TREATMENT OF PATIENTS WITH VON WILLEBRAND DISEASE WITH INHIBITORS

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Type 3 von Willebrand disease (VWD) is a severe, recessive bleeding disorder characterized by virtually undetectable plasma von Willebrand factor (VWF), and consequently reduced factor VIII. The incidence of type 3 VWD varies considerably among different populations, ranging from 0.11 to 0.55 per million in most European countries. Molecular defects responsible for type 3 VWD are scattered throughout the entire gene, and are heterogeneous, most of them resulting in null alleles. Large deletions are only responsible for a minority of VWD type 3 cases but several studies have reported a link between the development of alloantibodies and homozygosity for deletions. Detection of inhibitors in the laboratory is not easy. Severe allergic reactions have been reported following the infusion of concentrates or plasma products in such cases. Administration of recombinant activated factor VII has been used successfully to treat these rare patients.

An acquired form of VWD associated with lymphoproliferative and autoimmune diseases has also been reported, although an inhibitory antibody has been conclusively identified in only a minority of these cases. Coagulation factor concentrates can be used in the management of such cases, and the successful use of recombinant activated factor VII and infusions of intravenous immunoglobulin have been reported. There has been reported in association with a number of conditions, including hypothyroidism where the aetiology appears to be simply due to decreased production of VWF, rather tha nteh presence of inhibitors. The bleeding tendency will typically resolve promptly once treatment with thyroxine has been initiated. The use of sodium valproate for the prevention of epileptic seizures has also been reported to be associated with a reduction in plasma VWF levels and a bleeding tendency.