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 creatinine ranging from 5 to 12 mg/dl (mean ± 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.

<table>
<thead>
<tr>
<th>Time</th>
<th>F1+2 (nmol/l)</th>
<th>Lp(a) (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>2.4 ± 0.9</td>
<td></td>
</tr>
<tr>
<td>60</td>
<td>1.0 ± 0.4</td>
<td>30 ± 10.5</td>
</tr>
<tr>
<td>120</td>
<td>1.0 ± 0.4</td>
<td>30 ± 10.5</td>
</tr>
</tbody>
</table>

* Nadroparin i.v T I

Table 1. Effects on plasma levels of F1+2 and Lp(a) following a single intravenous injection of Nadroparin (4,100 IU aXa) (mean ± SD)
Fig. 1. Blood samples for Lp(a) and Fl+2 determinations collected before and 60 and 120 min after Nadroparin administration.

The decrease in Fl+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.

References

Announcement
Charles E. Culpeper Foundation Scholarships in Medical Science
The Charles E. Culpeper Foundation is currently accepting applications for its 1998 Scholarships in Medical Science Program designed to support the career development of academic physicians. Up to three awards of USD 100,000 per year for 3 years will be made to United States medical schools on behalf of candidates who are US citizens, have received their MD degree from a US medical school in 1989 or later (the 8-year rule may be waived when there are career interruptions for family and personal reasons), and are judged worthy of support by virtue of the quality of their research proposals. All scientific research relevant to human health is eligible for consideration. No institution may nominate more than one candidate.

In selecting awardees, emphasis will be on identifying young physicians with clear potential for making substantial contributions to science as academic physicians. Since January 1988, 29 physicians have been selected as Charles E. Culpeper Foundation Medical Scholars.

Deadline for applications is August 15, 1997. Awards will be announced by January 9, 1998, for activation on or about July 1, 1998. Application forms and instructions may be obtained by contacting the: