

# Self-monitoring of blood glucose significantly improves metabolic control in patients with type 2 diabetes mellitus: the Auto-Surveillance Intervention Active (ASIA) study

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## SUMMARY

**Objective:** Self monitoring of blood glucose (SMBG) in type 2 diabetes is a topic of current interest (imbalance between increased health-care costs and improvement in compliance with treatment and diet). An open label randomized prospective study was designed to compare changes in metabolic control over 6 months in patients managed with usual recommendations alone (conventional assessment group) or combined with SMBG.

**Research design and methods:** Patients not treated with insulin or previously self monitored, 40 to 75 years of age, with a diagnosis of type 2 diabetes > 1 year and standardized HbA<sub>1c</sub> level  $\geq 7.5$  and  $\leq 11\%$  were randomized to either a control group or SMBG group. They were followed up every 6 weeks over 24 weeks. Patients in the SMBG group were given the same device (Ascensia Esprit® Discmeter, Bayer) and were required to perform at least 6 capillary assays a week (3 different days of the week, including weekend). Management of patients was standardized, including drugs, diet and physical activity. The primary efficacy criterion was change in HbA<sub>1c</sub> level in Intent To Treat (ITT) patients. Assays were performed at baseline, at 3 and 6 months using the calibrated DCA 2000® device (Bayer).

**Results:** Two hundred sixty five general practitioners randomized 988 patients (ITT Population), but 689 patients were evaluable for the primary criterion. At the endpoint, HbA<sub>1c</sub> was lower in the SMBG group ( $8.1 \pm 1.6\%$ ) than in the conventional treatment group ( $8.4 \pm 1.4\%$ ,  $P = 0.012$ ). The change in HbA<sub>1c</sub> levels between baseline and endpoint was classified into two classes: improvement if a change  $> 0.5\%$  occurred, stability or worsening in case of a change  $\leq 0.5\%$ ; 57.1% of patients in the SMBG group vs 46.8% in the control group had an improvement in HbA<sub>1c</sub> level ( $P = 0.007$ ) after 3 months. A steady state was reached during the last 3 months. A multivariate logistic regression analysis was performed and identified factors predictive of improvement in HbA<sub>1c</sub> levels: HbA<sub>1c</sub> at baseline: odd ratio (OR) = 1.749 ( $P < 0.001$ ), SMBG group (reference value: SMBG group): OR = 0.665 ( $P = 0.015$ ), duration of diabetes: OR = 0.953 ( $P = 0.001$ ) and BMI: OR = 0.962 ( $P = 0.039$ ).

## RÉSUMÉ

### L'autosurveillance glycémique améliore significativement le contrôle métabolique du patient diabétique de type 2

**Objectifs :** La pratique de l'autosurveillance glycémique (ASG) chez le patient diabétique de type 2 reste débattue compte tenu du coût qu'elle représente mais aussi de l'amélioration de la compliance au traitement (diététique, médicamenteux) que l'on peut en attendre. Nous rapportons les données d'une étude ouverte randomisée prospective conduite sur 6 mois chez des patients diabétiques de type 2 effectuant uniquement un suivi traditionnel ou réalisant en association une ASG.

**Matériels et méthodes :** Les patients ont été randomisés dans le groupe suivi traditionnel ou le groupe ASG selon les critères d'inclusion suivants : patients non traités par de l'insuline ou ayant bénéficié antérieurement d'une ASG, âgés entre 40 et 75 ans, diagnostic de diabète porté depuis plus de 1 an, valeur d'HbA<sub>1c</sub>  $\geq 7,5\%$  et  $\leq 11\%$ . Les patients ont été suivis toutes les 6 semaines pendant 24 semaines. Les patients du groupe ASG bénéficiaient du même lecteur de glycémie (Ascensia Esprit® Discmeter, Bayer) et réalisaient au moins 6 glycémies par semaine (sur 3 jours différents de la semaine, incluant un jour du week-end). Le suivi standardisé des patients portait sur la prise des antidiabétiques oraux, la diététique et la fréquence de réalisation d'une activité physique. Le critère principal de jugement était la variation de la valeur de l'HbA<sub>1c</sub> en intention de traiter (ITT). Les mesures d'HbA<sub>1c</sub> ont été réalisées à l'inclusion, à 3 et 6 mois par une méthode standardisée (DCA 2000® ; Bayer).

