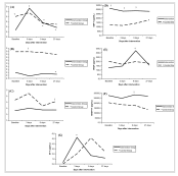
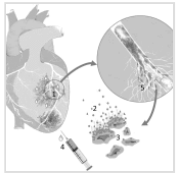
Outline

Figures (2)

Tables (4)

Table 1

Table 2
Table 3
Table 4

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VEGF gene therapy cooperatively recruits molecules from the immune system and stimulates cell homing and angiogenesis in refractory angina

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Highlights

- VEGF gene therapy is influenced by chronic inflammatory process.
- Immune system cell and angiogenic expression are time-dependent by gene therapy.
- VEGF gene therapy is influenced by continuous pharmacological treatment.
- Gene therapy provided an angiogenic process at time line.

Abstract

Background

New vessels are formed in response to stimuli from angiogenic factors, a process in which paracrine signaling is fundamental.

Objective

To investigate the cooperative paracrine signaling profile in response to Vascular Endothelial Growth Factor (VEGF) gene therapy in patients with coronary artery disease (CAD) and refractory angina.

Method

A cohort study was conducted in which plasma was collected from patients who underwent gene therapy with a plasmid expressing VEGF 165 (10) and from surgical procedure controls (4). Blood samples were collected from both groups prior to baseline and on days 3, 9 and 27 after the interventions and subjected to systemic analysis of protein expression (Interleukin-6, IL-6; Tumor Necrosis Factor-α, TNF-α; Interleukin-10, IL-10; Stromal Derived Factor-1 α, SDF-1α; VEGF; Angiopoietin-1, ANGPT-1; and Endothelin-1, ET-1) using the enzyme-linked immunosorbent assay (ELISA).

Results

Analysis showed an increase in proinflammatory IL-6 ($p = 0.02$) and ET-1 ($p = 0.05$) on day 3 after gene therapy and in VEGF ($p = 0.02$) on day 9. A strong positive correlation was found between mobilization of endothelial progenitor cells and TNF-α on day 9 ($r = 0.71$; $p = 0.03$). Furthermore, a strong correlation between β-blockers, antiplatelets, and vasodilators with SDF-1α baseline in the group undergoing gene therapy was verified ($r = 0.74$; $p = 0.004$).

Conclusion

Analysis of cooperative paracrine signaling after VEGF gene therapy suggests that the immune system cell and angiogenic molecule expression as well as the endothelial progenitor cell mobilization are time-dependent, influenced by chronic inflammatory process and continuous pharmacological treatment.

Keywords

Coronary artery disease; Refractory angina; Vascular endothelial growth factor; Gene therapy; Cell homing; Angiogenesis

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