The effect of glycemic variability on DNA damage in pediatric patients with type 1 Diabetes Mellitus

Gökhan GÖKMEN[1], Özgen KILIÇ ERKEK[2], Melek TUNÇ-ATA[2], Ayça ALTINCIK[1], Emine Kılıç TOPRAK[2], Vural KÜÇÜKATAY[2], Bayram ÖZHAN[1]

1. University of Pamukkale,Faculty of Medicine, Department of Pediatric Endocrinology ,Denizli, Turkey
2. University of Pamukkale,Faculty of Medicine, Department of Physiology, Denizli, Turkey

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INTRODUCTION

HbA1c reflects the average blood glucose levels and does not give any information about the glucose fluctuations called 'glycemic variability'. Increased glycemic variability (GV) is an important risk factor in terms of complications independent of HbA1c. Increased oxidative stress has been incriminated as a causative factor for the effects of GV. However, there is no data regarding the effect of GV on DNA damage.

AIM

The aim of this study was;

- investigate the relationship between continuous glucose monitoring system (CGMS) indices and clinical data
- investigate DNA damage in patients with diabetes
- evaluate the effect of glycemic variability on DNA damage.

METHOD

- Sixtytwo patients with T1DM, aged under 18 years old and 21 healthy control objects were included in the study.
- "Medtronic iPro™2, Enlite Glucose Sensor®" was inserted and continuous glucose monitoring (CGM) indices were calculated.
- Mean sensor glucose, standard deviation (SD), glucose management indicator (GMI), coefficient of variation (CV), time in range (TIR), time below range (TBR), time above range (TAR) indices were evaluated.
- Study group was designated into subgroup pairs according to following categorical variables: a) one year median HbA1c > 7.5% vs. HbA1c ≤ 7.5 %) b) TIR ≥70% vs.TIR<70% c) CV≥36% vs. CV<36%.
- DNA strand breaks and Fpg-sensitive sites were detected in leukocytes with single cell gel electrophoresis, the comet assay.
- DNA damage was determined by using the program Comet Assay IV system (AutoComet) by one physiologist blindly.

RESULTS

Twelve children who removed the CGM sensor because of local side effects (pruritus, pain) or due to incompatibility of CGM sensors were excluded from the study. Mean diabetes duration of the remaining 50 patient was 4,39±2,39 years and HbA1c was % 9,23±2,16. Clinical characteristics and CGM metrics of the participants are summarized in Table 1 & 2.

Table 1. Clinical characteristics of the participants

	Control (n=21)	T1DM (n=50)	p
Age (decimal age)	13,16±3,78	13,69±2,99	0,57
Female/Male	20/11	30/20	0,33
Prepubertal/Pubertal	6/15	14/36	0,96
Weight SDS	-0,25±1,50	0,02±1,20	0,40
Height SDS	-0,02±1,27	-0,04±1,09	0,92
BMI SDS	-0,28±1,24	1,19±5,66	0,43

Table 2. CGMS metrics of the patients with type 1 DM

	Mean ±SD	Median (Min-Max)
TIR (%)	58.88±15,04	55,5 (21-90)
TAR (%)	36,46±15,53	44,5 (10-79)
TBR (%)	4,64±4,51	4,5 (4-5)
Mean sensor glucose (mg/dl)	167,1±28,93	192 (129-255)
GMI (%)	7,45±1,01	8,3 (6,1-10,5)
SD	64,64±15,22	61 (29-93)
CV (%)	39,37±7,38	37,69 (21,16-54,22)

Head lenght (HL), tail length (TL), tail intensity (TI), tail moment (TM) and tail migration (TMi) were used for statistical analysis as parameters of DNA damage. There was no statistically significant difference between the two groups in terms of DNA damage parameters (Table3).

Table 3. Comparison of DNA damage parameteres between the control and diabates group.