**Résultats :** Deux-cent-soixante-cinq généralistes ont randomisés 988 patients (population ITT), mais 689 patients ont été évalués sur le critère principal de jugement. L'HbA<sub>1c</sub> à 6 mois était plus basse dans le groupe ASG ( $8,1 \pm 1,6\%$ ) que dans le groupe suivi traditionnel ( $8,4 \pm 1,4\%$ ,  $P = 0,012$ ). Les variations d'HbA<sub>1c</sub> entre l'inclusion et la fin d'étude ont été classées en 2 catégories : amélioration si la variation d'HbA<sub>1c</sub> était  $> 0,5\%$ , stabilité ou dégradation si la variation était  $\leq 0,5\%$  ; 57,1 % des patients du groupe ASG vs 46,8 % des patients du groupe suivi traditionnel ont présenté une amélioration de leur valeur d'HbA<sub>1c</sub> ( $P = 0,007$ ) après 3 mois. Une stabilisation de la valeur

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**Conclusions:** This study is the first multicenter, controlled, prospective trial conducted on a large number of patients demonstrating that SMBG was statistically associated with a better quality of metabolic control than usual traditional recommendations alone in type 2 diabetes.

**Key-words:** Self-monitoring blood glucose · Type 2 diabetes mellitus · Blood glucose control · HbA<sub>1c</sub>.

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The usefulness of Self Monitoring of Blood Glucose (SMBG) has been demonstrated in type 1 diabetes by improvement in control of blood glucose in patients and in the improvement of the long-term prognosis of this disease [1]. By extension, type 2 diabetic patients who, becoming insulin-dependent, will benefit from the SMBG with the aim of optimized control of blood glucose [2, 3]. However, SMBG remains debatable in type 2 diabetes mellitus treated with diet and oral antidiabetic agents only in term of improvement of metabolic control, as reported in a recently published meta-analysis by Faas *et al.* [4]. But, among the 11 former studies published, 5 were retrospective [5-9], and only 4 [10-13] of the 6 prospective studies [10-15] did not have methodological limits accounting for the difficulty in determining a significant difference (small sample size, insufficient duration of follow-up, reference group sometimes non diabetic, SMBG with reagent strips).

Theoretically, SMBG can improve compliance with recommendations on diet and exercise and medication regimens. The American Diabetes Association has recommended that the optimal frequency of SMBG for patients with type 2 diabetes should be adequate to facilitate reaching glucose goals [2]. This hypothesis is based on the fact that lifestyle changes are facilitated by SMBG. Under these conditions, we should expect an improvement of glycemic control [2, 16, 17]. SMBG increases patient management costs, and because of the high prevalence of type 2 diabetes, efforts to establish the efficacy of SMBG in type 2 diabetes mellitus are of greater relevance.

The aim of this 6-month study was to compare, over a 6-month period, metabolic control in patients with poorly controlled type 2 diabetes, managed either with usual recommendations alone (conventional assessment group) or combined with self monitoring of blood glucose (SMBG group).

d'HbA<sub>1c</sub> était observée durant les 3 mois suivants. Une analyse multivariée a été conduite afin de déterminer les facteurs prédictifs de l'amélioration de la valeur d'HbA<sub>1c</sub> : HbA<sub>1c</sub> à la randomisation : odd ratio (OR) = 1,749 ( $P < 0,001$ ), groupe ASG (valeur de référence : groupe ASG) : OR = 0,665 ( $P = 0,015$ ), durée d'évolution du diabète : OR = 0,953 ( $P = 0,001$ ) et IMC : OR = 0,962 ( $P = 0,039$ ).

**Conclusions :** Cette étude multicentrique contrôlée et prospective conduite sur une large population de patients diabétiques de type 2 démontre que la pratique de l'ASG est significativement associée à un meilleur contrôle métabolique comparativement aux seules recommandations de suivi traditionnel du patient diabétique de type 2.

**Mots-clés :** Autosurveillance glycémique · Diabète de type 2 · Contrôle glycémique · HbA<sub>1c</sub>.

## Research design and methods

### Overall study design

An open-label, randomized, prospective, controlled study was conducted on patients with type 2 diabetes poorly controlled with oral antidiabetic treatment.

