LETTER

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Association of postprandial and fasting plasma glucose with HbA1c across the spectrum of glycaemic impairment in type 2 diabetes

Dear Editor,

Management of diabetes requires an understanding of the association between fasting plasma glucose (FPG), postprandial plasma glucose (PPG) and HbA1c—a tripartite model known as the glucose triad.[1] A higher contribution of PPG relative to FPG in patients with HbA1c levels of ≤7% (53 mmol/mol) has been observed in a seminal article published in 2003[2] and further observed in several studies.[3] Collectively, such data seem to make a convincing case for targeting postprandial glucose excursions in patients with mild hyperglycaemia. However, it has been questioned whether there is yet adequate evidence from clinical trials to support the safety and effectiveness of such a strategy. Therefore, the aim of the current post hoc analysis of the IMPROVE study[4] was to utilise the large sample of patients with type 2 diabetes (N = 22,082) to assess the contribution of PPG and FPG to overall glycaemia and optimal glucose control. Cross-sectional associations between PPG or FPG and HbA1c were examined by crude and multiple linear regression analyses at baseline and final study visits. Associations between absolute and relative change in PPG/FPG with change in HbA1c were also analysed.

TABLE 1 Cross-sectional analysis of the impact of 1 mmol/L change in PPG or FPG on HbA1c at baseline and final visits

Continuous variable: PPG	Final visit		Baseline visit	
Adjustments	Estimate (95% CI)	P-value	Estimate (95% CI)	P-value
Crude	0.22 (0.22-0.23) r^2 .19	<.001	0.17 (0.16-0.17) r^2 .16	<.0001
Sex, age, country	0.21 (0.21-0.22)	<.0001	0.18 (0.17-0.18)	<.0001
Sex, age, country, prestudy therapy[a]	N/A	N/A	0.18 (0.17-0.18)	<.0001
Sex, age, country, prestudy therapy[a], BMI, diabetes duration	0.21 (0.21-0.22)	<.0001	0.18 (0.17-0.18)	<.0001
Sex, age, country, prestudy therapy[a], BMI, diabetes duration, FPG	0.10 (0.09-0.11)	<.0001	0.10 (0.09-0.10)	<.0001
Continuous variable: FPG	Final visit		Baseline visit	
Adjustments	Estimate (95% CI)	P-value	Estimate (95% CI)	P-value
Crude	0.37 (0.36-0.38) r^2 .22	<.0001	0.26 (0.25-0.27) r^2 .18	<.0001
Sex, age, country	0.35 (0.34-0.36)	<.0001	0.26 (0.25-0.26)	<.0001
Sex, age, country, prestudy therapy[a]	N/A	N/A	0.26 (0.25-0.26)	<.0001
Sex, age, country, prestudy therapy[a], BMI, diabetes duration	0.35 (0.34-0.36)	<.0001	0.25 (0.25-0.26)	<.0001
Sex, age, country, prestudy therapy[a], BMI, diabetes duration, PPG	0.26 (0.25-0.27)	<.0001	0.16 (0.15-0.17)	<.0001

BMI, body mass index; CI, confidence interval; FPG, fasting plasma glucose; HbA1c, glycated haemoglobin; N/A, not analysed; PPG, postprandial plasma glucose.

