TREATMENT OF HEMORRHAGIC DISORDERS

TREATMENT OF HEMORRHAGIC DISORDERS: CEREBRAL HEMORRHAGE

Marietta M, Pedrazzi P, Torelli G

Dept. of Hematology, Azienda Ospedaliero, Universitaria Policlinico di Modena, Italy

Intracerebral haemorrhage (ICH) accounts for 10-30% of all cerebral strokes, with an estimated incidence of about 12-15 cases per 100000 people per year, Thirty days survival rate after ICH is approximately 60%, but 80-90% of the survivors are left with serious neurological deficits. Intracerebral bleeding has been considered a monophasic event that is limited by clotting and tamponade effect of the surrounding regions.[1] However, it was recently reported that intracerebral haemorrhage expands over time for both a persisting bleeding from the primary source and a mechanical disruption of the surrounding vessels.[2] Therefore, it could be important to prevent the haematoma enlargement through an ultra-early haemostatic therapy given a few hours from the onset. On this regard, recombinant activated factor VII (rFVIIa) is very attractive because of its pan-haemostatic potential In a randomised, double-blind, placebo controlled study, treatment with rFVIIa within 4 h of ICH onset limited growth of the haematoma by about 50%. This was associated with a 38% reduction in mortality and an improvement of functional outcomes at 90 days.[3] rFVIIa has been also successfully used for the treatment of ICH in thrombocytopenic patients.[4]

Oral anticoagulation therapy (OAT) increases the risk of ICH five to ten times, doubles the risk of mortality and increases the risk of progressive bleeding and clinical deterioration. Failure to rapidly normalise the international normalised ratio (INR) to below 1.4 further increases these risks. Patients with ICH receiving warfarin should be reversed immediately with prothrombin complex concentrates or fresh frozen plasma and vitamin K.[5]

References

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3. Mayer SA et al. N Engl J Med 2005; 352: 777-85.
4. Busani S et al. Thromb Haemost 2005; 93: 381-2.
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ACQUIRED HEMOPHILIA

Baudo F

Thrombosis Hemostasis Unit, Niguarda Hospital, Milan, Italy

AH is an autoimmune syndrome characterized by acute bleeding in patients with negative family and personal history. Its incidence varies between 0.1 and 1.0 case per million/population per year with equal distribution between sexes except in the younger age because of the pregnacy-related cases. AH is associated with autoimmune diseases, solid tumours, lymphoprolipherative diseases, pregnancy; 50% of the cases idiopathic. Diagnosis is suggested by the clinical picture and confirmed by the laboratory tests. Spontaneous or after minor trauma severe bleeding associated with a prolonged APTT, not corrected by incubation with normal plasma, with a normal prothrombin time are the diagnostic hallmarks. Bleeding is unrelated to inhibitor titre or FVIII level; therefore they are not valuable in guiding therapy. The goals of management are the control of bleeding and the suppression of inhibitor. None of the available agents is effective in all the patients. Effective hemostasis can be achieved with correction of FVIII deficiency (FVIII concentrates, DDAVP), bypassing (APCC, rFVIIa), neutralizing (high dose Ig) or removal of the inhibitor (immunoadsorption or plasmapheresis). Combined modalities may be necessary. The main criteria for the anti hemorrhagic therapy are the site and the entity of bleeding. Bleeding-related mortality approaches 12.5%; therefore early diagnosis and treatment are essential. Prednisone + cyclophosphamide and other immunosuppressive agents are the standard intervention. Positive predictive factors are a low inhibitor level and a short interval between the appearance of the inhibitor and the start of therapy. Promising results have been reported with cyclosporine A, 2-CDA, anti-CD20 monoclonal antibody and immune tolerance. The majority of the cases of AH occurs in the general hospitals. Because of the rarity of the disorder, the complexity of treatment and the potential risk of the bleeding-related death, these patients should be managed in the hemophilia centers or under their supervision.

DESMOPRESSIN

Cattaneo M

Unità di Ematologia e Trombosi, Ospedale San Paolo, Università di Milano, Milan, Italy

Desmopressin (1-deamino-8-D-arginine vasopressin, DDAVP) is a synthetic analogue of the antidiuretic hormone vasopressin. Like the natural antidiuretic hormone, desmopressin increases the plasma levels of factor VIII and von Willebrand factor (vWF), with the advantage, compared to vasopressin, that it produces little or no vasoconstriction, no increase in blood pressure, and no contraction of the uterus or gastrointestinal tract, so that it is well tolerated when administered to humans. In 1977, desmopressin was used for the first time in patients with mild hemophilia A and von Willebrand disease (vWD) for the prevention and treatment of bleeding, first during dental extractions and then during major surgical procedures. The clinical indications for desmopressin rapidly expanded beyond hemophilia and vWD. The compound was shown to be efficacious even in bleeding disorders not involving a deficiency or dysfunction of factor VIII or vWF, including congenital and acquired defects of platelet function and such frequent abnormalities of hemostasis as those associated with chronic kidney and liver diseases. Desmopressin has also been used prophylactically in patients undergoing surgical operations characterized by large blood loss and transfusion requirements. Some of these indications have been strengthened by the experience accumulated, others have not been supported by rigorous clinical trials or have been overcome by the advent of more efficacious treatments.