The patients were randomized to two groups and followed-up by their general practitioner: (Group 1): patients received a conventional laboratory work-up based solely on laboratory measurement of HbA<sub>1c</sub> every 12 weeks, according to recommendations of the Agence Nationale d'Accréditation et d'Evaluation des Soins (ANAES) [3]; (Group 2): in addition to the conventional laboratory workup, patients underwent self-monitoring of blood glucose. These patients received specific initial training given by their general practitioner at the initial inclusion visit and were required to perform at least 6 capillary assays a week. The patients met the following eligibility criteria: type 2 diabetes with a known duration of over 1 year, insufficiently controlled with oral antidiabetic treatment ( $HbA_{1c} \geq 7.5$  and  $\leq 11\%$ ), age between 40 to 75 years, patient not previously treated with insulin (for more than 7 consecutive days) and not requiring insulin at inclusion, patient who did not previously receive blood glucose self-monitoring, patient able to carry out blood glucose self-monitoring. Exclusion criteria were: type 1 diabetes, MODY and secondary diabetes mellitus, recent weight loss of more than 3 kg during the last 3 months, impending complications of diabetes, pregnant women, patient unable to read or write, uncooperative or who did not consent to participate.

The patients were followed up every 6 weeks over 24 weeks. Five visits (V1 to V5) were conducted during the study. Clinical evaluations were carried out at each visit (weight, systolic blood pressure (SBP) and diastolic blood pressure (DBP)) and laboratory analyses at V1 (baseline), V3 (3 months) and V5 (6 months). At V3, each general practitioner could modify the treatments of diabetic patients accord-

ing to HbA<sub>1c</sub> value in keeping with ANAES recommendations [3]. At each consultation, patients were informed of their current blood glucose level, the necessity of good control of diabetes, and the importance of weight loss in combination with physical activity.

Two hundred and sixty five general practitioners randomized 988 type 2 diabetic patients (510 patients in SMBG group and 478 in conventional assessment group). Six hundred and eighty-nine randomized patients were evaluable for the primary criterion with at least two evaluations of HbA<sub>1c</sub> levels with a 2-month interval between the 2 evaluations (patients included in the modified Intent To Treat (ITT) population: 345 patients in SMBG group and 344 in the conventional assessment group). Written informed consent was obtained from all the patients at V1.

### Treatment components

Six hundred and eighty-six patients currently were taking at least one oral antidiabetic drug. Among treated patients, the most widely prescribed agents were sulfonylureas and biguanides (80.8% and 61.1% of patients, respectively); 30% of patients were receiving  $\alpha$ -glucosidase inhibitors. They were prescribed either alone or in combination; the most frequent combinations were sulfonylureas plus biguanides (32.4%) or a combination of the 3 treatments (14.3%). No statistical difference between groups was found. At inclusion visit, 573 patients (83.2%) were receiving at least one other treatment. The most frequently reported treatments were fibrates (n = 117), angiotensin-converting enzyme inhibitors (n = 115), HMG-CoA reductase inhibitors (n = 108) and  $\beta$ -blockers (n = 95). No statistically significant difference was found between groups in terms of concomitant treatments in the modified ITT population. All patients received dietary advice from their general practitioners based on their ideal body weight, and walking was encouraged as a form of exercise. 61.5% of the patients enrolled in the modified ITT population reportedly followed a diet. No statistical difference was found between the two groups (SMBG: 59.6% *vs* conventional assessment group: 63.5%, NS). The intensity of usual physical activity was reported as moderate by 33.1% of modified ITT population, intermediate by 26.2% and limited by 23.3%. No statistical difference between groups was found in the modified ITT population. Guidelines for self-adjustment of diet and low blood glucose values were given.

### Initial training and quality control of SMBG

Training in SMBG was also carried out by general practitioners who trained the diabetic patients at the time of the inclusion visit V1. Patients in the SMBG group received the same device (Ascensia Esprit®, Discmeter Bayer) and were required to perform at least 6 capillary assays a week (on 3 different days of the week, including weekends). A quality control was carried out by the investigator at the time of the

V2 visit for patients in the SMBG group: methodology used by the patient for conduct of SMBG, potential corrections, checking of the proper functioning of the device and calibration of the device using a standard solution.

### Laboratory measurements

Assay of HbA<sub>1c</sub> was performed by an immunoenzymological method in the same qualified laboratory for each patient, using a calibrated DCA 2000 (Bayer, France). Blood glucose was also measured in the same laboratory as HbA<sub>1c</sub> for each patient, by glucose oxidase method (Beckman, Fullerton, CA).

