Antifibrinolytic

Antifibrinolytics, such as aminocaproic acid (ε-aminocaproic acid) and tranexamic acid are used as inhibitors of fibrinolysis.

These lysine-like drugs interfere with the formation of the fibrinolytic enzyme plasmin from its precursor plasminogen by plasminogen activators (primarily t-PA and u-PA) which takes place mainly in lysine rich areas on the surface of fibrin. These drugs block the binding sites of the enzymes or plasminogen respectively and thus stop plasmin formation.

They are used in menorrhagia and bleeding tendency due to various causes. Their application may be beneficial in patients with hyperfibrinolysis because they arrest bleeding rapidly if the other components of the haemostatic system are not severely affected. This may help to avoid the use of blood products such as fresh frozen plasma (FFP) with its associated risks of infections or anaphylactic reactions.

Antifibrinolytics have gained increasing attention in minimizing blood loss and mitigating the risks associated with massive transfusions, including infection and coagulopathy in pediatric patients undergoing spine surgery. Nevertheless, the selection of optimal agent is still a matter of debate.

Aghajanian et al. aim to review the utility of these agents and compare the efficacy of antifibrinolytics in pediatric and adolescent spine surgeries. A comprehensive search was performed in Scopus, Web of Science, and MEDLINE databases for relevant works. Studies providing quantitative data on predefined outcomes were included. Primary outcome was perioperative bleeding between the groups. Secondary outcomes included transfusion volume, rate of complications, and operation time. Twenty-eight studies were included in the meta-analysis incorporating 2553 patients. The use of Tranexamic acid (RoM: 0.71, 95%CI: [0.62-0.81], $p < 0.001$, $I2 = 88\%$), Aprotinin (RoM: 0.54, 95%CI: [0.46-0.64], $p < 0.001$, $I2 = 0\%$), and Epsilon-aminocaproic acid (RoM: 0.71, 95%CI: [0.62-0.81], $p < 0.001$, $I2 = 60\%$) led to a 29%, 46%, and 29% reduction in perioperative blood loss, respectively. Network meta-analysis revealed higher probability of efficacy with Tranexamic acid compared to Epsilon-aminocaproic acid (P score: 0.924 vs. 0.571). The rate of complications was not statistically different between each two antifibrinolytic agent or antifibrinolytics compared to placebo or standard of care. The network meta-analysis suggests a superior efficacy of all antifibrinolytics compared to standard of care/placebo in reducing blood loss and transfusion rate. Further adequately-powered randomized clinical trials are recommended to reach definite conclusion on comparative performance of these agents and to also provide robust objective assessments and standardized outcome data and safety profile on antifibrinolytics in pediatric and adolescent pediatric surgeries [1)]

In 2010, the CRASH-2 trial showed that the antifibrinolytic drug tranexamic acid safely reduces mortality in bleeding trauma patients.

The antifibrinolytic drug aprotinin was abandoned after identification of major side effects, especially on kidney.

The indication for use of antifibrinolytic drugs is made with various methods. The most rapid and suitable one is thromboelastometry (TEM) in whole blood, which is even possible in patients on

heparin. With various assays, an enhanced fibrinolysis becomes visible in the curve signature (TEMogram) and from the calculated values, e.g. the maximum lysis parameter. A special test for the identification of increased fibrinolysis (APTEM) compares the TEM in the absence or presence of the fibrinolysis inhibitor aprotinin. In severe cases of activated fibrinolysis, this assay confirms the syndrome already in less than 15 min during the early phases of clot formation.

The influence of antifibrinolytic drugs (AFD) in the development of cerebral ischemia was also studied. AFD increased the risk of cerebral ischemia regardless of the admitting neurologic condition or the findings of CT. Among patients given AFD, impaired orientation or alertness was associated with a higher risk of ischemia. Other neurologic signs were not predictive of ischemia. Clinical features were not predictive of ischemia among patients not given AFD. Focal, thick collections of blood on CT were highly predictive of ischemia, whether or not patients received AFD. Admitting CT is the best prognostic indicator for the development of cerebral ischemia after SAH. It should be used to supplement the clinical examination in selecting patients best suited for therapy to prevent vasospasm [2].

1)
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2)
Adams HP Jr, Kassell NF, Torner JC, Haley EC Jr. Predicting cerebral ischemia after aneurysmal subarachnoid hemorrhage: influences of clinical condition, CT results, and antifibrinolytic therapy. A report of the Cooperative Aneurysm Study. Neurology. 1987 Oct;37(10):1586-91. PubMed PMID: 3658161.

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