effect on vascular cell..." is not substantiated.

Competing interests:

None declared.