### Statistical analyses

Results are expressed as the mean  $\pm$  SD for quantitative parameters, and frequency and percentage for qualitative parameters. The comparisons between groups before randomization were carried out using a *t* test when variables had a normal distribution and with a non-parametric Wilcoxon test in other cases. Chi<sup>2</sup> test for qualitative variables or Fisher's exact test in case of small theoretical samples < 5.

HbA<sub>1c</sub> level was measured at inclusion, after 3 months of follow-up (visit 3) and after 6 months of follow-up (visit 5). The primary efficacy criterion was the outcome in HbA<sub>1c</sub> level in modified intent to treat (ITT) patients with analysis of variance of the last known value (value at 3 or 6 months) and inclusion value as covariate. For secondary analyses, a repeated measure analyses and a paired *t* test were performed on data at 0, 3 and 6 months. The change in HbA<sub>1c</sub> level between baseline and endpoint has been analysed in two classes, improvement *vs* stability or worsening, in terms of a 0.5% decrease in HbA<sub>1c</sub> (improvement if change higher than 0.5%, stability and worsening if change  $\leq$  0.5%). A logistic analysis has been performed in order to identify factors predictive of the improvement in HbA<sub>1c</sub> level.

Additional criteria were changes in fasting blood glucose, frequency of asymptomatic and symptomatic hypoglycemia (capillary blood glucose < 3 mM/L), weight, blood pressure, observed diet and drugs (type of treatments, changes in doses of drugs). An analysis of safety was carried out in ITT by evaluating the number of patients who presented an adverse event (AE), and numbers of patients who presented a serious AE.

Sample-size estimates were calculated to detect a difference of 0.5% in HbA<sub>1c</sub> between the two groups, with type-error = 1.667 (two-tailed test with power of 90% and 5% significance level): 234 patients/group were required. Since the expected dropout rate was estimated at 35%, a total of 830 patients were required.

Statistical analyses were performed using Software SAS®, version 8.2, SAS Institute, NC, Cary, USA.

**Table I**  
Clinical and laboratory parameters at baseline.

	SMBG group (n = 345)	Conventional assessment group (n = 344)	P
Sex (M/W)(%)	53.7/46.3	56.6/43.4	NS
Age (years)	60.9 ± 9.4	62.2 ± 9.1	NS
Duration of diabetes (months)	92.3 ± 75.0	100.8 ± 79.6	NS
Weight (kg)	83.3 ± 15.7	82.0 ± 15.3	NS
BMI (kg/m <sup>2</sup> )	30.4 ± 6.1	29.7 ± 4.8	NS
Waist to hip ratio	0.96 ± 0.10	0.96 ± 0.08	NS
Systolic blood pressure (mmHg)	138.7 ± 11.7	140.5 ± 13.2	NS
Diastolic blood pressure (mmHg)	80.0 ± 6.8	80.8 ± 7.4	NS
HbA <sub>1c</sub> (%)	9.0 ± 1.3	8.9 ± 1.3	NS
Fasting blood glucose (mM/L)	7.2 ± 5.1	7.5 ± 4.8	NS

## Results

### Demographic data at baseline

Clinical and laboratory data of the patients studied are listed in *Table I*. No statistically significant difference was observed between the two groups, the SMBG and conventional assessment groups. At baseline, HbA<sub>1c</sub> levels were 9.0 ± 1.3% in SMBG group and 8.9 ± 1.3% in the conventional assessment group (NS).

### Drop-outs from therapy or assessment

Three hundred and three patients discontinued the study early (164 in SMBG group and 139 in the conventional assessment group: NS). Among the 303 patients who dropped out of the study, only 240 had a reason reported for discontinuation: adverse event (n = 6), patient non compliance (n = 33), consent withdrawal (n = 15), patient lost to follow-up (n = 19), death (n = 4), protocol violation (n = 21), lack of information on patients (n = 92), other reason (n = 110).

