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DOES LOW-DOSE PERI-OPERATIVE HEPARIN ADMINISTRATION AFFECT MORTALITY FOLLOWING MAJOR ABDOMINAL SURGERY? A.R. Hedges, C.J. Parker and V.V. Kakkar. Thrombosis Research Unit, King's College School of Medicine & Dentistry, Denmark Hill, London SE5 8RX, UK.

Current evidence suggests that peri-operative low-dose heparin administration reduces the post-operative frequency of fatal pulmonary embolism and may also reduce the frequency of fatal myocardial infarction. Evidence is now accumulating that anticoagulants affect the course of malignant disease, in particular the formation of metastases. Malignant cells disseminated during surgery may be responsible for metastasis formation.

The aim of this study was to discover whether administration of peri-operative low-dose heparin had any effect on mortality. A retrospective analysis of 1,232 patients undergoing elective abdominal surgery was performed. 658 patients received no heparin and 574 patients received heparin prophylaxis subcutaneously. The two groups were well matched for age, sex, type of operation performed and distribution of pre-existing disease. The number and causes of death are shown below.

CAUSE OF DEATH	HEPARIN	NO HEPARIN	X^2	P
Cardiopulmonary	15(2.6%)	29(4.4%)	2.733	NS
Disseminated malignancy	15(2.6%)	36(5.5%)	6.009	<0.02
Non-disseminated malignancy	11(1.9%)	11(1.7%)	0.291	NS
Miscellaneous	3(0.6%)	6(0.9%)	0.291	NS
Total	44(7.1%)	82(12.5%)	7.593	<0.01

Low-dose peri-operative heparin administration reduces post-operative mortality. This reduction is only partly explained by a reduction in cardiopulmonary cases, more significantly there is a reduction in death due to disseminated malignancy.

A prospective study is planned in patients undergoing operations for malignancy to confirm this finding.

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THROMBOEMBOLISM PROPHYLAXIS IN SPINAL CORD INJURY: FIXED VS ADJUSTED DOSE HEPARIN. D. Green (1), T. Cohn (2), P. Filbrandt (2), V. Ito (2), M. Y. Lee (2), J. Press (2), and W. C. Vandenberg (2). Departments of Medicine (1) and Physical Medicine and Rehabilitation (2), Rehabilitation Institute and Northwestern University Medical School, Chicago, Illinois, U.S.A.

We had previously estimated the incidence of deep vein thrombosis (DVT) in untreated spinal cord injury patients with complete motor paralysis to be 78% (Paraplegia 20:227, 1982). Therefore, we have begun to randomize patients to receive prophylaxis with either fixed dose heparin (5,000 u every 12 h subcutaneously) or adjusted dose heparin (mean dose, 13,890 u every 12 h). Treatment is started within 72 hrs of injury, and continued for 12 weeks. Nineteen subjects have received the fixed dose for 155 weeks, and 21 the adjusted dose for 153 weeks (p = N.S.). Patients have had daily clinical examinations for thromboembolism/bleeding, and weekly doppler flow and impedance plethysmography studies. All suspected DVTs have been confirmed by venography. The activated partial thromboplastin time (aPTT) with the fixed dose has average 26 ± 1.5s (S.D.) and with the adjusted dose, 39.6 ± 7.6s ($p < 0.001$). There have been 2 episodes of pulmonary embolism and 2 DVTs in the fixed dose group and 1 DVT in an adjusted dose patient whose aPTT never rose above 26s. The thromboses were noted after 2, 3, 3, 4, and 6 weeks of prophylaxis. Bleeding occurred in 2 patients on the adjusted dose regimen and required withdrawal of the heparin; no subject on the fixed dose bled. Our preliminary conclusion is that heparin prophylaxis significantly reduced the frequency of thromboembolism in spinal cord injury patients. While fewer and less severe thrombotic events have occurred in those receiving adjusted doses, the decrease has not yet reached statistical significance ($\chi^2 = 1.16$). Furthermore, there appears to be a small, but definite risk of bleeding on this regimen. Thus, additional patients are being studied to determine the optimum use of heparin in this population.

