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HAEMOSTASIS CHANGES FOLLOWING TOTAL HIP REPLACEMENT IN A RANDOMIZED TRIAL WITH LMW HEPARIN (KABI 2165) AND ADJUSTED DOSE STANDARD HEPARIN. M. Berruyer, M. Dechavanne. Laboratoire Hémobiologie, Institut Pasteur, Faculté A. Carrel, Lyon, France.

70 patients were randomized to 3 groups. Group I : patients received 5,000 IU calciparine^R subcutaneously given 2h before operation, twice a day for 3 days and then, doses were adjusted by heparin levels. Groups II and III : 2,500 IU Kabi 2165 were given instead of calciparine^R, but in group III, a single daily dose of 5,000 IU Kabi 2165 was administered from the third day. Fibrinopeptide A (FPA), FPA generation, D-dimers were measured in plasma by ELISA methods. Anti Xa activity, Xa generation, heparin cofactor II (HC II), antithrombin III (AT III) were assayed in plasma using amidolytic methods. Serial measurements were done : pre-operatively, 2 and 8h after the first heparin injection and on the 7th post-operative day, before heparin administration. Pre-operatively, the mean level of D-dimers was higher ($p<0.05$) in 9 patients with bleeding complications after surgery (0.83 ± 0.57 µg/ml) compared to other patients (0.42 ± 0.33 µg/ml) 2h after heparin injection : 1) Xa activity was lower ($p<0.001$) in group I (<0.05 IU/ml) than in groups II and III (0.137 ± 0.1 IU/ml) ; 2) inhibition of Xa generation decreased ($p<0.001$) in group I (11.7 ± 8%) compared to that in groups II and III (25.8 ± 13%) ; 3) inhibition of FPA generation was lower ($p<0.05$) in group I (27.1 ± 32.2%) than in groups II and III (45.7 ± 29.2%) ; 4) diminution of D-dimers under heparin (0.37 ± 0.28 µg/ml) was only significant ($p<0.05$) in groups II and III. 8h after the first heparin injection, in all groups : 1) D-dimers increased ($p<0.001$) compared to pre-operative values ; 2) AT III and HC II diminished ($p<0.001$) ; 3) no anti Xa activity and no inhibition of Xa and FPA generation were found. On the 7th day : 1) 4 patients with deep vein thrombosis had higher FPA than other patients ; 2) AT III but not HC II fell in group I ($p<0.05$) ; 3) no anti Xa activity and no inhibition of Xa and FPA generation were observed in all groups.
In conclusion : 1) although clinical results are similar in the 3 groups, Xa activity, Xa generation, FPA generation change differently according to the heparin used ; 2) the occurence of deep vein thrombosis is followed by an FPA increase and bleeding complications are correlated with a high level of pre-operative D-dimers.

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EFFICACY AND SAFETY OF A LOW MOLECULAR WEIGHT HEPARIN (L M W H KABI 2165) IN PROPHYLAXIS OF POSTOPERATIVE DEEP VEIN THROMBOSIS (D.V.T.) AFTER ONCOLOGICAL SURGERY. L. Grunebaum (1), J.-P. Fricker (2), M.-L. Wiesel (1), Y. Vergnes (2), J.-P. Cazenave (1), P. Barbier (3) and A. Kher (3). INSERM U 311, Service d'Hémostase et de Thrombose, Centre Régional de Transfusion Sanguine, Strasbourg, France (1), Centre Anticancéreux Paul Strauss, Strasbourg, France (2) and KabiVitrum, Noisy le Grand, France (3).

The effect of a LMWH - Kabi 2165 on thrombo-embolism prophylaxis was studied in a prospective, randomized trial of 74 patients scheduled for surgery due to malignant diseases. 38 patients received 2 500 anti-Xa units S.C. 2 hours before operation, then 12 hours after and then 5 000 anti-Xa units once a day for 10 days. 36 patients were given calcium heparin 5 000 i.u S.C. 2 hours before operation and then three time a day for 10 days. ^{125}I-Fibrinogen uptake test was used in all patients to detect D.V.T. Positive scan was controlled by phlebography. In the Kabi 2165 group, 2 patients had positive scan not confirmed by phlebography No pulmonary embolism was reported. In the calcium heparin group, 2 patients developed non fatal pulmonary embolism. The fibrinogen test was negative in all the patients. Intra and postoperative blood loss, transfusion requirements, wound hematomas and infectious complications did not differ significantly between the two groups. The mean values of hematocrit and hemoglobin preoperatively and post operatively (day 1, and 10) were similar for the two groups :

	KABI 2165	HEPARIN
Hemoglobin g/l day -1	130.0	128.8
Hemoglobin g/l day +1	137.9	142.1
Hemoglobin g/l day +10	120.3	119.0
Hematocrit (%) day -1	37.8	37.0
Hematocrit (%) day +1	39.8	41.2
Hematocrit (%) day +10	35.1	34.9

It is concluded that a single daily injection of 5 000 anti-Xa units of Kabi 2165 may provide a prophylaxis against postoperative venous thromboembolism as effective and as safe as 3 daily injections of 5 000 i.u. of calcium heparin in oncological surgery.

