Letters to the Editor

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Lack of a rationale for the Task Force recommendation regarding re-administration of streptokinase

Dear Sir

In the recently published Task force report, under section "Fibrinolytic regimens", the authors recommend not to re-administer streptokinase for at least 10 years. The reference supporting this statement is Ref. 51. After evaluating this paper and looking into the literature my comments are as follows:

The referenced publication only contains data up to 7.5 years. In so far any comment exceeding this period cannot be drawn from this publication.

Squire and his coworkers performed an excellent retrospective analysis, i.e. they analyzed blood samples of patients after discharge from a hospital. Evidently they measured single antibody titers at a given period after thrombolysis, but not reported the course of such titers over time. They definitely found a decrease of titer levels over time, but interestingly in their series, patients from 12 up to 35 month did not present SK-antibodies, the authors suggest for the inhibition of thrombolytic activity. In contrast, single patients after this period presented with high titers, which the authors suggest may negatively impact thrombolytic therapy.

Although the presence of Streptokinase antibodies in individual patients is an important observation, the origin of antibody elevation remains unclear and relation to a previous Streptokinase application is questionable. The absence of detectable antibodies against streptokinase in a relatively small control group is not a proof for persistence of antibodies.

I refer to the publications of Fears and coworkers, which in the Team-2 trial could not detect an influence of pretreatment antibodies on efficacy of streptokinase or anistreplase. The authors also evaluated safety parameters, but could not detect any additional risks arising from a reapplication of streptokinase, when applied according to the approved package information (i.e. no readministration between 5 days and 1 year).

In a second publication Fears and coworkers investigated the course of antibody titers. From their data the authors conclude that a streptokinase resistance is unlikely for 92% of the population after 12 months and 100% after 18 months after first application. Slightly elevated SK antibody titers are not preventive with regard to streptokinase efficacy. In the discussion the authors conclude as follows: 'Our results suggest that much of a second dose of SK might be neutralized up to six months after the first dose but not at 12 months'.

In conclusion, I recommend changing the respective paragraph of the Task Force publication. In my opinion, data for such a recommendation are inappropriate and definitely not supported by the reference. This view is further supported by the streptokinase antibody titer courses reported from the Terima investigators. My concern with the recommendation as mentioned is, that a large number of patients who still have a benefit after the first streptokinase application will be withheld from efficient therapy.

References


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Reply: Lack of a Rationale for the Task Force recommendation regarding Re-administration of Streptokinase

Dr Thimme questions the task force recommendation not to re-administer streptokinase (or anistreplase) in case of re-infarction.

Re-infarction due to re-oclusion of a previously recanalized coronary artery or to occlusion of another coronary vessel is a serious condition associated with a high morbidity and mortality. Therefore, optimal reperfusion therapy should be offered as soon as possible to these patients. If primary angioplasty is not available re-administration of lytic therapy is the only alternative. If a patient already received streptokinase or anistreplase at the time of the first infarction it is likely that neutralizing antibodies have developed which may reduce the efficacy for clot lysis after a second administration.

There is uncertainty regarding the incidence and the duration of the presence of these antibodies and large studies of the effect on clinical outcomes after re-administration are lacking. Antibodies have been detected up to 7.5 years after the first administration of streptokinase and there is no evidence that these antibodies may disappear completely. Indeed, Squire et al. conclude that ‘there is as yet no evidence of a time limit beyond which administration of streptokinase on a second occasion can be regarded as safe and likely to be effective’. In view of this, the Task Force recommends not to re-administer streptokinase or anistreplase at any time after the first administration. More effective reperfusion therapies such as primary angioplasty or the administration of a non-immunogenic fibrin-specific lytic agent should be offered to these high-risk patients.

References


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