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Assessment of glycemic control in nursing home patients with diabetes

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ABSTRACT:

OBJECTIVE

The objectives of this article were (1) to describe glycemic control in nursing home residents and (2) to evaluate the relevance of HbA1c in the detection of hypoglycemia risk which is considered as a major risk in this population.

DESIGN, SETTING, PARTICIPANTS

Clinical and biological data were recorded during a 4-month period in 2013-2014. 247 (14.5%) out of 1694 nursing home residents studied had diabetes. 236 residents were included in the study. Blood capillary glucose, HbA1c, geriatric assessment and diabetes treatment were recorded from medical charts.

MEASUREMENTS

Glucose control was divided into four categories: tight, fair, moderate or severe chronic hyperglycemia using the High Blood Glucose Index when enough capillary blood glucose were available or by frequency analysis of blood glucose in the other cases. Hypoglycemia episodes have been identified by medical or biological records.

RESULTS

Glucose control was tight in 59.3 % and fair in 19.1 % of the residents with mean HbA1c and blood glucose of 6.50 ± 0.77 and $7.74 \pm 1.03\%$, and 137 ± 24 and 173 ± 11 mg/dl, respectively. Chronic exposure to hyperglycemia was observed in 21.6 % of the residents, classified as severe in 9.7 % and moderate in 11.9 % with mean HbA1c and blood glucose values of 8.5 ± 1.0 and $8.1 \pm 1.3\%$ and 200 ± 21 and 230 ± 26 mg/dl, respectively. Hypoglycemia was noticed in 42/236 (17.8%), classified as severe (n = 8; 3.4 %) or mild (n = 34; 14.4 %). Hypoglycemia was associated with exposure to chronic hyperglycemia in 15/42 cases. HbA1c was lower than 6,5 % and 7,0 % in respectively 81,3 % and 75,0 % of the

residents with well-controlled diabetes without hypoglycemia. The relative risk of hypoglycemia was not different across various HbA1c values compared with the 7-7.9 % HbA1c interval. The relative risk of hypoglycemia was significantly ($P = 0.0095$) higher (2.78, 95% CI 1.44-5.36) for the patients with moderate chronic hyperglycemia compared to those with tight glucose control. The majority of residents with hypoglycemia episodes (38/42) or chronic hyperglycemia (44/51) were insulin-treated.

CONCLUSION

Our data show that glucose control was poor in 40% of the residents treated with insulin. They suggest that HbA1c is not the adequate marker for the detection of hypoglycemia risk. Therefore, blood glucose follow up should be recommended.

KEY WORDS: Diabetes mellitus; Hypoglycemia, Chronic hyperglycemia; Blood glucose in long term care home residents; HbA1c

INTRODUCTION

The prevalence of diabetes increases with aging and reaches 15-20 % in nursing homes for dependent elderly (1). Diabetes, which may be long-standing with onset in middle age or earlier or diagnosed after age 65 years (1), is usually not the first line pathology; however, it may be a significant burden in the management of these residents (2). Indeed, residents in these geriatric institutions tend to have high levels of physical and/or cognitive impairment, co-morbidities and polypharmacy, and their life expectancy is limited. The benefit of tight glucose control on microvascular and cardiovascular complications declines with rising co-morbidities and functional impairment (3). Besides, tight glucose control in older subjects with diabetes receiving oral anti-diabetic agents or insulin has been associated with a high risk of severe hypoglycemia because of a lack of awareness of warning symptoms

and a loss of coordinate response mainly related to cognitive impairment (4, 5). There is now a consensus to target HbA1c levels at a less stringent values in frail residents than in middle-aged adults and HbA1c levels up to 8.0-8.5 % (6-9) or 9 % (10, 11) are acceptable in order to avoid the risk of hypoglycemia. In care home residents, HbA1c at 7-8 % has been recommended by the Diabetes UK group (12).

Results of several evaluations in geriatric institutions suggest that a significant number of residents with diabetes are overtreated with HbA1c lower than 7 % with severe hypoglycemia events (13-16). Thus, most clinicians consider that the risk of hypoglycemia is higher among patients with low HbA1c levels. However, a detailed analysis of glucose control is not yet available in this population.

Hence, we carried out a retrospective study on diabetes control in residents of several public and private nursing homes in Marseilles (France) and surroundings in order (a) to describe glycemic control in nursing home residents and (b) to evaluate the relevance of HbA1c in the detection of hypoglycemia risk which is considered as a major risk in this population.

