Skin autofluorescence is increased in young people with type 1 diabetes exposed to secondhand smoking

Vollenbrock, Charlotte E; van Waateringe, Robert; Veeze, Henk J; Aanstoot, Henk Jan; Wolffenbutel, B.H.

Published in:
Journal of diabetes

DOI:
10.1111/1753-0407.12498

Publication date:
2017

Journal of Diabetes

Journal of Diabetes 9 (2017), 308–310

RESEARCH LETTER

Skin autofluorescence is increased in young people with type 1 diabetes exposed to secondhand smoking

Highlights
- Skin autofluorescence is increased in diabetes, rises with age, and predicts diabetes-related complications.
- Exposure to secondhand smoke, because one or more family members are smokers, further increases skin autofluorescence in children and young adults with type 1 diabetes.
- Elimination of passive smoking should be a goal in diabetes education.

Charlotte E. VOLLENBROCK,[1] Robert P. VAN WAATERINGE,[1] Henk J. VEEZE,[2] Henk-Jan AANSTOOT[2] and Bruce H.R. WOLFFENBUTTEL[1*]

[1]Department of Endocrinology, University of Groningen, University Medical Center Groningen, Groningen, and [2]Diabeter, Center for Pediatric and Adolescent Diabetes Care and Research, Rotterdam, The Netherlands

Keywords: autofluorescence, glycation, smoking.

To the Editor

Tobacco smoking is known to increase the risk of micro- and macrovascular complications, as well as mortality.[1] In adolescents with type 1 diabetes (T1D), active tobacco smoking worsens glycemic control and is associated with a poorer cardiovascular risk profile.[2] Less is known about the effect of exposure to secondhand smoking in T1D. Smoking and hyperglycemia both accelerate the formation of advanced glycation end products (AGEs),[3] the final products of non-enzymatic glycation and oxidative reactions of proteins, lipids, and nucleic acids.[4,5] The AGEs can be measured non-invasively in the skin with an AGE reader,[6] and its measure, skin autofluorescence (SAF), is a strong predictor of future cardiovascular morbidity and mortality. Several studies have shown elevated SAF levels in tobacco smokers compared with never smokers, because tobacco smoke causes oxidative stress and is an exogenous source of reactive glycation products itself.[6,7]

Recently, we demonstrated that secondhand smoking is associated with higher SAF levels in the general population.[7] The aim of the present study was to extend our previous findings by assessing secondhand smoking in children and young adults with T1D.

Correspondence:
Bruce H.R. Wolffenbuttel, Department of Endocrinology, University Medical Center Groningen, HPC AA31, PO Box 30001, 9700 RB Groningen, The Netherlands.
Tel: +31 50 3613962
Fax: +31 50 3619392
Email: bwo@umcg.nl
Received 20 October 2016; accepted 21 October 2016
doi: 10.1111/1753-0407.12498

Methods

We analyzed SAF data of 88 children and young adults (aged 5–26 years) with T1D treated at the outpatient clinic of Diabeter, a large, certified diabetes center in Rotterdam (The Netherlands). Data were collected in agreement with the Declaration of Helsinki and after approval of the Medical Ethical Review Board of the Erasmus MC Rotterdam. Participants and their guardians provided written informed consent. Personal and anthropometric data, including age, height, weight, blood pressure, and information about exposure to tobacco smoking in the household, were obtained from routine electronic patient charts.

An immunochemical assay (Vantage system; Siemens, Tarrytown, NY, USA) was used to measure HbA1c, whereas low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) were measured using an enzymatic colorimetric assay on a Hitachi Cobas C501 analyzer (Roche Diagnostics, Mannheim, Germany). An AGE reader (Diagnoptics Technologies, Groningen, The Netherlands) was used to measure SAF, as described previoiusly,[6] and SAF is reported in arbitrary units (AU).

Data are given as the mean ± SD or median (interquartile range [IQR]). Independent samples *t*-tests were used to compare baseline characteristics between those

exposed and those not exposed to secondhand smoking. Univariate and multivariate regression analyses were performed to assess associations between secondhand smoking and SAF. Two-tailed $P < 0.05$ was considered significant.

Results

The total population consisted of 41 males and 47 females aged 16 ± 4 years. Data on secondhand smoking were available for 73 subjects, 23 of whom were exposed to secondhand smoking; none of the study subjects were active smokers. No significant differences were observed between subjects exposed or not to secondhand smoke in terms of age, gender, body mass index, systolic blood pressure, HbA1c, and diabetes duration (see Table S1). In subjects exposed to secondhand smoking, SAF was 1.67 ± 0.45 AU, compared with 1.42 ± 0.34 AU in patients not exposed ($P = 0.03$). Those exposed to secondhand smoking had significantly higher LDL-C than those not exposed (2.70 mmol/L [IQR 2.10–3.40] vs. 2.30 mmol/L [IQR 1.90–2.70], respectively; $P = 0.01$). However, HDL-C was significantly lower in males, but not in females, exposed to secondhand smoking.

