Low-Molecular-Weight Heparin and Lipoprotein(a) in Patients with Chronic Renal Failure

A.	Andrea	Sagripanti
V.	Vincenzo	Cozza
G.	Giuliano	Barsotti

Istituto Clinica Medica I, Università di Pisa, Italy

Prof. Giuliano Barsotti, Istituto Clinica Medica I, Università di Pisa, via Roma 67, I-56126 Pisa (Italy)

Dear Sir,

Lipoprotein(a) (Lp(a)) has been recently implicated as an important risk factor for cardiovascular disorders both in the general population and in uremic patients [1,2], but the possible effects of low-molecular-weight heparin (LMWH) on plasma level of Lp(a) are not reported. We have investigated the acute effect of a LMWH, Nadroparin, on Lp(a) plasma level in a series of uremic patients on conservative dietary treatment. The prothrombin fragment 1+2 (F1+2), a specific index of in vivo thrombin generation, was also measured.

After obtaining informed consent, 16 chronic uremic patients (11 males and 5 females, aged 21-66 years), with plasma cre-atinine ranging from 5 to 12 mg/dl (mean $\pm$ SD 8.2 ± 1.9 mg/dl) were injected intravenously with a single dose of Nadroparin (Seleparina®, Italfarmaco, Milan, Italy; vials 0.4 ml = 4,100 IU aXa). Blood samples for Lp(a) and F1+2 determinations were collected immediately before and 60 and 120 min after Nadroparin administration (fig. 1).

The uremic patients presented baseline F1+2 plasma level higher than a normal control group (2.4 ± 0.9 vs. 1.0 ± 0.4 nmol/l; $p < 0.01$), according to the prothrombotic state of chronic renal failure [3]. In 10 out of the 16 patients (62.5%) the Lp(a) plasma level was higher than 30 mg/dl. As expected, Nadroparin caused a significant decrease in F1+2 plasma level at 120 min (fig. 1 and table 1); conversely, a significant increase in Lp(a) plasma level was observed at 60 min, as shown in table 1.

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Table 1. Effects on plasma levels of F1+2 and Lp(a) following a single intravenous injection of Nadroparin (4,100 IU aXa) (mean $\pm$ SD)

60 min
120

Fig. 1. Blood samples for Lp(a) and F1+2 determinations collected before and 60 and 120 min after Nadroparin administration.

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The decrease in F1+2 following Nadro-parin administration is in keeping with the well-known inhibition of activated factor X exerted by LMWH, thereby preventing the conversion of prothrombin into thrombin.

The unexpected finding of our study is the increase in Lp(a) circulating level following LMWH administration: this observation has not yet been reported in the literature. We can hypothesize that Lp(a) may be released from the endothelial vascular surface. This hypothesis is supported by the observation that Lp(a) is bound to glycosaminoglycans and to plasminogen receptor on the endothelial surface [4] and that LMWH can release lipoprotein lipase, anchored to the vascular endothelium through glycosamino-glycans, into the circulation [4]. A similar mechanism might be involved in the release of Lp(a) into the bloodstream after Nadro-parin administration.

In conclusion, we think that the effects of LMWH on Lp(a) require further investigation, since Lp(a) is emerging as an important risk factor for vascular disease in uremic patients.

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124
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Sagripanti/Cozza/Barsotti