Regulation of the Growth and Migration of Vascular Wall Cells by Heparin


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Introduction

It is well known that heparin and some of the heparinoids have anti-atherogenecity. Recently, it was reported that heparin inhibits the modulation of vascular smooth muscle cells (SMC) from the contractile state to the synthetic state and the proliferation of SMC (Chamley-Campbell et al., 1981), and that cultured vascular endothelial cells (EC) produce a heparin-like inhibitor of SMC growth (Castellot et al., 1981), probably heparan sulfates (HS). It is possible that HS secreted by EC have various regulatory effects on the blood and vascular wall components including medial SMC. EC produce and secrete a large amount of HS, and they are very similar to heparin in their molecular structure. Particularly, the HS secreted by EC are more heparin-like (i.e., more highly sulfated) than the HS produced by SMC (Gamse et al.).

In the present study, we report the effect of heparin on the migration and growth of bovine aortic EC and SMC.

Materials and Methods

Bovine fetuses were obtained from a slaughterhouse and the thoracic aorta was dissected under sterile conditions. EC and medial SMC were cultured by the explant method. Cells subcultured for several passages were used for the experiments.

![Graph showing effect of heparin on proliferation of EC and SMC]

Fig. 1 Effect of heparin on the proliferation of EC and SMC. DMEM supplemented with 10% calf serum was used as the culture medium.

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Results

Heparin inhibited the proliferation of SMC and EC dose-dependently (Fig. 1). The inhibitory effect of heparin on SMC proliferation was neutralized partially by protamine sulfate, suggesting that the polyanion charge of heparin is an important factor in the effect.

Heparin inhibited the migration of SMC dose-dependently. However, migration of EC was inhibited only in higher concentrations (Fig. 2).

References


Summary

1) We studied the effect of heparin on the migration and proliferation of fetal bovine aortic EC and SMC in culture.

2) Heparin inhibited the proliferation of SMC and EC dose-dependently. Although Castellot et al. reported that the effect was specific for SMC, it was not specific for SMC in our study. It is not known how the difference between the results can be explained.

3) The inhibitory effect of heparin on SMC proliferation was neutralized partially by protamine sulfate.

4) Heparin specifically inhibited the migration of SMC dose-dependently, but not of EC.

5) Our results suggest that anti-atherogenecity of heparin might be due not only to the fully-understood anti-coagulatory and lipemia-clearing effect, but also to the inhibitory effect on the migration and proliferation of medial SMC.

Key words: heparin, endothelial cell, smooth muscle cell, migration, proliferation.