HEPARINOID ORG 10172 ANTICOAGULATION FOR CARDIOPULMONARY BYPASS : A CASE REPORT.

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Introduction : Heparin-induced thrombocytopenia (HIT) is a not uncommon complication of heparin administration.There are two types of HIT.The first type is a mild transient thrombocytopenia of early onset.The patients are usually symptom-free,the thrombocytopenia usually improves and requires no therapy.The second type is a severe thrombocytopenia of delayed onset.This second type has the potential of serious thromboembolic complications (eg pulmonary embolism)(1).This type of thrombocytopenia requires treatment and heparin has to be stopped.The mechanism of this second type seems to be immune mediated.When patients with immune mediated HIT are rechallenged with heparin within 12 months of the initial event,recurrent thrombocytopenia and/or thrombosis may occur. We were presented with a patient requiring elective aortocoronary bypass surgery who had developed immune mediated HIT nine months before the anticipated date of surgery.Haematological investigation suggested that heparinoid Org 10172 should be a safe alternative to heparin anticoagulation for cardiopulmonary bypass (CPB) in this patient.
Methods : We obtained informed consent from the patient.Preoperatively the plasma of the patient demonstrated heparin-induced platelet aggregation in vitro as measured by standard platelet aggrego-metry.Additional in vitro aggregation studies with low-molecular-weight-heparins and heparinoids demonstrated that heparinoid Org 10172 produced the least aggregation.In vivo testing of Org 10172 did not induce thrombocytopenia or disseminated intravascular coagulation (DIC) in this patient. Therefore Org 10172 was utilized to achieve anticoagulation for CPB.The patient was given 10.000 anti-Xa units of Org 10172 intravenously (at time T0) and 2.500 anti-Xa units were added to the priming fluid.Every hour on CPB an additional bolus of 1.250 anti-Xa units of Org 10172 should be given in order to maintain a proper level of anticoagulation during CPB.Haemodynamic parameters,whole blood platelet count,thrombin time (TT),activated partial thromboplastin time (aPTT) and prothrombin time (PT) were measured immediately after induction of anaesthesia (T-30'),5 minutes before (T-5') and after (T+5') the first administration of Org 10172 (T0),and at T+30', T+55',T+69',T+79',T+90',T+97',T+127' and at one hour intervals after surgery,the first and second postoperative day (POD).Fibrinogen levels,antithrombin III activity (ATIII),factor V activity (fV),antiplasmin activity (AP),fibrinogen degradation products (FDP) and the ethanol gelation test were also measured at these time intervals.
Results : Intravenous injection of 10.000 anti-Xa units of Org 10172 did not cause cardiovascular problems.At T+5':platelet count,fibrinogen level, ATIII,fV and AP did not change significantly in respect to the values of these parameters at T-5' aPTT increased by 96%,TT increased by 53% and PT increased by 36%.At T+12' CPB was instituted without problems.At T+30' there was a "normal" decrease of the platelet count;aPTT,TT and PT remained elevated;fibrinogen level,ATIII,fV and AP were decreased by an amount which can be attributed to hemodilution.At T+57' 1.250 anti-Xa units of Org 10172 were given via the CPB circuit as dictated by the protocol.At T+75' however,and despite that aPTT,TT and PT were still prolonged, the surgeon observed some clots in the peri-cardial cavity.Therefore an additional bolus of 1.250 anti-Xa units of Org 10172 was given via the CPB circuit.At T+90' CPB was terminated without problems and transfusion of packed cells (PC) and fresh frozen plasma (FFP) was started. No protamine was administered.At T+120' surgery was terminated and the patient was transferred to the postoperative care unit (POCU) in a stable haemodynamic condition.The first two hours in the POCU were characterized by excessive bleeding. Blood loss was compensated by transfusions of PC and FFP.The platelet count returned to subnormal level.aPTT,TT,PT,fibrinogen level,ATIII,fV and AP returned to normal values probably because of the administration of FFP.There was a thrombocyto-penia on the first POD (70.10e9/l) and on the second POD (46.10e9/l).From the fourth POD the platelet count gradually returns to normal values.
Discussion : Heparinoid Org 10172 is a sulphated mucopolysaccharide from pig intestinal mucosa. Org 10172 has an anti-Xa/anti-thrombin ratio between 80 and 100.Although it is claimed that Org 10172 is virtually devoid of anti-thrombin activity and does not have an effect upon blood platelet function,we did observe a prolongation of the aPTT and TT,and a postoperative thrombocytopenia.Furthermore the anticoagulation for CPB with Org 10172 is unpredictable as the surgeon observed some clots in the pericardial cavity after the second bolus of Org 10172.
Conclusion : We demonstrated that anticoagulation for CPB can be achieved with Org 10172.Because the above-mentioned problems we cannot,however, recommend Org 10172 as a safe alternative for heparin anticoagulation for CPB in patients in whom heparin is relatively contra-indicated.

(1)Chong BH,Pitney WR,Castaldi PA : Heparin-induced thrombocytopenia : Association of thrombotic complication with heparin-dependent IgG antibody that induces thromboxane synthesis and platelet aggregation. Lancet 2 : 1246-1248,1982.