Acta Diabetol (2015) 52:813–815
DOI 10.1007/s00592-014-0683-y

LETTER TO THE EDITOR

Erythrocyte glutathione transferase in uremic diabetic patients: additional data

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Received: 28 October 2014 / Accepted: 30 October 2014 / Published online: 16 November 2014

Dear Editor,

We found that erythrocyte glutathione transferase, an enzyme devoted to the body detoxification from endogenous and exogenous toxins, is overexpressed in humans in case of increased blood toxicity as it occurs in kidney dysfunctions and environmental pollution [1–3]. In a recent paper, we also reported that erythrocyte glutathione transferase (e-GST) may be an early biomarker for kidney dysfunction in diabetic patients [4]. More precisely, we found that a statistically significant increase in e-GST activity is present in diabetic patients even in the absence of an increase in traditional biomarkers of kidney damage i.e., albuminuria [4]. Evidence was also given that the observed increase is not caused by diabetes per se. The hypothesis that e-GST may indicate an incipient defect in the kidney functionality is a fascinating idea that must be corroborated by further investigations and epidemiologic studies. In this context, we explored the possibility that e-GST hyperexpression could correlate with some of the many biomarkers usually tested in diabetic diseases. In Table 1 are summarized the possible correlation of some clinical parameters between the different groups (healthy subjects, diabetic non-nephropatic patients, and diabetic nephropatic patients). Table 2 shows that no evident correlation is present among e-GST and some clinical parameters. The absence of correlation confirms that e-GST must be considered a novel biomarker which reveals an incipient kidney defective function in case of diabetic disease. The early increase in the e-GST activity in diabetic patients without any apparent signal of renal damage can be explained by assuming an elevation of the circulating toxins and not as a consequence the modification of other classical parameters. Recently, e-GST, present in the erythrocytes and easily measured, has disclosed new possible use as biomarker of kidney status in transplanted patients that will be object of future investigations.

Managed by Antonio Secchi.

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Conflict of interest The authors declare that they have no conflict of interest.

Ethical standard The study was approved by the Ethical Committee of our Institution (Comitato Etico Indipendente dell'Azienda Ospedaliera Universitaria Policlinico Tor Vergata).

Human and animal rights All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 [5].

Table 1 Correlation of clinical parameters among the control group, the diabetic non-nephropatic patients, and the nephropatic patients

Laboratory parameters	Control group (1)	Non-nephropatic diabetic patients (2)	Nephropatic diabetic patients (3)	*P*1 versus *P*2	*P*1 versus *P*3	*P*2 versus *P*3
Creatinine (mg/dl)	0.80 ± 0.01	0.83 ± 0.03	1.6 ± 0.09	ns	$P < 0.05$	$P < 0.05$
Albuminuria (mg/24 h)	5.4 ± 2.3	9.8 ± 3.9	229 ± 509	ns	$P < 0.001$	$P < 0.001$
GFR (ml/min)	117 ± 2	107 ± 3	60 ± 4	ns	$P < 0.001$	$P < 0.001$
e-GST (U/g Hb)	5.6 ± 0.4	6.8 ± 0.5	8.3 ± 0.5	$P < 0.05$	$P < 0.001$	$P < 0.05$
e-CAT (U/g Hb)	204 ± 4	217 ± 7	218 ± 7	ns	ns	ns
Glycemia (mg/ml)	68 ± 4	144 ± 55	135 ± 48	$P < 0.001$	$P < 0.001$	ns
Fructosamine (mmol/l)	201 ± 5	268 ± 4	273 ± 5	$P < 0.05$	$P < 0.05$	ns
Hb glycate (%)	4.6 ± 0.4	7.4 ± 0.2	7.5 ± 0.2	$P < 0.001$	$P < 0.001$	ns
HDL-cholesterol (mg/dl)	54 ± 11	54 ± 12	49 ± 14	ns	ns	ns
Cholesterol total (mg/dl)	176 ± 25	189 ± 26	193 ± 30	ns	ns	ns
Hs-CRP (mg/dl)	0.02 ± 0.01	0.5 ± 0.9	0.7 ± 1.2	ns	ns	ns

