INTRAMYOCARDIAL INJECTION OF BASIC FIBROBLAST GROWTH FACTOR INCREASED REGIONAL MYOCARDIAL BLOOD FLOW AND SALVAGED INFARCTED MYOCARDIUM IN DOGS

MASARU MIYATAKA, KINJI ISHIKAWA, IWAO OGAWA, HIRONARI KOKA, SHOJI NAKAI, HIROFUMI KINO, MASAHIKO INAGAKI, AKIO KIMURA, TAKAYA HASEGAWA, KOJI KITAYAMA, and RYO KATORI

Kinki University School of Medicine

Summary. We studied whether basic fibroblast growth factor (bFGF) might increase regional myocardial blood flow (Qm) at the infarcted myocardium. In eight dogs, bFGF 300 µg was injected into the myocardium supplied by the left anterior descending coronary artery (LAD), and the artery was ligated. In 12 dogs, saline was injected (control group). Nonradioactive colored microspheres were used to determine Qm. The amount of viable myocardium and the extent of fibrosis in the infarcted area four weeks after occlusion were measured histologically. In the outer layer, the Qm values immediately after and four weeks after occlusion were 26 ± 2% and 70 ± 6%, respectively, in the control group, and 46 ± 5% and 121 ± 13%, respectively, in the bFGF group. The Qm at both times in the bFGF group was significantly higher than the corresponding control group values (p < 0.01). The Qm at four weeks in the inner and middle layers also significantly increased in the bFGF group. There was more viable myocardium (control vs. bFGF group: 41 ± 5% vs. 61 ± 7%, p < 0.05) and less fibrosis (3.1 ± 0.2 vs. 2.0 ± 0.4, p < 0.01) at the outer layer in the bFGF group. bFGF caused a marked increase of the Qm, an increase of viable myocardium, and a decrease of fibrosis at the infarcted myocardium. We conclude bFGF was effective in limiting infarct size in acute myocardial infarction.

INTRODUCTION

In 1992, Yanagisawa-Miwa et al. [1] performed a provocative study in dogs showing that basic fibroblast growth factor (bFGF) 10 µg injected into the circumflex coronary artery twice after ligation of the left anterior descending coronary artery (LAD) reduced the myocardial infarct size, preserved good left ventricular function, and promoted abundant collateral development. Although they did not measure the...
regional myocardial blood flow (Qm) at the infarcted myocardium, their results suggested that bFGF can be a useful therapeutic measure to augment the myocardial supply in coronary artery disease. Several investigators measured Qm at the infarcted myocardium treated by bFGF [2-4], and some reported an increased response of Qm [2,3], while others reported that the duration of this increase was limited (to four weeks) [4]. In the study reported here, we clarify the effect of bFGF on the Qm and provide a brief review of the effect of bFGF on acutely ischemic myocardium in experimental animals.

MATERIALS AND METHODS
The details of this study will be presented in a separate paper. Briefly, the LAD of dogs was occluded by suture. In the bFGF group, human recombinant bFGF (Kaken Pharmaceutical Co., Tokyo, Japan) dissolved in 1.75 mL of physiological saline was injected in the LAD area in eight dogs, while saline was similarly injected in 12 dogs as a control. The LAD was occluded approximately one minute after these intramyocardial injections. The dogs were maintained as usual for four weeks. To measure the Qm, nonradioactive colored microspheres were injected into the left atrium [5].

After sacrifice of the dogs by pentobarbital, the myocardium surrounded by the LAD and second diagonal artery was removed to calculate the Qm and for histological analysis. The Qm was expressed as a ratio to the value of normal noninfarcted myocardium (Qm; % of noninfarcted) as an index of myocardial blood flow as follows:

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Q_m = \frac{Q/Q_{preocclusion}}{Q/Q_{preocclusion}} \times 100 \%
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Histological specimens of the infarcted myocardium were photographed at \( \times 100 \), the amount of viable myocardium was counted with a point-counting system with a grid of 100 cross points. In totally necrotic areas, the myocardium score is near zero, and in normal myocardium near 100. Using these photographs, the extent of fibrosis was scored visually as 0, 1, 2, 3, 4, or 5, where 0 indicates fibrosis not present and 5 indicates all fibrosis.

RESULTS
The results will be presented in detail in the separate paper. Briefly, the Qm was markedly reduced immediately (five seconds) after coronary occlusion, especially at the inner layer, in both groups (figure 1). At the outer layer, the Qm immediately after occlusion in the bFGF group was approximately twice the value of the control group. The Qm at four weeks in the bFGF group was significantly greater than in the control group (figure 1). Myocardial fibrosis was significantly less in the bFGF group than in the control group at all three layers (figure 2). The amount of viable myocardium (myocardium score) was significantly greater in the bFGF group compared with the control group at the middle and outer layers (figure 2).