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Brief report

Predictors of postprandial blood glucose response to biphasic insulin analogue therapy

Vito Borzì[a,*], Marian Benroubi[b], Janusz Gumprecht[c], Ryuzo Kawamori[d], Robert Ligthelm[e], Joseph Shaban[f], Siddharth Shah[g], Marina Shestakova[h], Yang Wenying[i], Paul Valensi[j], on behalf of the IMPROVE™ Study Expert Panel

[a] Department of Internal Medicine, Vittorio Emanuele Hospital, Catania, Italy
[b] Diabetes Centre, General Hospital of Athens 'POLYKLINICI', Athens, Greece
[c] Department of Internal Diseases, Diabetology and Nephrology, Medical University of Silesia, Zabrze, Poland
[d] Department of Metabolism and Endocrinology, Juntendo University School of Medicine, Tokyo, Japan
[e] EHM Clinic, Hoofddorp, The Netherlands
[f] Endocrinology and Metabolism, Windsor Regional Hospital, Windsor, ON, Canada
[g] Department of Endocrinology, Bhatia S. L. Raheja Hospital, Mumbai, India
[h] Institute of Diabetes, Federal Scientific Centre of Endocrinology, Moscow, Russia
[i] Department of Endocrinology, China-Japan Friendship Hospital, Beijing, China
[j] Department of Endocrinology-Diabetology-Nutrition, Jean Verdier Hospital, AP-HP, Paris Nord University, CRNH-IdF, Bondy, France

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ABSTRACT

Biphasic insulin aspart 30 (BIAsp 30) has been shown in randomised controlled trials and the IMPROVE™ observational study to reduce postprandial blood glucose (PPBG) – thought to be an independent risk factor for cardiovascular disease. We used multivariate regression analysis to identify predictors of PPBG reduction in the IMPROVE™ study. A total of 52,419 type 2 diabetes patients were enrolled in the IMPROVE™ study (pre-study therapy subgroups: no pharmaceutical therapy, $n = 8966$; oral antidiabetic drugs [OADs] only, $n = 33,797$; insulin ± OADs, $n = 9568$; missing information on pre-study therapy, $n = 88$). Mean change from baseline in PPBG (mean of three meals) in the global cohort was −6.3 mmol/L; reductions in subgroups were: no pharmaceutical therapy, −8.8 mmol/L; OADs only, −6.0 mmol/L; insulin ± OADs, −5.1 mmol/L. High baseline PPBG was consistently and strongly predictive of PPBG response; lower baseline HbA1c and body mass index, greater age and shorter diabetes duration were also significant predictors of PPBG change. The novel findings from this study indicate that most patients can be expected to achieve a PPBG response with BIAsp 30 irrespective of baseline characteristics or previous therapy with an expected larger PPBG reduction when baseline PPBG is higher.

* *Corresponding author at*: Department of Internal Medicine, Vittorio Emanuele Hospital, Via Plebiscite 628, Catania 95100, Italy. Tel.: +39 0957 435 216; fax: +39 0957 435 216.
E-mail address: vitoborzi@gmail.com (V. Borzì).
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1. Introduction

Elevated postprandial blood glucose (PPBG) levels are a feature of type 2 diabetes (T2D) from the earliest stages of the disease, and evidence suggests that elevated PPBG is an independent risk factor for cardiovascular disease (CVD) [1]. Biphasic insulin aspart 30/70 (BIAsp 30 [NovoMix® 30, Novo Nordisk A/S, Denmark], comprising 30% rapid-acting insulin aspart and 70% intermediate-acting protaminated aspart) has been shown in randomised controlled trials (RCTs) to reduce PPBG more than optimised oral antidiabetic drug (OAD) therapy [2,3] or other insulins (basal insulin or human premix, respectively) [4–7]. Results from the largest observational study of BIAsp 30 in routine practice to date, the IMPROVE™ study, confirmed the PPBG results from RCTs [8–10]. Our aim in the current analysis was to identify baseline predictors of PPBG reduction in this large population in order to provide information about treatment strategies and optimise use of BIAsp 30 therapy.