### Primary efficacy criteria

At endpoint, HbA<sub>1c</sub> level was lower in the SMBG group (8.1 ± 1.6%) than in traditional assessment group (8.4 ± 1.4%) ( $P = 0.012$ ). The covariance analysis demonstrated a significant effect of baseline value ( $P < 0.001$ ) and a significant effect of group ( $P < 0.005$ ). The difference between groups was statistically significant ( $P = 0.005$ ). A repeated measures analysis of variance was also carried out on the three values (at baseline, 3 months and 6 months) and found a significant decrease in HbA<sub>1c</sub> level over time ( $P < 0.001$ ), a significant effect of Time\* Group interaction ( $P = 0.022$ ), but no significant effect of group (*Fig 1*).

The mean change between inclusion and endpoint was -0.88 ± 1.54% in the SMBG group and was -0.60 ± 1.54%

in the conventional assessment group. The change between the two groups was significant ( $P = 0.009$ ). When a comparison was made between the inclusion visit and the intermediate visit (3 months), we found that the improvement occurred mainly during the first 3 months, with a steady state reached in the last 3 months of the study. At V3, HbA<sub>1c</sub> was lower in the SMBG group (8.3 ± 1.5%) than in the conventional assessment group (8.4 ± 1.4%), and the mean change in HbA<sub>1c</sub> was -0.70 ± 1.28% in the SMBG group at 3 months compared to -0.45 ± 1.27% in the conventional assessment group ( $P = 0.013$ ). On the contrary, the mean changes in HbA<sub>1c</sub> were not statistically different between the two groups at 3 and 6 months.

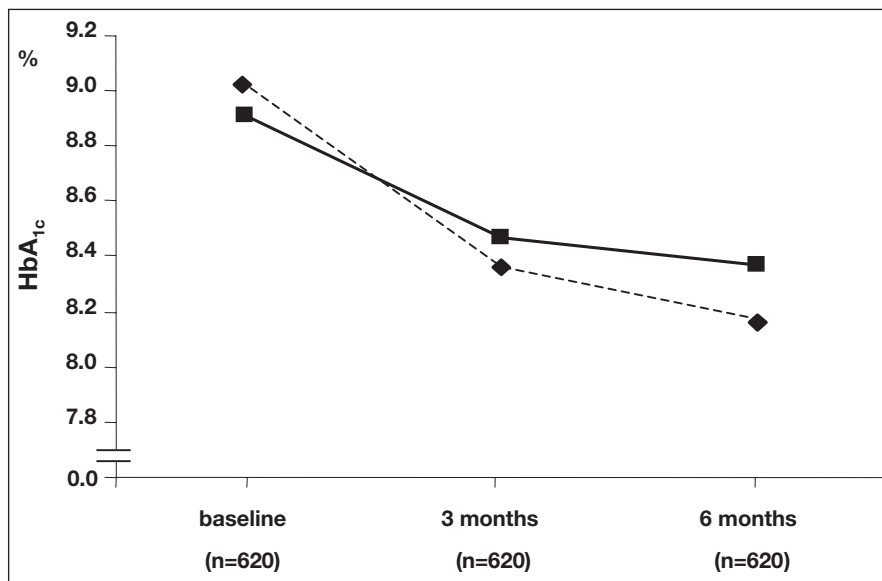
### Outcome of HbA<sub>1c</sub> levels

An improvement of HbA<sub>1c</sub> between baseline and endpoint was shown in 52.0% of patients (57.1% in the SMBG group and 46.8% in the conventional assessment group) and stability or worsening was found in 48% of patients (42.9% in the SMBG group and 53.2% in the conventional assessment group) ( $P = 0.007$ ) (*Fig 2*). At 3 months, 50.3% of patients in the SMBG group showed an improvement in HbA<sub>1c</sub> level *vs* 41.6% in the conventional assessment group ( $P = 0.026$ ).

The multivariate analysis determined factors predictive of improvement in HbA<sub>1c</sub> (> 0.5%): HbA<sub>1c</sub> level at baseline: odd ratio (OR) = 1.749 ( $P < 0.001$ ); SMBG group (reference value = SMBG group): OR = 0.665 ( $P = 0.015$ ); duration of diabetes in years: OR = 0.953 ( $P < 0.001$ ) and BMI (kg/m): OR = 0.969 ( $P = 0.039$ ).

### Secondary efficacy criteria

No statistically significant difference was found in fasting blood glucose levels at endpoint between the two groups (SMBG: 6.66 ± 4.83 *vs* conventional group: 6.91 ± 4.56 mM/L, NS). In all, 78 patients reported at least one episode



**Figure 1**

HbA<sub>1c</sub> change during study, in modified ITT population with 3 evaluations (620 patients) at baseline, 3 and 6 months in SMBG (◆) and conventional assessment (■) groups.

