ated with effective transfusions in approximately 50% of occasions. In disorders of platelet function such as Glanzmann’s thrombasthenia, Bernard-Soulier, gray platelet and Scott syndromes and storage pool disease, other interventions, including the use of DDAVP, corticosteroids and antifibrinolytic agents, might be necessary. Unfortunately, in these conditions specific triggers for platelet transfusion cannot be easily identified because platelet count may be normal. Therefore, in these cases careful observation of the clinical development of hemorrhage is of utmost importance and the ultimate target is to restore sufficient platelet function. The lack or incomplete expression of specific glycoproteins in some platelet function disorders has raised the concern that the administration of normal platelets could trigger the development of antibodies capable of decreasing the efficacy of future platelet transfusions. However, this seems quite uncommon and is not considered a reason to withhold platelet support. In conclusion, use of good quality products, regular monitoring of patients and close co-operation between the clinical staff and the transfusion service are the cornerstones of effective platelet transfusion.

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References

Desmopressin in the treatment of patients with defects of platelet function

Desmopressin (1-deamino-8-D-arginine vasopressin, DDAVP) is a synthetic analog 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 vasconstriction, no increase in blood pressure, and no contraction of the uterus or gastrointestinal tract, so that it is well tolerated when administered to humans.1 In 1977, desmopressin was used for the first time in patients with mild hemophilia A and von Willebrand’s disease (VWD) for the prevention and treatment of bleeding. The clinical indications for desmopressin quickly expanded beyond hemophilia and VWD. The compound was shown to be efficacious even in bleeding disorders not involving a deficiency or dysfunc tion 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 superceded by the advent of more
Efficacious treatments. Desmopressin in the treatment of congenital disorders of platelet function. Desmopressin shortens or normalizes the bleeding time of most patients with congenital defects of platelet function. There is usually a good response in patients with defects of the release reaction and in those with isolated and unexplained prolongations of the bleeding time. Most patients with storage pool deficiency respond to desmopressin but a few do not, in particular those with severe deficiencies of platelet α-granule content. Negative results have been reported in most patients with Glanzmann’s thrombasthenia. The documented efficacy in patients with Bernard-Soulier syndrome, who lack the GPIb-IX-V complex, the platelet receptor for VWF that is essential for platelet adhesion to the vessel wall at high shear, supports the contention that desmopressin can shorten the prolonged bleeding time through mechanism(s) that are independent of released VWF (see later). Whether the effect on a laboratory test such as the bleeding time corresponds to a hemostatic effect is not well established. Although there are anecdotal reports of desmopressin successfully stopping or preventing bleeding in these patients, a clinical trial is necessary to determine the clinical efficacy of desmopressin. The mechanisms by which desmopressin induces shortening of the bleeding time in patients with normal factor VIII/VWF are unclear.

Released VWF; a biologically plausible, but as yet unproven, mediator. It is biologically plausible that the favorable effects of the compound may be mediated by increased platelet adhesion to the vessel wall due not only to the rise of plasma VWF but also to the abluminal secretion of the protein toward the subendothelium and to the fresh appearance in plasma of ultralarge VWF multimers. These ultralarge VWF multimers are hemostatically very effective because they support platelet adhesion to the vascular subendothelium to a higher degree than other VWF multimers and induce platelet aggregation under conditions of high shear. In fact, it has been shown that infusion of desmopressin improves the formation of platelet aggregates that form at the high shear rate levels that can be found in the microcirculation. This effect of desmopressin can be observed not only in patients with type 1 VWD, but also in patients with normal VWF but impairment of platelet aggregation at high shear due to congenital or drug-induced abnormalities of the secretory mechanisms or of the interaction of released ADP with its platelet receptors. The improvement of platelet aggregation at high shear after desmopressin administration to these patients correlated with the shortening of the bleeding time and the increase in the plasma levels of VWF with ultralarge multimers, suggesting that these changes in VWF could indeed be responsible, at least partly, for the observed effects of desmopressin on primary hemostasis.

Mechanisms independent of released VWF: proven, but as yet uncharacterized. If the potentiation of platelet function that is mediated by desmopressin-induced release of VWF is biologically plausible, there is no direct evidence that it is responsible for the effects of the drug observed in vivo. In contrast, clear and direct evidence exists that other, as yet unknown, mechanisms are operating in vivo. In 1987, it was shown that desmopressin infusion in patients with type 3 VWD further shortened their prolonged bleeding times, which had been partially corrected by the administration of cryoprecipitate. Since type 3 VWD patients lack VWF in tissue stores, the effect of desmopressin on their bleeding time was not associated with an increase in plasma VWF levels or the appearance of ultralarge VWF multimers. These results unequivocally indicated that the drug can affect primary hemostasis independently of released VWF. Subsequent studies in rabbits, who do not respond to desmopressin infusion with an increase in the plasma levels of factor VIII and VWF, gave further support to the concept that the drug can affect primary hemostasis independently of released VWF. In fact, in rabbits whose bleeding times had been prolonged by combined treatment with aspirin and the thrombolytic streptokinase, desmopressin infusion shortened the prolonged bleeding times without increasing the plasma levels of VWF. Another, more indirect demonstration of a released VWF-independent mechanism comes from the finding that desmopressin shortens the prolonged bleeding times of patients with Bernard-Soulier syndrome, who lack GPIb, the platelet receptor for VWF which is essential for platelet adhesion and activation at high shear. Effects of desmopressin on the platelet count or on agonist-induced platelet aggregation have been ruled out by many studies. Several putative mechanisms or mediators have been proposed, but their role is uncertain.

Conclusions. Desmopressin is efficacious in mild hemophilia and type 1 VWD and usually permits the avoidance of factor concentrates, with significant reductions in costs and the risk of transmitting blood-borne viral diseases. Desmopressin has been used successfully to prevent or stop bleeding in patients with defects of primary hemostasis not associated with abnormalities of VWF. However,
there is still no well-designed clinical trial that truly shows efficacy of the compound in these conditions.

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References


Advances in the pathogenesis and treatment of idiopathic thrombocytopenic purpura

Several articles published in this journal in the last two years have described new insights into the pathogenesis and treatment of idiopathic thrombocytopenic purpura (ITP).1-13 This issue contrasts an interesting paper by Veneri et al.14 on the association between Helicobacter pylori (HP) and ITP. Helicobacter pylori, besides being implicated in the pathogenesis of gastritis, peptic ulcer and lymphoproliferative disorders,15,16 has more recently been found to be associated with a number of autoimmune disorders, including adult ITP. The study by Veneri et al.14 provide some additional indirect supportive evidence of the pathogenetic role of HP infection in ITP and the therapeutic role of HP eradication, at least in a proportion of patients with ITP. The available evidence supports the conclusion that the search for HP infection and its eradication might be advisable in ITP patients. However, prospective clinical studies are required to establish the impact of the above observations on current clinical practice.17,18

References

8. Leung AY, Hawkins BR, Chim CS, Kwong YYL, Liang RH. Genetic analysis of HLA-typing in Chinese patients with...
increasingly employed for the treatment of multiple myeloma.

Reduced costs in patients with multiple myeloma resulted from this autologous transplantation, with half of the cases never requiring readmission and febrile episodes being less frequent. Therefore, this program might safely be offered to patients with multiple myeloma, resulting in better quality of life and reduced costs.

References


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