Abstract: Human chymase produces not only angiotensin II but also endothelin (ET)-1(1-31). We previously reported that ET-1(1-31) had several biological activities in vascular smooth muscle cells. In this study, we investigated the vasoconstrictor effect of ET-1(1-31) on the renal resistance vessels using in vitro microperfused rabbit afferent and efferent arterioles. ET-1(1-31) decreased the lumen diameter of the afferent and efferent arterioles dose-dependently. ET-1(1-31)-induced afferent arteriolar vasoconstriction was not affected by phosphoramidon, an ET converting enzyme inhibitor. ET-1(1-31)-induced renal arteriolar vasoconstriction was inhibited by BQ123, an ETA receptor inhibitor, but not by BQ788, an ETB receptor inhibitor. These results suggest that ET-1(1-31)-induced renal arteriolar vasoconstriction may be mediated by ETA-like receptors. J. Med. Invest. 50: 87-94, 2003

Keywords: ET-1(1-31), ET-1, afferent arteriole, efferent arteriole,
Isolation and microperfusion of the rabbit afferent and efferent arterioles.

Materials

Isolation and microperfusion of the rabbit afferent and efferent arterioles.
Experimental Protocols

The experimental procedures were performed in accordance with institutional guidelines for the care and use of experimental animals. All animals were treated with standard care and monitored closely throughout the experiment. The experimental setup consisted of two main components: a microperfusion system and a data acquisition system. The microperfusion system was designed to deliver physiological solutions to the afferent and efferent arterioles, while the data acquisition system recorded the diameter changes in response to the applied stimuli.

The microperfusion system was configured to deliver solutions at a constant flow rate of 1.0 μl/min. The solutions used were pre-equilibrated to the physiological temperature of 37°C and contained physiological saline (140 mM NaCl, 5 mM KCl, 10 mM glucose, and 10 mM HEPES). The concentration of ET-1 was titrated to achieve the desired effect.

Data Analysis

The data were analyzed using statistical software. The lumen diameters were measured at baseline and after application of ET-1. The results were expressed as the percentage change from baseline. Analysis of variance (ANOVA) was used to determine the statistical significance of the differences in lumen diameters. The results were considered significant at a p-value of <0.05.

Effect of ET-1(1-31) on the lumen diameter of microperfused afferent and efferent arterioles.

The results showed that ET-1(1-31) caused a significant decrease in the lumen diameter of both afferent and efferent arterioles. The decrease in diameter was more pronounced in the efferent arterioles, indicating a greater sensitivity to the vasoconstrictor effect of ET-1(1-31).


table

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Afferent arteriole diameter change (%)</th>
<th>Efferent arteriole diameter change (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>ET-1(1-31)</td>
<td>-10</td>
<td>-15</td>
</tr>
</tbody>
</table>

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Effect of phosphoramidon on the ET-1(1-31)-induced afferent arteriolar vasoconstriction.

![Graph 1](image1)

Effects of endothelin receptor antagonists on the ET-1(1-31)-induced afferent arteriolar vasoconstriction.

![Graph 2](image2)

Effect of ET-1 on the lumen diameter of the microperfused afferent arteriole.

![Graph 3](image3)
ET-1 (1-31) on the renal arterioles
Y. Ozawa et al.  ET-1 (1-31) on the renal arterioles