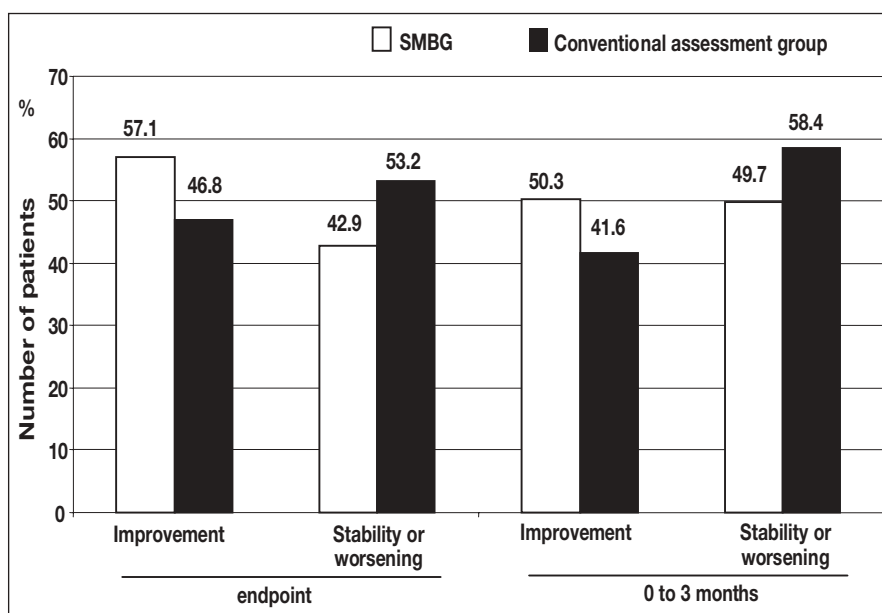
of hypoglycemia (symptomatic or asymptomatic) during the study; 53 (10.4%) patients in the SMBG group and 25 (5.2%) patients in traditional assessment group. These proportions were statistically different ( $P = 0.003$ ) due to the difference between groups solely for asymptomatic hypoglycemia ( $P = 0.001$ ). No serious episode of hypoglycemia was reported during this study.

Mean change in weight between the inclusion and endpoint was  $-0.93 \pm 4.35$  kg in the SMBG group *vs*  $-0.83 \pm 4.87$  kg in the conventional group; mean change in SBP between the inclusion and endpoint was  $-1.20 \pm 11.4$  mmHg in the SMBG group *vs*  $-2.72 \pm 12.03$  mmHg in the conventional group; mean change in DBP between the inclusion and endpoint was  $-0.62 \pm 7.71$  mmHg in the SMBG

group *vs*  $-1.00 \pm 7.89$  mmHg in the conventional group. No difference was found between the groups, and no time effect was found with the repeated measures analysis of these parameters.

### Changes in prescription of antidiabetic treatments and other treatments

At the last visit, information was available on 668 patients for their oral antidiabetic treatment. Eighty four percent of the modified ITT population were currently taking sulfonylureas, 64.1% were taking biguanides and 37.4% were taking  $\alpha$ -glucosidase inhibitors; in the two groups, the percentage of patients taking an antidiabetic treatment increased sig-



**Figure 2**

HbA<sub>1c</sub> change in classes (improvement and stability or worsening), in modified ITT population, at end-point and at 3 months.

nificantly during the study, whatever the treatment used, but no statistical difference between groups was found. The combinations of treatment the most frequently reported were sulfonylureas plus biguanides (31.4%) and the 3 types of treatments together (19.6%). Prescription for another concomitant treatment at visit 5 was reported in 83.5% of the modified ITT population. The most frequent drugs prescribed were the same as at baseline. No statistically significant difference was found between groups.

### Diet and physical activity compliance

At the last visit (V5), 58.3% of patients in the modified ITT population were asked to follow a diet. No statistically significant difference between the 2 groups was found during the study in terms of diet prescribed. However, the percentage of patients following dietary instructions remained stable in the SMBG group during trial, whereas this frequency decreased significantly in the conventional group ( $P = 0.045$ ). The intensity of usual physical activity was reported as moderate by 29.5% of the modified ITT population, intermediate by 33% and limited by 18.8%. No statistical difference was found between groups.

