BMC Geriatrics

MEETING ABSTRACT Open Access

Long-term diabetic complications in elderly patients with variable levels of HMGA1 expression

E Chiefari*, C Capula, F Paonessa, S Iiritano, A Nocera, B Arcidiacono, K Possidente, D Foti, A Brunetti

From de Senectute: Age and Health Forum
Catanzaro, Italy. 5-7 December 2009

Background

Type 2 diabetes mellitus is a very common metabolic disorder affecting ~200 million people worldwide [1]. Chronic complications of the disease due to poor metabolic control are specifically associated with long-term damage, dysfunction and failure of various organs, causing blindness, renal failure, amputations, and increased risk of cardiovascular diseases [2]. Previously, we reported a novel genetic flaw that markedly reduced the intracellular expression of the high mobility group A1 (HMGA1) protein, and adversely affected insulin receptor expression in cells and tissues, leading to human diabetes [3]. Also, the involvement of HMGA1 in the transcriptional regulation of genes essential in both the inflammatory response and atherosclerosis is well known [4]. Herein we have investigated the prevalence of chronic complications in an elderly diabetic population according to the expression levels of HMGA1.

Materials and methods

The study was performed in 125 elderly patients (aged over 65 years) with type 2 diabetes consecutively attending our outpatient diabetes clinic, in Catanzaro. 50 unrelated age-, sex-, and ethnically-matched healthy controls were enrolled. Periodic clinical and biochemical examinations were performed on every patient, before and during the time of investigation. Total RNA was prepared from peripheral-blood mononuclear cells of

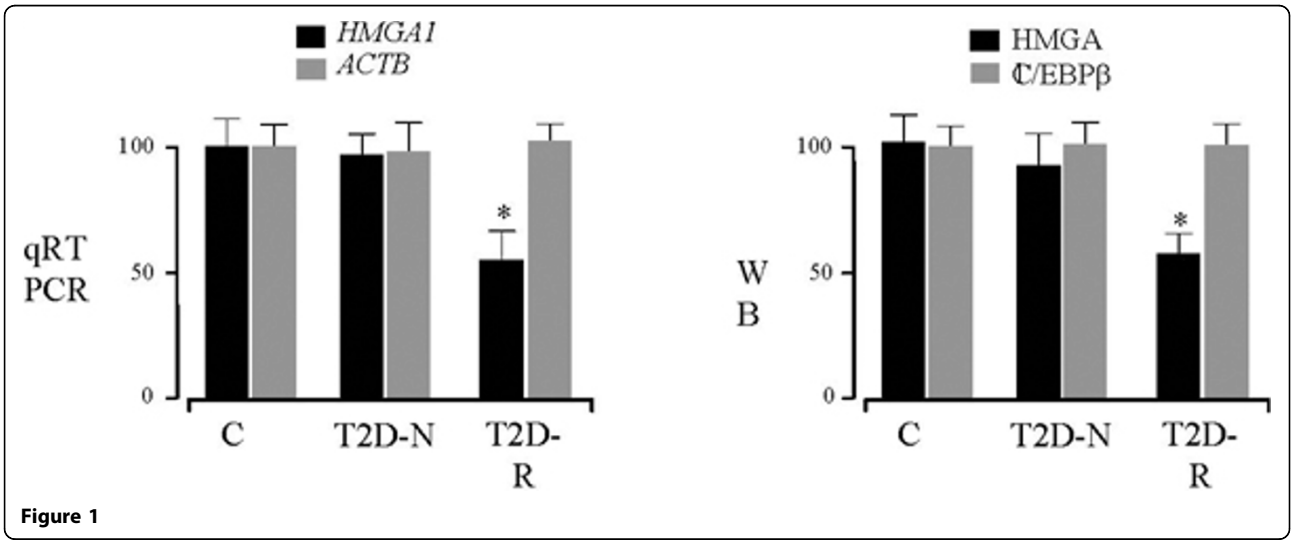

Figure 1

Department of Clinical and Experimental Medicine "G. Salvatore", University of Catanzaro "Magna Græcia, Catanzaro, Italy

Table 1

	T2D-N (n = 111)	T2D-R (n = 14)	p* value
Patients affected	86 (77.5%)	10 (71.0%)	0.03
Long term complications			
macroangiopathic[1]	36 (32.4%)	3 (21.4%)	0.03
microangiopathic[2]	75 (67.6%)	8 (57.1%)	0.01

[1] Include coronary heart disease, myocardial infaction and stroke.
[2] Include retinopathy, nefropathy, neuropathy and foot problems.
* Yates' chi-square test.

patients and controls, cDNA was synthesized and used for HMGA1 real-time PCR (qRT-PCR) amplification. Western blot (WB) analysis of HMGA1 was performed on nuclear extracts from peripheral lymphomonocytes as previously described [5,6]. The study was approved by the local ethics committee (Comitato Etico Regione Calabria, Azienda Ospedaleria "Mater Domini," Catanzaro) and informed consent was obtained from all individuals.

Results

In 111 patients with type 2 diabetes (88.8%), HMGA1 mRNA and protein expression levels were similar to those of normal subjects (see Figure 1). In contrast, HMGA1 expression was significantly reduced in 14 diabetic patients (11.2%) in which a mean reduction of 50% in HMGA1 content was observed in peripheral lymphomonocytes (see Figure 1).

HMGA1 mRNA (left) and protein (right) levels from healthy control individuals (C), and type 2 diabetic patients without (T2D-N) or with (T2D-R) defects in HMGA1 expression. -actin (ACTB) and C/EBP, controls. mRNA and protein abundance are expressed as percent of maximal control value (100%). *$p < 0.05$ vs C.

A negative correlation was observed between reduced HMGA1 expression and long-term diabetic complications such as retinopathy, nephropathy, neuropathy, and cardiovascular disease (see Table 1).

Conclusions

A deficit of HMGA1 in affected diabetic patients may confer a less severe course of the disease in terms of long-term chronic complications of diabetes.

Published: 19 May 2010

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doi:10.1186/1471-2318-10-S1-A91
Cite this article as: Chiefari *et al.*: Long-term diabetic complications in elderly patients with variable levels of HMGA1 expression. *BMC Geriatrics* 2010 **10**(Suppl 1):A91.