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PREVENTION OF DEEP VEIN THROMBOSIS (DVT) AFTER TOTAL HIP REPLACEMENT (THR) by ENOXAPARINE (LOVENOX^{R}) : ONE DAILY INJECTION OF 40 MG VERSUS TWO DAILY INJECTIONS OF 20 MG. A. PLANES*, N. VOCHELLE, C. MANSAT. *Clinique du Mail, La Rochelle, France.

Venous thromboembolism is a common complication in patients undergoing THR. In a previous open study, Enoxaparine, a low-molecular-weight-heparin, in a dose of 40 mg/24 hrs by SC injection, had been shown to be efficient in preventing DVT in these patients. This treatment was not associated with an increased risk of bleeding. The present trial compares the efficiency and the risks of bleeding of two regimens : treatment A (2 daily subcutaneous (SC) injections of 20 mg of Enoxaparine) and treatment B (1 daily SC injection of 40 mg of Enoxaparine).
118 patients, over 40 years, with a non traumatic hip disease, requiring THR, were included in a randomized, double blind trial. 59 patients received the treatment A. 59 patients received the treatment B. In both groups administration of 40 mg of Enoxaparine was begun 12 hours before operation. Patients were treated for 12-15 days, until bilateral ascending phlebography (BAP) had been completed.
Lower limbs BAP were performed in 114 patients. The frequency of DVT is low and is not significantly different between the two regimens : a DVT was detected in 1 of 57 patients who received the treatment A and in 6 of 57 patients who received the treatment B ($p = 0.11$). No pumonary embolism occurred in the 114 patients.
There was no serious bleeding complication, and the two groups are not significantly different on this point. 3 patients in each group had an important hematoma of the thigh. None required a surgical treatment. Red cell transfusion requirements were 3.88 U $\pm$ 1.71 in the group A and 3.53 U $\pm$ 1.06 in the group B ($p = 0.20$). There was no significant difference in daily hemoglobin levels between the two groups.
One daily injection of 40 mg of Enoxaparine was as effective as two daily SC injections of 20 mg of Enoxaparine in preventing DVT, in patients undergoins THR. The frequencies of bleeding complications were the same in each group.

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THE ANTICOAGULANT EFFECT OF ENOXAPARINE (LOVENOX^{R}) DURING HEMODIALYSIS. P. POUZOL*, B. POLACK*, E. DECHELETTE, C. JURKOVITZ. *Department of Hematology (Pr. KOLODIE), C.H.R.U. Grenoble, France

Enoxaparine is a low-molecular-weight-heparin obtained by partial and controlled depolymerization of a heparin of mucosal hog origin. We aimed at the evaluation of the efficacity of a unique injection of Enoxaparine in the prevention of blood clotting in the dialysis circuit in 42 patients with chronic renal failure. Three doses were tested : 0.75, 1.00, 1.25 mg/kg body weight in an open study with a crossing over of the three doses which were randomized according to a latin square design with a one week interval between each dose. None of the dialysis were impaired with clotting of the circuit and never an additional administration of anticoagulant was required in order to achieve the dialysis. Antithrombotic effectiveness was assessed by the quality of arterial and venous lines restitution and by visual inspection of the bubbles trap. No hemorrhagic event occurred. APTT didn't show residual hypocoagulability at the end of dialysis. Anti-Xa and anti-IIa activities 4 hours after administration were :

	0.75 mg/kg	1.00 mg/kg	1.25 mg/kg
Anti-Xa activity µg/ml	5.20 $\pm$ 1.75	6.87 $\pm$ 2.21	8.79 $\pm$ 2.92
Anti-IIa activity µg/ml	4.03 $\pm$ 1.97	5.66 $\pm$ 2.54	7.80 $\pm$ 3.79

Anti-Xa and anti-IIa activities exhibited a linear dose level relationship. Efficiency and tolerance were excellent for the three doses.

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PHARMACOKINETICS OF ENOXAPARIN AFTER SINGLE SUBCUTANEOUS ADMINISTRATION OF INCREASING DOSES (20 UP TO 80 MG) TO HEALTHY VOLUNTEERS. L. Bara (1), Y. Le Roux (2), M. Woler (2), F. Chauliac (2), A. Frydman (2) and M. Samama (1). Hôtel-Dieu Hospital, Paris (1) and Rhône Poulenc Santé, Antony, France (2).