### Adverse events (AE)

In all, 92 patients (9.3%) presented at least one adverse event during the study, i.e. 144 adverse events: 39 patients (33.3%) presented one AE involving metabolism and nutrition; 17 patients (14.5%) presented at least one disorder of general health and 16 patients (13.7%) presented one AE involving the cardiovascular system. Of these 92 patients, 23 patients (2.3%) presented at least one AE considered as serious: in 8 patients, the problem involved the cardiovascular system and in 6 patients it involved a disorder of general health. In 6 patients (0.6%), the treatment was permanently discontinued. In 4 patients, the outcome of AE was death. For the two patients who experienced an AE leading to death, the cardiovascular system was the cause (stroke and cardiac arrest). For one of the other two patients, cirrhosis with oedema was reported as cause of the death.

### Conclusions

This multicenter controlled prospective trial demonstrates that self monitoring of blood glucose is statistically associated with a slight but significant improvement of metabolic control. The benefit was greater in patients with higher initial HbA<sub>1c</sub> levels, lower BMI and lower duration of diabetes. This is the first study on a large number of patients and designed to analyze the influence of self monitoring of blood glucose on metabolic control in type 2 diabetes, according to dietary, lifestyle and drug regimen recommendations. Our results are similar to those of a previous study also conducted in general practice [13]. This approach has proven to be acceptable and feasible [18], and its objective

was to achieve care of type 2 diabetic patients as close as possible to their own home environment. The patients were trained to monitor their blood glucose which would give them the necessary feedback to support a change in lifestyle.

The use of SMBG is increasingly recommended in type 2 diabetes mellitus by endocrinologists. For type 2 diabetic patients treated with insulin, we have to apply the same recommendations for SMBG as that for type 1 diabetic patients. SMBG has also demonstrated its effectiveness in selected patients and under conditions such as pregnancy, intensive insulin therapy, and self-awareness of hypoglycemic symptoms. SMBG may also be used in some situations: to avoid hypoglycemic episodes during dose modifications, in case of illness which can alter glucose control, to sensitize the patients to the treatment or diet compliance, and to assess the effect of physical activity. However, trials investigating the effects of SMBG in type 2 diabetes mellitus treated with diet or oral anti-diabetic agents only did not find any real benefit for metabolic control or weight loss. Currently, a moderate use of SMBG is recommended in these patients and some authors conclude that the high costs of SMBG in these patients are not justified and that SMBG is a waste of time and money [9, 15, 16].

Based solely on the randomized controlled trial, which is the best methodological instrument for measuring efficacy, a meta-analysis reported that among 6 randomized controlled trials, only one demonstrated a benefit of SMBG on blood glucose control [4]. In 5 studies out of the 6, patients were treated with diet alone or in combination with oral antidiabetic agents. The sixth study included type 2 diabetic patients, half of whom were receiving insulin [10]. All studies but one [14] had a follow-up period of 6 months or longer. The mean HbA<sub>1c</sub> at the beginning of these studies ranged from 6.1 to 12.4%. The equipment used was reagent strips in two studies [10, 13], strips on blood glucose meters in two other studies [11, 12], and was not specified in the last two studies. In all 6 randomized controlled studies, patients received technical training in how to use the meter device, but in only three of them (and also in our study), a check on the accuracy of the patients' performance (technique of use and the accuracy of the data) was carried out [10, 12, 13]. Lastly, education of the patients in how to use the results to guide their daily behavior (diet and physical activity) was applied in 4 studies [10, 12-14]. The number of glycemic determinations per day or per week was variable according to studies.

Among the 3 studies comparing the effectiveness of the SMBG in comparison to a standard group, only the study by Rutten and al. showed the effectiveness of SMBG on the outcome of HbA<sub>1c</sub> levels and weight [13]. Two other studies also showed an improvement in HbA<sub>1c</sub> and weight in a group using SMBG, but the differences were not significant [11, 12]. There are several explanations why SMBG did not lead to improved blood glucose control in these studies. First, it is possible that compliance with the technique or its

accuracy were insufficient [14]. A second explanation is that patients in the SMBG group were monitoring their blood glucose levels but not using the information to regulate their intake or exercise [10]. In most of the previous studies, the size of the diabetic populations was small, from 12 to 73 type 2 diabetic patients. Finally, frequent methodological discrepancies were reported in most of the studies (ambiguous formulation of variables, lack of statement about reliability and validity of measurements, and no clear definition of the included population). Only 4 studies met all methodological qualitative criteria [10-13]. But recently, a prospective, randomized, controlled multicenter study has shown that meal-related self-monitoring of blood glucose in combination with an eating diary and a structured counseling program improved significantly glycemic control in the majority of type 2 diabetic patients [19].