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THROMBOSIS PROPHYLAXIS WITH LOW MOLECULAR WEIGHT HEPARIN (KABI 2165) AND CALCIUM HEPARIN IN PATIENTS WITH TOTAL HIP REPLACEMENT.
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In a prospective controlled randomized trial efficacy and safety of a low molecular weight heparin (Kabi 2165) and calcium heparin were compared in 80 patients with total hip replacement. 40 patients were given Kabi 2165 : 2,500 anti-Xa Units S.C. 2 hours before operation and then every 12 hours for 10 days. 40 patients received calcium heparin : 5,000 iu S.C. 2 hours before operation, then every 8 hours during the first post operative day and then heparin doses were adjusted according to the activated partial thromboplastin time and the thrombin time for 10 days. Bilateral venography was performed routinely on all patients between the ninth and tenth post operative day. The two groups were well matched for risk factors which could predispose to risk of developing venous thrombosis. 7 patients in Kabi 2165 group (17,5 %) and 4 patients in calcium heparin group (10 %) developed D.V.T. ($p = 0.33$). In 3 patients (7,5 %) of Kabi 2165 group and in 2 patients (5 %) of calcium heparin group, the thrombi extented to the popliteal-femoral vein. The incidence is not significantly different ($p = 0,50$). There were no significant differences in postoperative mean estimated blood losses, and mean blood units transfused. Mean hemoglobin levels and mean hematocrit values at the day before operation, the 1st, 5th, and 10th day after operation were :

	KABI 2165	HEPARIN
Hemoglobin g/l day - 1	140,2	141,4
Hemoglobin g/l day + 1	120,2	124,4
Hemoglobin g/l day + 5	114,8	119,5
Hemoglobin g/l day +10	114,4	117,5
Hematocrit (%) day - 1	41,5	41,6
Hematocrit (%) day + 1	35,2	36,5
Hematocrit (%) day + 5	33,7	34,6
Hematocrit (%) day +10	34,0	34,8

These differences were not statistically significant. Incidence of wound hematomas was similar in both groups No thrombocytopenia was reported in this study. In conclusion, Kabi 2165 2,500 anti Xa Units twice daily seems as efficient as adjusted-dose of calcium heparin thrice daily.

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USE OF A LOW MOLECULAR WEIGHT HEPARIN (LMWH) KABI 2165 DURING HAEMODIALYSIS : DETERMINATION OF LOWEST EFFECTIVE DOSE-MEMBRANE DEPENDANT DOSAGE REGIMEN. G. Potron (1), O. Toupance (2), C. Droulle (1), J. Chanard (2), A. Kher (3), P. Barbier (3). Laboratoire Central d'Hématologie (1), Unité d'Hémoldialyse (2) CHU 51090 REIMS France KabiVitrum Noisy le Grand (3)

The L.M.W.H., Kabi 2165 was compared to standard heparin in stable chronic haemodialysis patients in order to determine the lowest effective dose.
An initial dose of 1,000 to 2,500 anti-Xa units followed by an additional dose of 750 to 1,500 anti-Xa units, 1 or 2 hours after the start of the dialysis was associated with clotting and bleeding complications on 156 dialysis performed in 8 patients: 33 partial coagulations of extracorporeal circulation and 16 minor bleeding events. This dosage regimen corresponds to half of that of standard heparin needed in the same patients to prevent clinical problems.
In 9 patients treated with haemodialysis for 4 hours or less using cuprophane membrane, a single dose of 80 anti-Xa units/kg given at the start of dialysis achieved a sufficient antithrombotic effect on 195 dialysis, but minor bleeding complications were observed in 4 cases.
On 270 dialysis perfomed in 12 patients using polyacrylonitrile membrane, it was necessary to increase by 1,000 anti-Xa units this previous dosage to obtain satisfactory effectiveness.

The biological activities measured in this study indicates that : rises in fibrinopeptide A and platelet factor 4 were associated with clotting in the extracorporeal circulation.
Increased levels of factors VIII : RAg and decreased levels of prekallierein in the predialysis blood sanples were corrected by Kabi 2165 .

In conclusion, Kabi 2165 would appear to be an effective and easier antithrombotic agent in patients on chronic haemodialysis.