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**Clinical Experience with Recombinant Human Thrombopoietin in Chemotherapy-Induced Thrombocytopenia**

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An important question with regard to the treatment of cancer patients with chemotherapy is whether recombinant thrombopoietin (rhTPO) can improve the platelet count and shorten the period of thrombocytopenia induced by chemotherapy. Both full-length rhTPO and a truncated version of the molecule, known as pegylated recombinant human megakaryocyte growth and development factor, have been evaluated in phase I/II clinical trials in cancer patients receiving chemotherapy. The development of neutralising antibodies and clinically significant thrombocytopenia in some patients treated with the truncated molecule has led to discontinuation of the trials in the USA. Clinical experience with rhTPO has shown that the full-length molecule is remarkably well tolerated and has a favourable safety profile; rhTPO exhibited dose-dependent increases in the platelet count and the number of megakaryocytes in the bone marrow before chemotherapy. There was also an increase in the frequency and proliferation of bone marrow progenitor cells and mobilisation of progenitors into the peripheral blood. Early results also showed that rhTPO can attenuate chemotherapy-induced thrombocytopenia and reduce the need for platelet transfusions. However the optimal schedule of rhTPO administration may depend on the length of the regimen and anticipated timing of the platelet nadir. These initial results indicate that rhTPO is a safe and potentially useful agent in the prevention and management of chemotherapy-induced thrombocytopenia.

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**Human Coagulation Factor FVIIa (Recombinant) in the Management of Limb-Threatening Bleeds Unresponsive to Alternative Therapies: Results from the NovoSeven Emergency-Use Programme in Patients with Severe Haemophilia or with Acquired Inhibitors**

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Achieving and maintaining haemostasis in patient with haemophilia and inhibitors to factors VIII or IX continues to be a major challenge to physicians. The open-label emergency-use study with recombinant factor VIIa (rFVIIa) evaluated the efficacy and safety of this factor (NovoSeven) in treating limb-threatening joint or muscle bleeds in 17 patients with haemophilia A or B and in 6 patients with acquired inhibitors to factor VII or IX. All patients had previously failed to respond to one or more alternative therapies (porcine factor VIII, prothrombin concentrates etc.). rFVIIa administration was effective or partially effective in controlling joint or muscle bleeds in 34 of 35 (97%) bleeding episodes in 23 patients; 14 of 17 (82%) muscle bleeds and 16 of 18 (89%) joint bleeds were effectively controlled. These findings suggest that rFVIIa is an effective and well-tolerated therapeutic option in the management of joint or muscle haemorrhage in patients with severe haemophilia and in patients with inhibitors.

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**Transfusions of Polymerized Bovine Hemoglobin in a Patient with Severe Autoimmune Hemolytic Anemia**


Hemoglobin solutions have several advantages as substitutes for red cells for transfusion over other such substitutes. Polymerised forms of bovine hemoglobin, such as HBOC201, are particularly promising. They have a molecular structure similar to that of human hemoglobin but have lower concentrations of organic phosphates, resulting in more pronounced oxygen unloading in ischemic tissue and increased binding of carbon dioxide in the deoxygenated state. The affinity of bovine hemoglobin for oxygen is also partially regulated by serum chloride ions, whereas that of human hemoglobin is influenced by 2,3-diphosphoglycerate. This results in excellent oxygen-transport properties. In this report the treatment is described of a 21-year-old woman with very severe autoimmune hemolytic anemia and ITP (Evans’ syndrome) and a period of septic shock due to cyclophosphamide-induced neutropenia. The anemia was refractory to all known forms of treatment. A total of 11 units of HBOC-201 (330 g, 4 g/kg) were administered over a 7-day period. A peak plasma level of HBOC-201 was attained after the ninth unit. There were no adverse effects, i.e. no rise in systemic or pulmonary arterial pressure. Five of the units were given because of clinical evidence of ischemia; three units as part of volume resuscitation during an episode of septic shock and three to maintain Hb levels above 4 g/dl. The clinical response to HBOC-201 was very favorable and appears to have been a life-saving treatment. The absence of red cell alloantigens is an added advantage in the treatment of severe autoimmune hemolytic anemia.
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Comparison of Solvent/Detergent-Inactivated Plasma and Fresh Frozen Plasma under Routine Clinical Conditions
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It has been shown that in solvent/detergent (SD)-treated plasma, the levels of protein S (PS) and of α2-antiplasmin (α2-AP) are reduced by 50%. Thus treatment with S/D plasma might induce an imbalance of plasma coagulation factors and inhibitors. To study this problem, 40 patients (23 receiving fresh frozen plasma, FFP, and 17 S/D plasma, random distribution by a list calculated by statisticians) who suffered from dilution coagulopathy, liver disease, disseminated intravascular coagulation or were connected to extracorporeal circulation were investigated. The following markers for activated coagulation (MAC) were measured: prothrombin fragments F1 + 2, fibrin monomers, D-dimers, thrombin-antithrombin and plasmin-α2-AP. Blood was taken just before and 1 h after the first plasma (2 units). No additional blood products were transfused before the second sample. Pre- and posttransfusion values were compared within the same group and between the two groups. Pretransfusion values for all inhibitors were in the same range in both groups of patients and increased after transfusion, except for PS in both groups. Whereas the pre-/posttransfusion values did not differ significantly in the FFP group, α2-AP (p = 0.02) showed a significantly higher increase in the S/D plasma group. There were no significant pre-/posttransfusion differences between the two groups of patients. This was also true for MAC pre- and posttransfusion. It is concluded that S/D plasma behaves as FFP under the study conditions employed.

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A multicenter study to evaluate the performance characteristics of these three methods. It concerned a two-phase study in which 10 centers located in the USA and Europe participated. Coded samples of RBCs and platelets were distributed by 24-hour (phase 1) or 2-day (phase 2) courier service. Samples were prepared to include concentrations of WBCs slightly below or above the concentration corresponding to the threshold standards for WBC-reduced RBC and platelet concentrates. All centers tested the samples by Nageotte hemocytometry plus one or both automated methods. Both flow cytometry and microfluorometry gave better results than Nageotte hemocytometry in freshly prepared samples. At WBC concentration >5/µl (RBCs) or >3/µl (platelets), the intersite CV was 20% for the automated methods but >30% for the Nageotte method (p < 0.001). Accuracy was greater for the automated methods than for Nageotte hemocytometry (p < 0.001). Nageotte hemocytometry showed a bias to underestimation relative to the results obtained with the automated methods. All methods had poorer results in testing samples that required 2 days’ shipment than in testing those requiring overnight shipment. These results are important in view of the fact that routine leuko-reduction of all cell concentrates is being considered. Optimal methods of counting residual WBCs are essential aspects of quality control.