Secondhand smoking was significantly associated with higher SAF in univariate regression analyses ($P = 0.01$; Fig. 1). After correction for other significant determinants of SAF, secondhand smoking remained significantly associated with higher SAF ($P = 0.043$). In addition to secondhand smoking, age was associated with higher SAF ($P = 0.002$; Table 1).

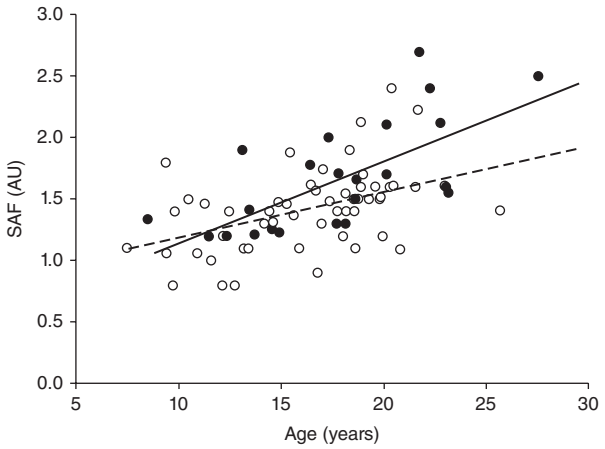

Figure 1 Association between age and skin autofluorescence (SAF), in arbitrary units (AU), in young people with type 1 diabetes exposed (black dots) and not exposed (open dots) to secondhand smoke. Regression lines show correlations between these parameters in exposed (solid line) and not exposed (dashed line) patients.

Table 1 Univariate and multivariate regression analyses for the association between clinical parameters and skin autofluorescence

Determinants	β Coefficient	SE	*P*-value	R^2
Univariate				
Secondhand smoking	0.247	0.095	0.01	8.7
Age	0.048	0.009	<0.001	26.6
Male gender	−0.112	0.082	0.175	1.0
BMI	0.029	0.010	0.007	7.0
HbA1c	0.030	0.027	0.267	0.3
Diabetes duration	0.037	0.008	<0.001	19.0
LDL-C	0.138	0.131	0.298	1.3
HDL-C	−0.223	0.133	0.097	3.2
TG	−0.029	0.087	0.737	0.1
SBP	0.007	0.003	0.016	6.5
Multivariate				
Secondhand smoking	0.164	0.080	0.043	41.1
Age	0.044	0.013	0.002	
BMI	−0.012	0.013	0.353	
Diabetes duration	0.016	0.010	0.112	
SBP	0.001	0.003	0.673	

Data show β coefficients per arbitrary unit (AU) increase in skin autofluorescence (SAF), and R^2 is used as an index of the percentage variance explained by each of the variables.
BMI, body mass index; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; SBP, systolic blood pressure; TG, triglycerides.

Together, these variables explained 41.1% of the variance in SAF.

Discussion

In the present study we showed that in non-smoking children and young adults with T1D, SAF is significantly increased by age and exposure to secondhand smoke. All data were obtained from structured medical files and were independent of whether the relative or person in the household smoked inside or outside the house, because it has been indicated that toxic molecules released during smoking outside the house can still be transmitted to the child, for example via clothing.[8]

We cannot exclude additional sources of secondhand smoke. However, the children in the present study typically spend the largest part of the day at school, where exposure to smoke is minimal. Earlier studies from our group have shown the effects of exposure to secondhand smoke on SAF in the general population.[7] We did not have information on coffee consumption, a significant determinant of SAF,[6] in the present study. However, in children and adolescents, coffee consumption is generally low in The Netherlands.

Journal of Diabetes published by John Wiley & Sons Australia, Ltd and Ruijin Hospital, Shanghai Jiaotong University School of Medicine.

Increased SAF is a strong predictor of future complications in diabetes. The strong effect of passive smoking on SAF and its possible long-term sequelae suggest that cessation of smoking by parents is an important issue for attention in diabetes education.

Acknowledgement

The authors wish to thank all patients and their guardians/parents for their interest and participation in this study.

Disclosure

None declared.

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Supporting information

Additional Supporting Information may be found in the online version of this article:

Table S1. Clinical characteristics of the study population.