	Control	T1DM	*p*
Head lenght (µm)	30,18±2,22	30,43±3,10	0,74
Tail lenght (µm)	36,07±7,03	32,52±9,79	0,14
Tail intensity (%)	25,10±10,63	20,78±11,56	0,15
Tail moment (µm)	4,89 ±2,99	3,92±3,55	0,28
Tail migration (µm)	21,02±7,67	17,34±9,93	0,24

Correlation analyses between DNA damage parameters and CGMS metrics among T1DM patients revealed that, %CV was moderately correlated with TL, TI, TMi (table 4). There was no statistically significant difference between subgroups [(CV<36% vs. CV≥36%) & (TIR≥70% vs.TIR<70%)] in terms of DNA damage parameters. HL was significantly higher in the HbA1c ≤ 7.5 % group (n=32) than in the HbA1c > 7.5% group (table 5 & 6 & 7).

Table 4. Correlation analysis between CGMS metrics and DNA damage parameters

		Mean glucose	TIR	TAR	TBR	GMI	CV
Headlenght (µm)	r	0,00	0,07	-0,03	-0,12	0,00	-0,10
	p	0,98	0,62	0,83	0,39	0,97	0,48
Taillenght (µm)	r	-0,12	0,04	-0,09	0,18	-0,12	0,29
	p	0,39	0,77	0,53	0,20	0,39	**0,04**
Tailintensity (%)	r	-0,12	0,02	-0,07	0,19	-0,12	0,30
	p	0,40	0,88	0,61	0,17	0,40	**0,03**
Tailmoment (µm)	r	-0,14	0,08	-0,11	0,13	-0,14	0,25
	p	0,33	0,57	0,42	0,35	0,33	0,08
Tail migration (µm)	r	-0,11	0,01	-0,07	0,21	-0,12	0,32
	p	0,42	0,89	0,60	0,15	0,41	**0,02**

Table5. Comparison of DNA damage parameters between subgroups regarding CV%

	%CV <36 (n=14)	%CV≥36 (n=36)	*p*
Headlenght (µm)	30,65±3,11	30,35±3,14	0,77
Taillenght (µm)	30,10±9,52	33,42±9,86	0,30
Tailintensity (%)	17,48±12,70	22,01±11,05	0,23
Tailmoment (µm)	3,23±4,23	4,17±3,29	0,42
Tail migration (µm)	14,66±9,74	18,34±9,95	0,25

Table 6. Comparison of DNA damage parameters between subgroups regarding TIR %

	TIR>%70) (n=11)	TIR<%70 (n=39)	p
Headlenght (µm)	30,88±3,16	30,30±3,11	0,59
Taillenght (µm)	33,21±13,95	32,32±8,41	0,79
Tailintensity (%)	20,88±17,08	20,76±9,67	0,97
Tailmoment (µm)	4,58±5,69	3,72±2,7	0,48
Tail migration (µm)	17,58±14,66	17,27±8,31	0,93

Table 7. Comparison of DNA damage parameters between subgroups regarding HbA1c %

	HbA1c<%7,5) (n=11)	HbA1c>% 7,5 (n=39)	p
Head lenght (µm)	32,28±2,43	29,88±3,09	0,02
Tail lenght (µm)	31,12±7,24	32,94±10,4	0,59
Tail intensity (%)	16,86±9,18	21,95±12	0,20
Tail moment (µm)	3,19±2,48	4,13±3,81	0,44
Tail migration (µm)	15,18±7,78	17,99±10,4	0,41

CONCLUSIONS

In our study, a positive correlation was found between % CV and DNA damage parameters tail length, tail intensity and tail migration. This data supports that, DNA damage increases as glycemic variability increases. No study has been found in the literature that investigates the relationship between glycemic variability and DNA damage. Our study is unique in this aspect, and new studies are needed regarding the mechanism by which glycemic variability increases DNA damageust highlight this text and replace with your own text.

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CONTACT INFORMATION

Ayça ALTINCIK, MD e-mail:saltincik@pau.edu.tr