GFR glomerular filtration rate, *Hs-CRP* high sensitivity C-reactive protein, *ns* not significant

Data are expressed as mean ± standard deviation

$P < 0.05$ is considered statistically significant

Table 2 Correlations between e-GST values and some clinical parameters

Parameters vs	e-GST		Parameters vs	e-GST	
	R^2	*P*		R^2	*P*
Age	0.000897	0.677	Chloride ion	0.00511	0.3308
Vitamin B_{12}	0.00020	0.9288	Sodium ion	0.01122	0.1469
Hb	0.05895	0.0006	Kalium ion	0.0762	0.0001
MCH	0.09178	<0.0001	Ht	0.05349	0.0012
MCHC	0.02374	0.0320	MCV	0.08135	<0.0001
PLT	0.04357	0.3605	RDW-CV	0.02787	0.0200
White Blood Cells	0.00218	0.5181	Red Blood Cells	0.000046	0.9256
Eosinophils	0.00072	0.711	Basophils	0.0106	0.154
Neutrophils	0.0113	0.1401	Monocytes	0.0156	0.0828
Transferrin	0.0156	0.0877	Lymphocytes	0.00786	0.2188
Sideremia	0.01402	0.1047	Ferritin	0.01421	0.1140
Total protein	0.01718	0.0738	Pre-albumin	0.00056	0.7616
Albumin (by nephelometer)	0.0955	<0.0001	Albumin	0.00031	0.8113
Γ-GT	0.00299	0.4503	GPT/ALT	0.02317	0.0341
GOT/AST	0.00395	0.3853	LDL-Cholesterol	0.01804	0.2411
BMI	0.00127	0.6599	Triglycerides	0.00256	0.4840
HDL-Cholesterol	0.00793	0.2159	PCR-hs	0.0334	0.0130
Cholesterol	0.01476	0.0907	Fructosamine	0.0234	0.0388
α-acid glycoprotein	0.1509	0.0001	BUN	0.1679	<0.0001
Glycate hemoglobin	0.0184	0.0606	Albuminuria	0.0196	0.0567
Glycemia	0.00746	0.2298	Cystatine C	0.1400	<0.0001
GFR	0.09558	<0.0001	Magnesium ion	0.0166	0.0902
Creatinine	0.1426	<0.0001	Calcium ion	0.00003	0.9403
Uric Acid	0.0003	0.8101	Inorganic phosphorous	0.1044	0.0007
PINI index	0.0849	0.0001			

GFR glomerular filtration rate, *Hs-CRP* high sensitivity C-reactive protein

Informed consent Informed consent was obtained from all patients for being included in the study.

References

1. Dessì M, Noce A, Dawood KF, Galli F, Taccone-Gallucci M, Fabrini R, Bocedi A, Massoud R, Fucci G, Pastore A, Manca di Villahermosa S, Zingaretti V, Federici G, Ricci G (2012) Erythrocyte glutathione transferase: a potential new biomarker in chronic kidney diseases which correlates with plasma homocysteine. Amino Acids 43:347–354
2. Noce A, Ferrannini M, Fabrini R, Bocedi A, Dessì M, Galli F, Federici G, Palumbo R, Di Daniele N, Ricci G (2012) Erythrocyte glutathione transferase: a new biomarker for hemodialysis adequacy, overcoming the Kt/V(urea) dogma? Cell Death Dis 3:e377
3. Fabrini R, Bocedi A, Del Grosso E, Morici L, Federici G, Palleschi A, Ricci G (2012) Erythrocyte glutathione transferase: a novel biomarker to check environmental pollution hazardous for humans. Biochem Biophys Res Commun 426:71–75
4. Noce A, Fabrini R, Dessì M, Bocedi A, Santini S, Rovella V, Pastore A, Tesauro M, Bernardini S, Di Daniele N, Ricci G (2014) Erythrocyte glutathione transferase activity: a possible early biomarker for blood toxicity in uremic diabetic patients. Acta Diabetol 51:219–224
5. Rid A, Schmidt H (2009) The newly revised declaration of Helsinki: what do the changes mean from an ethical perspective? Dtsch Med Wochenschr 134:2525–2528