Deep Venous Thrombosis and Left Ventricular Thrombosis Prophylaxis by Low Molecular Weight Heparin in Acute Myocardial Infarction

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Low molecular weight heparins (LMWH) and unfractionated heparins have shown a similar antithrombotic effect [1]. Several trials of a low-dose heparin prophylaxis after acute myocardial infarction (AMI) clearly indicate a significant reduction of deep venous thrombosis (DVT) of the lower limbs [2–4]. Moreover, a recent paper [5] showed a significant reduction of left ventricular thrombosis using full-dose subcutaneous standard heparin. Many published trials with a LMWH have been conducted in high-risk surgical patients. However, to our knowledge, the use of LMWH in the prevention of DVT and left ventricular thrombosis after AMI has not been reported. Thus, we present here the preliminary results of a pilot study performed over 1 year in patients treated with subcutaneous LMWH (Fragmin®; Kabi 2165) twice daily.

The study was designed as an open randomized standard heparin-controlled trial and was approved by the local ethical committee. Thirty-nine patients (30 males, 9 females, mean age 69 ± 11.3 years) with an AMI of less than 48 h were included after informed consent was given, regardless of the site of myocardial infarction. Patients were not included in case of thrombolysis. The two groups were comparable with regard to all factors examined; none presented a history of DVT. The patients were treated for 7 days either by subcutaneous injections of LMWH (120 aXa IU/kg twice daily; n = 20) or continuous intravenous infusion of standard heparin adapted to maintain the activated partial thromboplastin time (APTT) between 1.5 and 2.5 times the control value (n = 19). Prolonged thyroid gland saturation (3 weeks) was obtained by an intravenous administration of 150 mg sodium iodide (day 0). DVT was diagnosed by daily 125I-fibrinogen scanning, as described by Negus et al. [6], from day 1 to day 6. To diagnose left ventricular thrombosis, an echocardiography was performed between day 3 and day 6. All patients were confined to bed from day 0 to day 6.
Twenty-five patients completed the trial, 13 in the LMWH group and 12 in the standard heparin group. Six patients died during the study, 3 in each group, of cardiac arrest. Four were excluded for technical reasons. Investigational drugs were prematurely interrupted in 4 patients: in 1 for acute heart failure (standard heparin), in 1 for gastrointestinal bleeding (LMWH), and in 2 for unstable angina (1 standard heparin, 1 LMWH).

In both groups (n = 25) no DVT or left ventricular thrombosis was found during the trial. Moreover, no thrombosis was reported in the 14 patients excluded before the end of the study. Biological data are expressed as mean ± SD. In both groups initial APTT and plasma anti-Xa activity were similar. In the standard heparin group, the APTT was maintained with a mean range of 1.6–2.5 times the control value. In the LMWH group, the plasma anti-Xa activity increased from < 0.1 U/ml before treatment to 0.63 ± 0.30 on day 2 of treatment and was on the 6th day of treatment 0.44 ± 0.18 U/ml. The APTT significantly increased with an average of 1.4 ± 0.23 times the control value on day 2 (p < 0.001, paired Student’s t test) and was 1.25 ± 0.18 times the control value on day 6 (p < 0.001). The local tolerance was good in both groups. No thrombocytopaenia was reported during the study. One patient of the LMWH group suffered from moderate gastrointestinal bleeding due to an oesophago-gastric stress ulcer. No coagulation abnormality was found in this patient. He died a few days later of cardiac arrest. One patient of the standard heparin group had acute anaemia, without external haemorrhage on day 6.

The interest of DVT prophylaxis by standard heparin after AMI is well known. LMWH is effective in the prevention of surgical and nonsurgical DVT, especially in an elderly population confined to bed. Despite the small sample size, the results of this pilot study are in favour of DVT and left ventricular thrombosis prophylaxis in AMI, either by fixed dose of LMWH or adapted dose of standard heparin. Probably, no monitoring is needed for LMWH therapy because the anti-Xa plasma levels were found to be more stable with LMWH than APTT with standard heparin. Also we used a fixed dosage of LMWH, whereas the dosage of standard heparin was adjusted to APTT. Thus, LMWH appears to be promising in the prevention of DVT and left ventricular thrombosis in AMI and to be able to reduce the treatment costs. A larger multicentre trial would be required to ascertain whether LMWH as well as intravenous or subcutaneous unfractionated heparin reduce the incidence of DVT and left ventricular thrombosis in this indication and may authorize alleviation of platelet monitoring.

References


