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LOW MOLECULAR-WEIGHT HEPARIN CY216 IN THE TREATMENT OF ACUTE MASSIVE PULMONARY EMBOLISM. A CASE REPORT. G. Zambon (1), M. Vigo (2) M. Scatigna (1), C. Di Giacomo (1) and P. Prandoni (1). Clinica Medica II (1) and Radiologia II (2), University of Padova, Italy.

A 68 years old women presented to our Department with signs and symptoms suggestive of acute massive pulmonary embolism twenty days after knee fracture. She was in shock: heart rate, respiratory rate and blood pressure was 140/m, 36/m and 70 mmHg respectively. Two months before she had a severe episode of cerebral haemorrhage. Clinical suspicion was confirmed by a pulmonary digital subtraction angiography (DSA) and computerized tomography (CT), which showed a large filling defect in the right main pulmonary artery and a high degree of fascular sequestration of the lung (Miller index = 18). After rejecting the use of thrombolytic drugs, it was decided to treat the patient with low molecular-weight heparin CY216, due to the possible weaker bleeding potential with respect to the unfractionated heparin, and a dose of 17,500 U anti-Xa Choay was administered subcutaneously two times daily. A significant clinical improvement (decrease of heart and respiratory rate and increase of blood pressure) was observed within the first 48 hours of treatment. Pulmonary DSA and CT scan, repeated after 7 days of treatment, showed an important reduction of the above-mentioned defects (Miller index = 7). Not any bleeding complication developed and the patient was discharged within 15 days from the Hospital on warfarin therapy.

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INTER-INDIVIDUAL PHARMACOKINETIC VARIATIONS AFTER INTRAVENOUS (IV) AND SUBCUTANEOUS (SC) INJECTION OF CY 216 IN HEALTHY SUBJECTS. B. Boneu (1), G. Houin (2), M. Rostin (2), J.L. Montastruc (2), P. d'Azemar (3), B. Bayrou (4). Laboratoire d'Hémostase, Centre de Transfusion Sanguine (1) and Laboratoire de Pharmacocinétique (2) Hôpital Purpan 31052 Toulouse Cédex, Laboratoire Choay (3) and Institut Choay (4) 75782 Paris Cédex 16, FRANCE.

We investigated the pharmacokinetic parameters and their inter individual variations of a low molecular weight heparin (LMWH) derivative (CY 216, Fraxiparine R, Choay). In a cross-over study, 100 anti Xa IC u*/kg were injected in 12 healthy volunteers, either by IV or SC route, at one week interval. The pharmacological effects were followed on 12 serial citrated samples for 24h: - anti factor Xa (AXa) activity (chromogenic assay calibrated against CY 216); - APTT and thrombin clotting time prolongation. The main pharmacokinetic parameters (elimination half-life ($T_{\frac{1}{2}}$); clearance (cl); distribution volume (Vd); bioavailability F (SC/IV)) were calculated from the anti Xa activity curves using conventional methods. The results (mean, range) indicated below confirm some classical properties of CY 216: poor anticoagulant effect (APTT-TT), even after IV injection, longer half-life than standard Heparin (SH), distribution volume similar to plasma volume, excellent bioavailability of the drug.

	$APTT_{max}$ sec.	C_{max} AXa u/ml	$T_{\frac{1}{2}}$ h	Vd l	cl ml/min	F (SC/IV) %
IV	21	1.9	2.2	3.6	19.5	-
	16-53	1.4-2.3	1.5-2.9	2.5-4.9	15.4-23.9	-
SC	2	0.61	3.8	-	22.8	88
	0-12	.48-.89	1.5-6.4	-	14.5-33.8	58-117

We also emphasize important inter-individual variations between volunteers, as known for the pharmacological effects of SH in vitro and ex-vivo. From those results it could be assumed that, as for SH, close monitoring of treatment with LMWH would be suitable with higher dosages, after validation of the correlations between those biological tests and clinical results.

* anti Xa IC u : anti factor X activated Institut Choay unit.

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TREATMENT OF PROXIMAL DEEP VEIN THROMBOSIS (DVT) OF THE LOWER LIMBS BY CY 216* (LMWH) VERSUS UNFRACTIONATED HEPARIN (UFH) Duroux P. MD, Paris, France.

Preliminary clinical data showed CY 216 could be effective in the treatment of established DVT. Thus, we undertook an European collaborative controlled randomised study to assess the efficacy and tolerance of this new antithrombotic agent.

140 patients presenting a **proximal** DVT of less than 5 days confirmed by phlebogram, are randomly allocated into 2 groups, one treated by UFH with constant pump infusion, at doses daily adapted to laboratory tests, the other one by CY 216 at a mean daily dosage of 450 aXa IC u** calculated at onset of treatment on body weight, administered daily by 2 sub-cutaneous injections during 10 days, without dosage adaptation whatever the lab. tests results.

The efficacy is assessed on comparison on both phlebograms (Marder and Arnessen Indexes) and lung Scans performed before inclusion and after end of treatment. In addition, tolerance is appreciated on the incidence of bleeding complications. Furthermore, incidence of clinical DVT recurrence is assessed at 12th week.

The present study is still in progress, 130 patients are included ; the preliminary results tend to show that CY 216 at fixed doses, body weight adapted, is an effective and safe treatment of proximal deep vein thrombosis.

* CY 216 : Fraxiparine R Choay

** Axa IC u : anti-factor Xa Institut Choay unit.

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TOLERANCE OF CY 216 AS THROMBO-EMBOLIC DISEASE PREVENTION : EVALUATION OF LOCAL HAEMORRHAGIC RISK IN OPHTAL SURGERY - Preliminary results - Morin Y., Internal Medecine Department, and Limon S., Ophtalmology Department, Centre Hospitalier National d'Ophtalmologie des Quinze-Vingt, 28 rue de Charenton, 75012 PARIS.

The specific biological activity of low-molecular weight heparin prompted using CY 216 in ophtalmological surgery for thrombo-embolic prevention. We report preliminary results on 31 patients (9 males, 22 females, mean age 74,4) treated from 06/86 to 12/86 with a daily 0,3 ml sub-cutaneous injection of CY 216 started 2 hours prior to surgery until day 7, or day 10 for 7 patients. Coagulation tests included TCa and anti-Xa activity. All patients were checked daily for ocular haemorrnagies and thrombo-embolic manifestations. Anaesthesia was general in 16 cases and local in 15. Surgery was performed on 21 cataracts (67 %), 8 retinal detachments (26 %), 2 glaucomas (6 %).

No patient developped any clinical thrombo-embolism condition. In that particular surgery where frequent local haemorrhagic complications occur and delay the onset of heparinotherapy, CY 216 treatment exhibited 3 minor eyelids ecchymosis, 1 choroïd hematoma and 5 subconjonctival suffusions, all transient and not impacting specific surgical results ; and all already known as possible mechanical vascular aggression independant of heparinotherapy. 2 hyphemas (6 %) also occured, for which CY 216 was discontinued, still not impacting surgical results, and without excessive hypocoagulation according to tests. These biological tests showed no adverse effects ; TCa never raised more than 6" above controls, and anti-Xa activity raised to 4 times pre-treatment values ; in 3 patients, high values did not induce any haemorrhagic complications, a very strong argument in favor of excellent tolerance of CY 216 therapy.

At this stage of preliminary results, the tolerance of CY 216 concerning local haemorrhagic risk in eye surgery can be evaluated as near to excellent.