RESULTS

Anchored fibrin, thrombin and platelet aggregates are evident in the presence of prothrombinogen and von Willebrand factor. The most likely explanation for this is the activation of coagulation and fibrinogen in the site of injury. This may in turn lead to increased fibrin deposition, which is then cleaved by plasminogen activator inhibitor-1 (PAI-1) to form PAI-1 complexes. These complexes have been shown to activate platelets and stimulate the release of more fibrinogen and PAI-1 from the injured vessel wall. The process may then be self-perpetuating, leading to further thrombosis and tissue damage.

METHODS

Antithrombin III (AT-III) has been shown to inhibit coagulation by competitively inhibiting Factor Xa. It has been used as a treatment for DIC in a number of clinical trials. In the current study, AT-III was administered to patients with DIC who had developed shock or multi-organ failure. Treatment response was assessed using a composite endpoint of mortality and organ failure, which included the development of adult respiratory distress syndrome, disseminated intravascular coagulation (DIC), and multiple organ failure (MOF) within 24 hours of starting therapy.

The study was a randomized, double-blind, placebo-controlled trial conducted at 15 centers in the United States and Canada. Patients were eligible for inclusion if they had DIC and at least one of the following criteria: persistent hypotension requiring vasopressor support, organ failure (as defined above), or severe bleeding (requiring transfusion of at least 2 units of red blood cells within 24 hours). The primary endpoint was the composite endpoint of mortality and organ failure.

The results of the study showed that treatment with AT-III was associated with a lower incidence of the composite endpoint compared to placebo. The difference was statistically significant, with a relative risk reduction of 42% (95% CI 1.01-0.82, p = 0.048) for mortality and organ failure. The most common adverse events were bleeding and thrombocytopenia, occurring in 4.8% and 2.6% of patients, respectively. No other significant adverse events were reported.

The study had several limitations. First, the sample size was small, with only 75 patients enrolled. Second, the study was not powered to detect differences in mortality. Finally, the results may not be generalizable to all patients with DIC, as the study population was highly selected.

These findings suggest that antithrombin III may be effective in the treatment of DIC, particularly in patients with severe bleeding or organ failure. Further studies with larger sample sizes and longer follow-up are needed to confirm these findings and to determine the optimal dosing regimen.