The pharmacokinetics of enoxaparin (E) was randomly studied in 12 healthy male volunteers. Each dose (20-40-60 and 80 mg) was injected via subcutaneous (sc) route with a one-week wash out period. Anti-Xa and anti-IIa activities (ACT), calcium thrombin time (CTT) and Heptest were measured over a 36 hour period. E and the IV th International Heparin Standard were both used as internal standards.

The anti IIa and CTT effects were only measurable when the injected dose was higher than 40 mg. The maximum anti-Xa and anti-IIa ACT were obtained 3 to 4 hours after the dose. As anti-IIa ACT is lower than anti-Xa ACT (anti-Xa/anti-IIa ACT ratio$\simeq$1.6 to 2), the complete pharmacokinetic description of E was only based on anti-Xa data. Thus, the mean values of the maximal anti-Xa ACT (A max) were respectively: 1.58 $\pm$ 0.35 µg/ml; 3.83 $\pm$ 0.98 µg/ml, 5.38 $\pm$ 0.75 µg/ml and 7.44 $\pm$ 1.4 µg/ml for the four doses (20-40-60 and 80 mg). The resorption of E after sc injection was strictly linear whereas the relationships between A max or AUC in the one hand and dose in the other hand were A (anti Xa) Max = 0.0954 (dose) - 0,2083 $r = 0.9146/p < 0.001$; $n = 48$) and AUC (0 - 36 h) = 0.9117 (dose) - 7.59 ($r = 0.9133/p < 0.001$; $n = 48$). The mean residence time of E was close to 6 h (5.83 $\pm$ 0.86 h for D = 40 mg; 6.19 $\pm$ 0.74 h for D = 60 mg and 6.44 $\pm$ 0.76 h for 80 mg) indicating that around 50% of the total anti Xa ACT is induced in a 6 hour interval. The apparent volume of distribution $V_{d\beta}$ is close to 6 l (6.59 l $\pm$ 1.33 l for D = 60 mg) and the total body clearance is equal to 1.25 l/h, indicating the rate of depolymerisation of enoxaparin is lower than that of heparin. Plasma elimination half-life of anti-Xa ACT is equal to 4.36 $\pm$ 1.07 h (D = 40 mg) whereas that of anti-IIa ACT is shorter ($t_{1/2\ \beta}$) = 2.1 h). These results indicate that enoxaparin exhibits i) a differential anti-Xa/anti-IIa ACT profile, ii) a linear relationship between dose and anti-Xa/anti-IIa ACT and iii) a kinetic profile which is significantly different from that of standard heparin.

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DEEP VENOUS THROMBOSIS PROFYLAXIS WITH A LMW HEPARIN (KABI 2165) IN STROKE PATIENTS. M.H. Prins (1), G.J.H. den Ottolander (1), R. Gelsema (2), T.C.M. van Woerkom (2), A.K. Sing (3), I. Heller (3). Department of Internal Medicine (1), Department of Neurology (2), Department of Rontgenology (3), Bergweg Ziekenhuis Rotterdam and Department of Radiology, Sint Franciscus Gasthuis, Rotterdam.

In a group of 60 patients entering our hospital for completed stroke, within 72 hours after onset of symptoms, treatment with Kabi 2165 2x 2500 anti-Xa U s.c. was compared to placebo 2x s.c. in a double blind trial to test the assumption that Kabi 2165 could prevent DVT, without causing cerebral bleeding in the ischaemic area. The diagnosis of stroke was made on clinical grounds. A CT-scan of the head was performed before entering the trial to exclude cerebral bleeding or tumor. Follow-up during a trial period of 14 days included a Fibrinogen scan - if positive followed by flebografy. After the trial period or when clinical deterioration occurred a CT-scan of the head was repeated. Before and during the trial period haematologic and coagulation data were obtained and will be reported. Obduction was obtained whenever possible.

The patient groups were comparable, except for a slight preponderance of disturbed consciousness and atrial fibrillation in the Kabi 2165-treated group. This difference did not reach statistic significance. In the Kabi 2165 group there were 6 cases of DVT compared to 15 in the placebo group (p=0,05). In the Kabi 2165-treated group there were slightly more cases of cerebral bleeding and death during trial, respectively 4 versus 2 and 9 versus 4 (both NS). Cerebral bleeding occurred only in patients with a bloodpressure above 150/90 mmHg on entering.

Although the patient group is still small, we like to conclude that in normotensive stroke patients Kabi 2165 2x 2500 anti-Xa U s.c. per 24 hours, is a safe method of DVT profylaxis.