

CGRP and ET-1 plasma levels in normal subjects

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Abstract. – *Objective:* Calcitonin gene-related peptide (CGRP) is a 37 aminoacid peptide displaying about 50% homology with amylin which is secreted from the pancreatic islets of Langerhans. The main form, the beta-CGRP, is produced by the enteric nervous system and perivascular nerves of the vasa-vasorum. It represents one of the most powerful vasodilator yet discovered but its role is not yet completely clarified. High levels of this peptide have been shown in patients affected with thyroid medullary carcinoma, pheochromocytoma and lung carcinoma. Recently circulating levels of CGRP have been found in normal subjects.

Endothelin-1 (ET-1), a potent vasoconstrictor peptide, isolated from porcine endothelial cells, is an important regulator of the vascular tone acting in physiological antagonism with atrial natriuretic hormone (ANH). With this study we intended to investigate the presence of any correlation between CGRP and ET-1 in normal subjects.

Patients: For the study we considered 20 normal subjects (11 males and 9 females) aged 23 to 50.

Measures: Plasma levels of CGRP and ET-1 were measured by radioimmunological Kit.

Results: A positive and significant correlation between calcitonin gene-related peptide and endothelin-1 was found.

Conclusions: Our results confirms that CGRP and ET-1 have opposing actions on vessels and that they can act together in haemodynamic regulation.

Key Words:

CGRP, ET-1, Haemodynamic.

quence of the gene related to calcitonin synthesis. It can be considered an alternative primary RNA post transcriptional product of the calcitonin gene^{1,2}.

Immunoreactive CGRP and its binding sites were found in the central nervous system³ and in nerves supplying the heart and systemic blood vessels^{4,5}.

Circulating levels of CGRP probably originate from different tissues and are normally released into the circulation from the perivascular nerve terminals^{2,6,7}.

CGRP has been found in the plasma of normal subjects⁸ and high levels of this peptide have been shown in patients affected with thyroid medullary carcinoma⁹⁻¹², pheochromocytoma^{13,14} and lung carcinoma¹⁵.

The wide distribution of CGRP receptors in the cardiovascular system^{4,16-21} indicate that CGRP is a potent cardiovascular regulatory peptide.

Endothelin-1 (ET-1) is a peptide with vasoconstrictor properties isolated from porcine endothelial cells^{22,23} and it is well known that it is an important regulator of the vascular tone acting in physiological antagonism with atrial natriuretic hormone (ANH)²⁴. On the other hand CGRP stimulates ANH secretion²⁵⁻²⁷.

CGRP influences the renin angiotensin system stimulating renin secretion²⁸ and inducing a significant decrease in plasma aldosterone levels both in vivo, and in isolated rabbit glomerulosa cells²⁹. Conversely ET-1 has been demonstrated to stimulate aldosterone^{30,31} secretion and, although the results are not always in agreement, an inhibitory effect on renin release has however been shown³².

Aim of this study was to measure plasma CGRP and ET-1 levels in normal subjects in order to assess any correlation.

Introduction

Calcitonin gene-related peptide (CGRP) is a 37 aminoacid neuropeptide. Its existence was predicted analyzing the nucleotide se-

Methods

Twenty normal subjects aged 23 to 50 (11 males and 9 females) were considered for the study.

Blood samples were collected into a chilled syringe and transferred into a polypropylene tube containing EDTA (1 mg/ml) and aprotinin (500 KIU/ml). They were then centrifuged at $3000 \times g$ for 15 min. at 0°C and stored at -70°C until assay.

Measurement of ET-1

Plasma ET-1 levels were determined by radioimmunoassay (Peninsula Labs). A specific antibody, cross reacting 100% with human and porcine ET-1 and 17% with big endothelin was used. The sensitivity of this assay was 18.0 pg/tube. Recovery was approximately 90% by this method.

Concentrations of ET-1 have been expressed in pg/ml.

Measurement of CGRP

CGRP plasma concentrations were measured using a competitive radioimmunoassay Kit (Peninsula Labs). A rabbit antibody cross-reacting 100 % with human-CGRP was used.

Results

The mean plasma CGRP level was 42.80 ± 7.12 pg/ml. The mean plasma ET-1 level was 3.58 ± 0.32 pg/ml. A positive significant correlation ($r = 0.650$, $p < 0.001$) between the plasma levels of the two peptides was found (Figure 1).

Discussion

Although CGRP is released into circulation from the perivascular nerves, its function as a circulating hormone is still uncertain.

ET-1 has mostly an autacoid role, acting as an autocrine-paracrine hormone but there has been much evidence that circulating levels exert an endocrine action.

Plasma circulating levels of both CGRP and ET-1 may be considered, on the whole, reliable parameters of vasal activity.

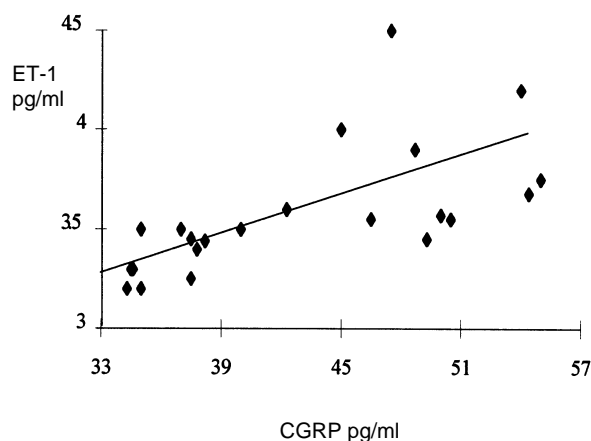


Figure 1. Relation between CGRP and ET-1.

We have demonstrated a significant and positive correlation between CGRP and ET-1 plasma levels. Although the cross section of the population under study is limited and the correlation found is not very close this finding may support the view that these two peptides are involved in the physiological control of vasculature as antagonists.

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