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PREVENTION OF MYOCARDIAL REINFARCTION BY LOW DOSE HEPARIN. G.G. Neri Serneri (1), F. Rovelli (2), G.F. Gensini (1), S. Pirelli (2), M. Carnovali (1) and A. Fortini (1). Clinica Medica I, University of Florence, Italy (1) and Divisione di Cardiologia, Centro De Gasperis, Ospedale di Niguarda, Milan, Italy (2).

The effectiveness of low dose heparin in the prevention of myocardial reinfarction was investigated in a multicentric randomized controlled study. After having given their informed consent to undergo daily subcutaneous heparin administration, 728 patients of both sex aged 50-75 years, who had suffered from a transmural myocardial infarction 6-18 months before the enrollment and were in the I or II NYHA class were randomized. 365 patients (control group) were on the therapy usually performed by the 21 experimental centers partecipating in the study and 363 (heparin group) were treated with subcutaneous calcium heparin (Calciparina®) 12,500 IU daily in addition to the usual therapy of the centers. During enrollment the balancement of the two groups was periodically checked for age, sex, serum cholesterol, cigarette smoking, blood pressure, site of infarction, arrhythmias and drug regimen. The prospectively established end-points were: transmural reinfarction as primary end-point; general mortality and mortality for cardiovascular events as accessory end-points over a mean follow-up period of 24 months. Statistical analysis was foreseen both on drug efficacy (DE) and intention to treat (IT) basis. Patients of both groups underwent periodical examinations during the study. Adherence to the therapy and bone mineral content (bone density by double isotope technique) were also checked. At the end of the study the balancement for the factors considered was satisfactory and the drop-outs were 7.7% in heparin group and 6.3% in control group (ns). In heparin group the reinfarction rate was lower by 62.92% than in control group. At life table analysis the difference was statistically significant ($p < 0.05$ DE and $p=0.05$ IT). Mortality rate was reduced by 47.61% (DE) in heparin group ($p < 0.05$ at life table analysis). Cardiovascular mortality was not significantly reduced (-33.06%), but the mortality attributable to thromboembolism was reduced in heparin group ($p < 0.05$). Sixty patients (16.5%) discontinued heparin treatment, but only in 23 patients (6.3%) suspension was due to side effects.

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MAY LMWH (CY 216) BE ADMINISTERED DURING PREGNANCY ? F. Forestier (1), F. Daffos (1), M. Rainaut (1), P. Cornu (2), A. Deschamps (2), F. Toulemonde (3). Centre de Diagnostic Prénatal et de Foetologie, Hôpital N.D. de Bon Secours, Paris (1) Laboratoire d'Hématologie, Hôpital Necker, Paris (2) and Institut Choay, Paris, France (3).

One of the main problems related to the use of fractionated heparin during pregnancy concerns its transplacental passage.

Previous studies showed LMW heparin fraction CY 216 has no teratogenic effects, and when labelled, does not cross the placental barrier in animal, and does not appear into the milk.

We studied the transplacental passage following subcutaneous administration of large dosage (17.500 AXa IC u) in 7 women who where going to have an abortion during the third trimester of gestation because of severe fetal malformation, after informed consent.

Blood samples were taken before and 3 h after injection from the mother , from the fetuses 3 h after mother injection -using ultrasound guidance of the needle and aspiration of blood in the umbilical vein.

Biological assays showed that the effects are clearly observable in mother, whereas no change was observed from the fetus.

Activity	Mother before (n = 7)	Mother after (n = 7)	Fetus (n = 7)	Fetus control (n = 63)
Anti-Xa µg/ml)	0.03 ± 0.08	4.16 ± 1.35	< 0.05	< 0.05
Anti-IIa (IU/ml)	0.03 ± 0.03	0.06 ± 0.04	< 0.05	< 0.05
APTT (sec.)	34.9 ± 8.0	39.3 ± 10.6	91.1 ± 4.5	93 ± 9

Thus, it was justifiable to treat, for several reasons, 22 patients using CY 216 during a period of 2 to 5 weeks before delivery. Treatments were successful and no complication has been observed. The cord blood samples at birth never showed any biological activity.

These data seem to clearly indicate that there is no passage through the placental barrier of CY 216 which offers a new possibility of treatment during pregnancy.