[a]Prestudy therapy only adjusted for in baseline visit analyses.
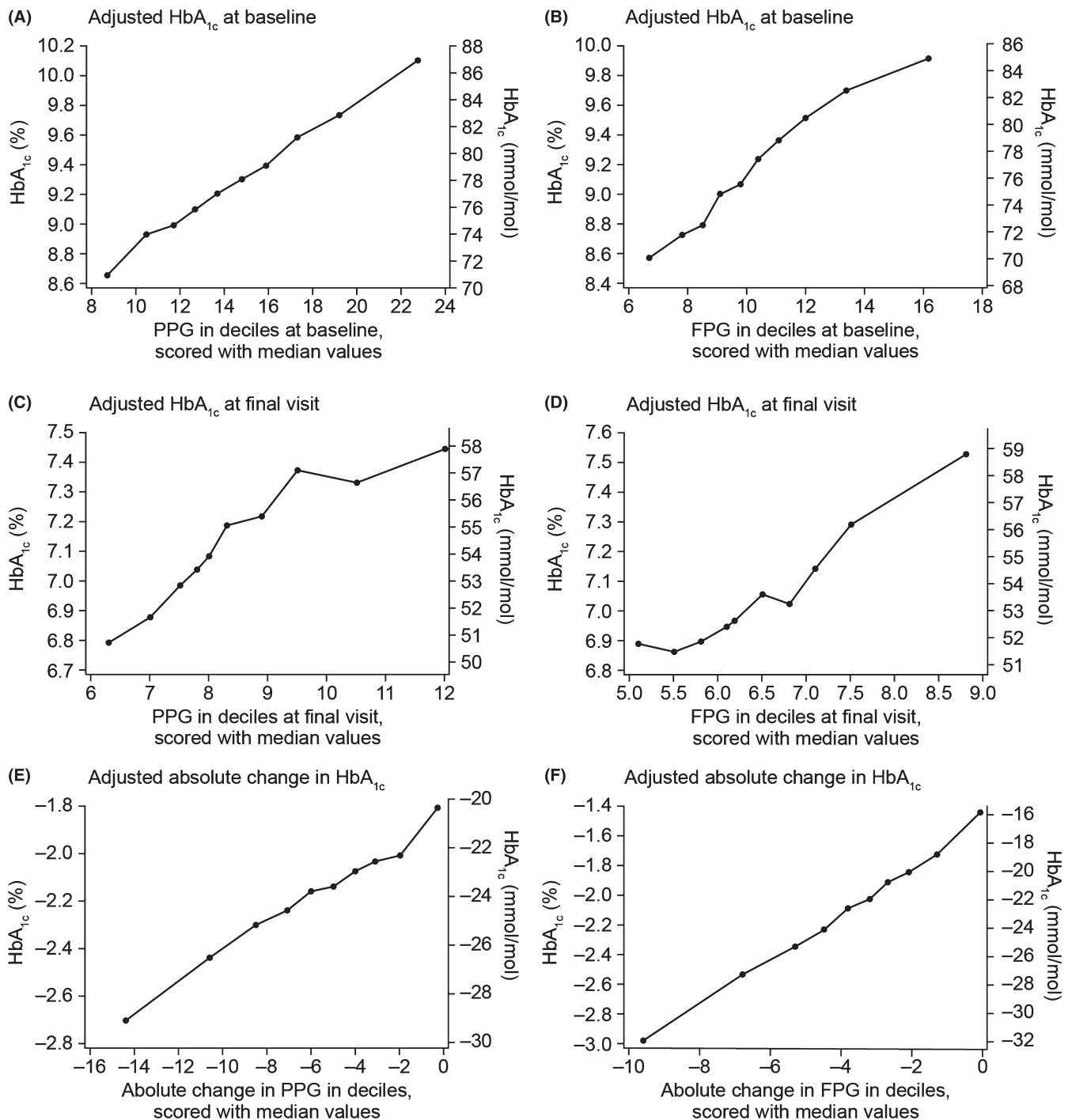
FIGURE 1 Cross-sectional analysis of (A) baseline PPG (in deciles) and HbA1c (adjusted for sex, age, country, prestudy therapy, BMI, diabetes duration, FPG); (B) baseline FPG (in deciles) and HbA1c (adjusted for sex, age, country, prestudy therapy, BMI, diabetes duration, PPG); (C) final visit PPG (in deciles) and HbA1c (adjusted for sex, age, country, BMI, diabetes duration, FPG); (D) final visit FPG (in deciles) and HbA1c (adjusted for sex, age, country, BMI, diabetes duration, PPG); (E) absolute changes in PPG and HbA1c (adjusted for baseline HbA1c, baseline PPG, sex, age, country, prestudy therapy, BMI, diabetes duration, baseline FPG absolute change in FPG); and (F) absolute changes in FPG and HbA1c (adjusted for baseline HbA1c, baseline FPG, sex, age, country, prestudy therapy, BMI, diabetes duration, baseline PPG absolute change in PPG). BMI, body mass index; FPG, fasting plasma glucose; HbA1c, glycated haemoglobin; PPG, postprandial plasma glucose

In the crude and adjusted analysis of the overall population, there was a statistically significant association between PPG (breakfast) and HbA1c, both at baseline and final visit (Table 1, Figure 1). Similarly, crude analysis in the overall population showed a significant association between FPG and HbA1c, both at baseline and final visit (Table 1, Figure 1). The associations between exposures and outcomes were only slightly affected and remained significant in a step-wise adjustment (Table 1). The associations were attenuated by

mutual adjustments for FPG and PPG, but remained significant and independent (Table 1). Both crude and adjusted analysis in the overall population showed an association between absolute changes in PPG (breakfast) and HbA1c after 26 weeks of biphasic insulin aspart 30 (BIAsp 30) treatment, where a larger reduction in PPG or FPG was associated with larger reductions in HbA1c (Figure 1). In the crude analysis, a 1 mmol/L decrease in PPG at breakfast between baseline and final visits was associated with an absolute reduction in HbA1c of 0.17% (2 mmol/mol). A 1 mmol/L reduction in FPG was associated with an absolute HbA1c reduction of 0.27% (3 mmol/mol). Similar results were observed when analysing the associations between relative changes in PPG and HbA1c: estimate 0.28 (95% confidence interval [CI] 0.27-0.28), along with relative changes in FPG and HbA1c: estimate 0.34 (95% CI 0.33-0.35). Finally, associations between PPG and HbA1c, or change in PPG and change in HbA1c, after 26 weeks of BIAsp 30 treatment did not seem to be modified by FPG level.

When seeking to contextualise our findings within the body of existing research, the findings differ from a meta-analysis which indicated a stronger association between PPG and HbA1c compared with FPG and HbA1c.[2] Regarding the reasons for this discrepancy, it can be argued that, depending on the method used for assessment of PPG (ie, after breakfast, lunch or dinner; at 1 or 2 h after the start of the meal), the impact of PPG can appear as slightly lower or greater than that of FPG. This is particularly true when the impact is crudely estimated using the calculation of linear correlations, as in the current analysis.

In conclusion, in a large population of patients with type 2 diabetes and poor glycaemic control at baseline, there was a statistically significant association between PPG (breakfast) and HbA1c, and between FPG and HbA1c, as well as between the changes in PPG and FPG with those of HbA1c. We believe these results demonstrate the importance of considering treatments that address both fasting and postprandial glucose in states of hyperglycaemia and mild dysglycaemia.

DISCLOSURES

Paul Valensi has served as chairman to the advisory board of the IMPROVE study, has given lectures for Novo Nordisk, and his department has received grants from Novo Nordisk. Lise Lotte N. Husemoen is an employee of Novo Nordisk. James Weatherall owns shares in Novo Nordisk A/S. Louis Monnier declares that he has no conflicts of interest.

AUTHOR CONTRIBUTIONS

Lise Lotte N. Husemoen contributed to the design of the study, performed the statistical analysis, and contributed to the interpretation of data and revision of the manuscript. Paul Valensi, James Weatherall and Louis Monnier contributed to the design of the post hoc study, and contributed to the interpretation of data and critical revision of the manuscript.

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