Previous research has concluded that most patients prefer blood testing rather than urine testing [6, 20]. But, it has been demonstrated that the SMBG is 12 times more expensive than urine testing [12]. Because of the high prevalence of type 2 diabetes mellitus and the added cost of SMBG over routine urine testing, efforts to establish the efficacy of SMBG in type 2 diabetes mellitus take on greater relevance. Two studies have reported a relationship between the number of reagent strips used by the patients and the decrease of HbA<sub>1c</sub> in type 2 diabetic patients [10, 11], as has already been demonstrated in type 1 diabetic patients [21, 22]. Unfortunately, in our study it is regrettable that it was not possible to recover patients' diaries in which blood glucose was recorded and to analyze capillary blood glucose. This lack of information on the quality and frequency of SMBG represents a limitation of our study when compared to other studies where compliance with SMBG was strictly evaluated [10, 12, 13].

Our study was conducted by general practitioners who received initial training for the follow-up of the patients and who were trained in SMBG as well as their patients enrolled in this study. This is a possible explanation for the large percentage of patients who discontinued the study (30.6%). But, the drop-out rate in this study was close to that observed in other studies (range 10-26%) [10, 15]. In addition, our population was representative of patients with type 2 diabetes in France, in terms of the latest epidemiological data recently published [23]. As the clinical and laboratory characteristics of the studied population were similar to those of type 2 diabetics followed-up in routine practice, we speculate that our conclusions could be applied to the whole population of patients with type 2 diabetes mellitus.

We also reported that the dietary instructions were more frequently applied by patients from the SMBG group than by patients undergoing conventional assessment, suggesting that maintaining dietary compliance was facilitated by SMBG. On the contrary, as the increase in antidiabetic treatment prescription was similar in the two groups, we can

speculate that these treatments had no direct impact on the differences observed in metabolic control between the two groups. Our results are in agreement with those reported by the Diabetes Prevention Program Research on the influence of lifestyle intervention to prevent diabetes mellitus or to achieve metabolic control [24].

The American Diabetes Association did not indicate which subgroup of type 2 diabetes SMBG can be used [2]. We found as factors predictive of the improvement of HbA<sub>1c</sub>, high HbA<sub>1c</sub> level at baseline, low BMI and short known duration of diabetes. For example, this means that a patient with an HbA<sub>1c</sub> level of 9.5%, a duration of diabetes of 7 years and a BMI of 22 will have approximately (based on OR of each parameter) 10.8 more chances to see an improvement if he is in the SMBG group and 7.2 more chances to see an improvement in his HbA<sub>1c</sub> level if he is in the conventional assessment group. A previous study has performed logistic regression analysis to try to identify which patient characteristics might predict success or failure of SMBG [12]. In this study, although none of the characteristics were significant, age and educational level approached statistical significance. The analysis concluded that younger, better educated patients might benefit from a program of intensive SMBG with at least 36 blood glucose determinations per month. The patient education should essentially be aimed at behaviour which is reported as more effective in achieving improved patient compliance [25]. However, some studies have demonstrated a "drop-off effect" whereby patients regressed to pre-intervention behaviour after a certain time without reinforcement [26, 27].

In our study, no standard rules for adjusting behaviour to the results of SMBG were given to patients who were expected to decide which changes to make in diet and physical activity in order to modify their glucose levels. So, we think that the improvement of HbA<sub>1c</sub> levels observed in the SMBG group is directly linked to the practice of regular SMBG and compliance with dietary recommendations. By monitoring their blood glucose levels, patients can obtain immediate and accurate feedback on the effect of food and exercise patterns on blood glucose control. This feedback may serve to reinforce efforts at changing their lifestyle in the long run.

In conclusion, this study is the first multicenter controlled prospective trial conducted on a large number of patients demonstrating that SMBG was statistically associated with better quality of metabolic control than usual recommendations alone in patients with type 2 diabetes.

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