2. Materials and methods

IMPROVE™ was a 6-month, non-randomised, non-interventional, observational study designed to investigate the effectiveness and safety profile of BIAsp 30 in routine clinical practice [11]. Individuals were enrolled into IMPROVE™ if their physician decided to initiate treatment with BIAsp 30 as part of their diabetes treatment [11]. At the time of this analysis, a total of 52,419 T2D patients were enrolled from eight countries (China, Japan, Poland, Italy, India, Canada, Russia, Greece) from the following pre-study therapy subgroups: no pharmaceutical therapy ($n = 8966$, diabetes duration 2.0 years, baseline HbA1c 9.9%); OADs only ($n = 33{,}797$, diabetes duration 7.4 years, baseline HbA1c 9.2%); and insulin ± OADs ($n = 9568$, diabetes duration 10.4 years, baseline HbA1c 9.3%). Information on pre-study therapy was missing for 88 patients. At final visit, HbA1c (no pharmaceutical therapy −3.1%, OADs only −2.1% and insulin ± OADs −2.0%), fasting blood glucose (FBG: no pharmaceutical therapy −5.9 mmol/L; OADs only −4.1 mmol/L and insulin ± OADs −3.3 mmol/L) and PPBG (no pharmaceutical therapy −9.0 mmol/L; OADs only −6.1 mmol/L and insulin ± OADs −5.1 mmol/L) were significantly reduced from baseline [10]. In addition, major hypoglycaemia was reduced in all the subgroups while minor hypoglycaemia rates was reduced in those patients on prior insulin treatment but was increased in those patients who were previously insulin-naïve [10]. There was no mean weight gain in the study (−0.1 kg for all three prior-treatment subgroups) [10]. Using these data, multivariate regression analyses were applied to mean PPBG reduction from baseline (averaged over three meals) at final visit for the global cohort and the three pre-study therapy groups, as well as for PPBG reduction at each of three meals. Baseline factors entered as potential predictors were age, duration of diabetes, HbA1c, PPBG, FBG and body mass index (BMI). Country effects were controlled for in the analysis of the change in overall mean PPBG. Multivariate regression was carried out on patient data when values for the endpoint and all the covariates in the model were available. Outliers were excluded on a per-covariate basis.

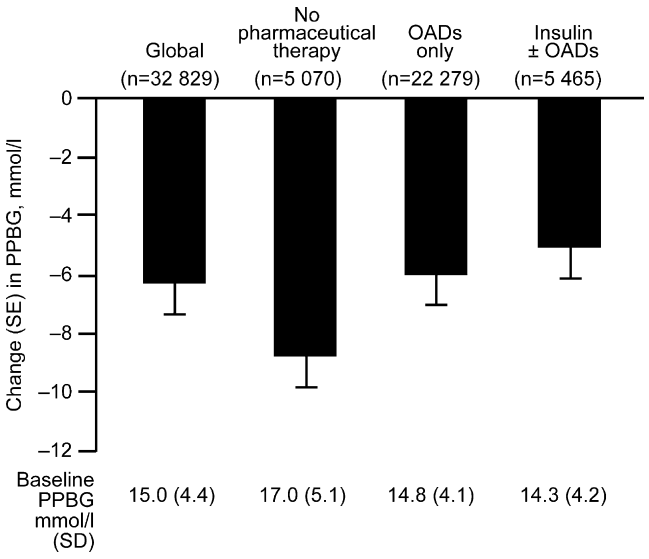

Fig. 1 – Changes in mean postprandial blood glucose (PPBG) values (averaged over three meals) for patients in the IMPROVE™ study: subjects with baseline and final visit measurement available.

3. Results

Large reductions from baseline in PPBG were observed in the global cohort and in the three pre-study therapy subgroups of the IMPROVE™ study (Fig. 1). In the global cohort, lower baseline HbA1c, FBG and BMI, greater age, shorter diabetes duration and higher baseline PPBG were significant predictors of greater reduction in PPBG; all $p < 0.001$ (Table 1, data summarised in Fig. 2). Similar relationships were observed in the pre-study therapy subgroups, except that baseline FPG, age or BMI were no longer significant predictors of PPBG change in subjects previously on no pharmaceutical therapy. Baseline age or BMI were also not significant predictors for those on prior insulin ± OAD. Multivariate regression using a model excluding baseline HbA1c as predictor yielded similar results (data not shown). The magnitude and direction of correlations were maintained when considering PPBG change at each of breakfast, lunch and dinner, although BMI was strongly correlated only with PPBG changes at breakfast and dinner, FBG correlated only with change in dinner PPBG and age correlated only with breakfast and lunch PPBG (Table 2, data summarised in Fig. 3). Breakfast and lunch PPBG reduction significantly correlated with the number of BIAsp 30 injections, and was larger in patients receiving three BIAsp 30 injections and smaller in those receiving one BIAsp 30 injection than in those receiving BIAsp 30 twice daily (Table 2 and Fig. 3). Number of BIAsp 30 injections was not a significant predictor of PPBG response at dinner.

4. Discussion

In this analysis, reductions in PPBG with BIAsp 30 were predicted by higher baseline PPBG, regardless of pre-study therapy. This association seems reasonable, since there is