P1-69. OXIDIZED LIPID-ASSOCIATED PROTEIN DAMAGE IN CHILDREN AND ADOLESCENTS WITH TYPE 1 DIABETES MELLITUS: NEW DIAGNOSTIC/PROGNOSTIC CLINICAL MARKERS

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INTRODUCTION

Type 1 diabetes mellitus (DM1), a chronic metabolic disorder of autoimmune origin, has been associated with oxidative stress (OS), which plays a central role in the onset, progression and long-term complications of the disease[1]. The markers of OS lipid peroxidation products, lipid hydroperoxides (LOOH), and also malondialdehyde (MDA) and thiobarbituric reactive substances (TBARS) that oxidatively modify proteins (Pr) (i.e., PrMDA and PrTBARS, respectively), have been associated with DM2, DM1, diabetic neuropathy, and microalbuminuria[2,3].

AIM

The aim of the present study was to investigate LOOH, PrMDA and PrTBARS as diagnostic and prognostic markers of DM1 in 50 children and adolescents with DM1 and 21 controls.

METHOD

Fifty children and adolescents with DM1 (2.58 to 17.5 years old, (mean ± SD: 10.99 ± 3.48)) and 21 healthy age-matched controls (2 to 14 years old, (mean ± SD: 9.05 ± 3.66) were recruited from the Department of Paediatric Endocrinology of the University Hospital of Patras in Greece. Lipid peroxidation was assessed by the direct marker lipid hydroperoxide (LOOH) and by its decomposition aldehyde products that are bound to oxidized proteins, such as malondialdehyde (PrMDA) and other aldehydes (PrTBARS; protein-bound thiobarbituric reactive substances). The employed assay was developed by our group for the determination of LOOH and PrMDA, and applied after modification for the measurement of PrTBARS for the first time in the present study. The determination of the aforementioned markers was performed in blood serum.

RESULTS

The novel OS marker PrTBARS was assessed for the first time in children and adolescents with DM1. LOOH and the pair PrMDA/PrTBARS, representing early and late peroxidation stages, respectively, are found to be significantly higher (130%, 50/90%, respectively, at p<0.001) in patients with DM1 compared to controls (Figure 1). The studied OS parameters did not differ with age, age at diagnosis, sex, duration of DM1, presence of recent ketosis/ketoacidosis, or mode of treatment (Table 1).

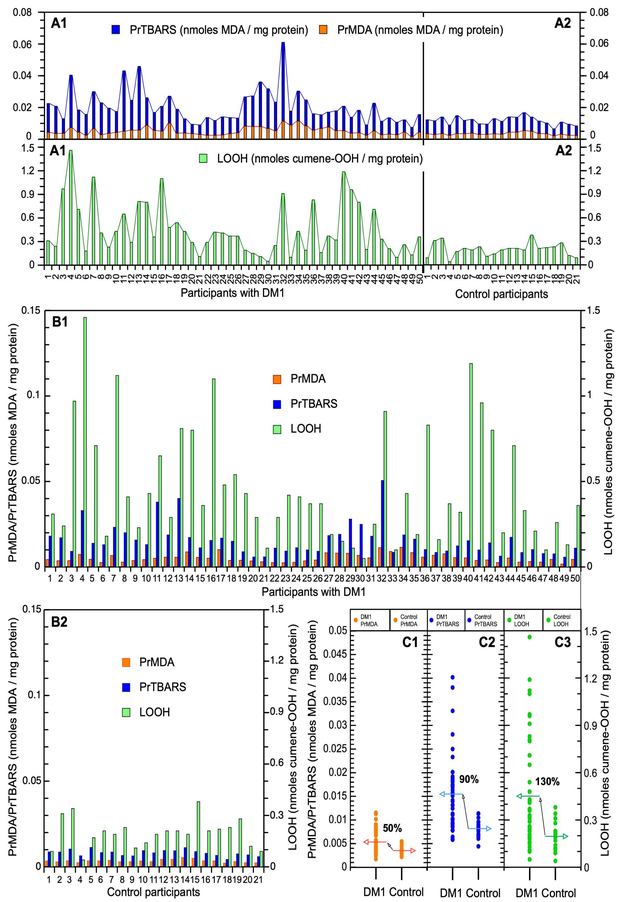

Figure 1. PrMDA, PrTBARS and LOOH concentrations in serum of patients with DM1 and controls. A. Composite stacked column histogram, consisting of PrMDA stacked with PrTBARS markers (in orange and blue, respectively) and that of LOOH marker (in green). B. Column histogram in column triplets of PrMDA, PrTBARS, LOOH markers. C. Scatter plots separate for the PrMDA, PrTBARS, LOOH markers, and their median value marked with horizontal arrows both for DM1 patients and controls, and expressed as % increase for DM1 patients vs the 0%-controls.

	PrMDA (nmoles MDA/mg protein)	PrTBARS (nmoles MDA/mg protein)	LOOH (nmoles cumene-OOH/mg protein)
Male (N=21) Mean (SD)	0.0054 (0.0017)	0.0137 (0.0047)	0.47 (0.33)
Female (N=29) Mean (SD)	0.0047 (0.0024)	0.0169 (0.0012)	0.45 (0.035)
p-value	0.105	0.898	0.461
Insulin MDI (N=43) Mean (SD)	0.0052 (0.0021)	0.0163 (0.0010)	0.48 (0.36)
Insulin pump (N=7) Mean (SD)	0.0041 (0.0023)	0.0137 (0.0054)	0.31 (0.16)
p-value	0.224	0.743	0.622
No recent ketosis (N=44) Mean (SD)	0.0048 (0.002)	0.0163 (0.0010)	0.46 (0.34)
Recent ketosis (N=6) Mean (SD)	0.0061 (0.0025)	0.0138 (0.0054)	0.50 (0.37)
p-value	0.612	0.676	0.905

Table 1. Oxidative stress markers (PrMDA, PrTBARS and LOOH) by sex, by mode of treatment and at initial diagnosis (recent ketosis) or post-initial diagnosis (no recent ketosis) in the patients with DM1. PrMDA: protein-bound malondialdehyde, PrTBARS: protein thiobarbituric acid reactive substances, LOOH: lipid hydroxyperoxides.

CONCLUSIONS

We propose that LOOH, PrMDA and the new marker PrTBARS could serve as potential diagnostic clinical markers for identifying OS in children and adolescents with DM1, and may, perhaps, hold promise as a prognostic tool for future complications associated with the disease.

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