PATIENTS AND METHODS

Study population

The study was approved by the Ethical Committee of the Departmental Geriatrics Center. The study population consisted of patients with diabetes living in 3 public and 12 private nursing homes in Marseilles and surroundings.

Data collection

Age, sex, geriatric assessment (GA) and diabetes management were recorded from medical charts. GA includes functional and cognitive status, comorbidities and medications. Burden of comorbidities was recorded using the Charlson comorbidity index. Functional status was assessed by the 1-6 "Autonomie Gerontologie Groupe Iso Ressources" (AGGIR)

composite scale (17). This scale used in French geriatric setting estimates the ability of aged persons to perform cognitive and daily-life activities without the help of someone else. The residents were ranked in heavily (scores 1-2) or mildly (scores 3-4) functional dependent. Polypharmacy as well as specific treatment for diabetes and cardiovascular complications were noticed. Glomerular function rate were determined with the Cockcroft formula.

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A total of 24,682 capillary blood glucose have been collected during a 4 month period. Patients receiving 3-4 insulin injections/day were checked for blood glucose before each meal. For those receiving 1-2 insulin injections/day, blood glucose was measured at least before breakfast and dinner. Patients treated with oral antidiabetics agents (OAA) were usually tested twice a week before breakfast and dinner. In untreated subjects, fasting blood glucose was tested at least once a week. HbA1c was assayed at the end of the blood glucose measurement period.

The quality of glycemic control was assessed using high blood glucose index (HBGI, respectively) in patients with 2-4 capillary glucose measurements (18). In other patients, with fewer blood glucose determination, the frequency distribution of blood glucose was calculated using the following classes: ≤ 50 mg/dl; 51-70 mg/dl; 71-180 mg/dl; 181-250 mg/dl; 251- 350 mg/dl; > 350 mg/dl (19). A correlation between these different percentages and HBGI has been calculated from the group with high blood glucose measures frequency (not shown).

The levels of glycemic control were classified into four categories determined by the HBGI or equivalent during the 4-month period whatever the patients had hypoglycemia or not:

- tight glycemic control: this group was identified by an HBGI < 5 or more than 80 % of the blood glucose comprised between 71 and 180 mg/dl;

- fair glycemic control: defined by an HBGI between 6 and 9 or by 65-79 % of the blood glucose values between 71 and 180 mg/dl;
- moderate chronic hyperglycemia: defined by an HBGI between 10 and 15 or by 18-28 % of blood glucose higher than 250 mg/dl;
- severe chronic hyperglycemia: identified by a HBGI higher than 15 or by more than 28 % or 8% of glucose values higher than 250 mg/dl and 350 mg/dl, respectively.

Averaged blood glucose values were calculated for each resident and were used for statistical analysis.

The hypoglycemia episodes were divided into two categories on the basis of their effect on neuroendocrine activation (20, 21). Mild hypoglycemia was defined by typical symptoms of hypoglycemia such as sweating, tachycardia, tremuloriness, hunger and/or dizziness, relieved by feeding or by blood glucose levels between 70 mg/dl and 51 mg/dl (3.85 and 2.75 mmol/l, respectively) or by a low blood glucose index (LBGI) above 1.1. Severe hypoglycemia was defined by the loss of consciousness or other major changes in mental status that required the assistance of another person to correct hypoglycemia signs or by a blood glucose below 51 mg/dl (2.75 mmol/l). Both groups were combined for statistical analysis purposes.

Statistical analysis:

Results are given as mean $\pm$ standard deviation. The potential effect of diabetes medications and biological and clinical factors (kidney function, co-morbidities, polypharmacy...) were analyzed. Between groups comparisons were tested for statistical significance with the χ^2 test for categorical variables and with the Mann-Whitney U test for continuous variables as appropriate. Relative risk of hypoglycemia was calculated across HbA1c values and glucose control groups. Statistical significance was determined at $p < 0.05$. Statistical analysis was performed with the Graph Pad Prism 5 software (La Jolla, CA).

RESULTS:

Demographic characteristics of patients:

The prevalence of diabetes was 14.5% (247 patients with diabetes out of 1694 residents). HbA1c values were not available at the end of the 4-month period of blood glucose follow-up in 11 residents who were not included in the study. 236 residents were included in the study separated into 79 male (mean age: 78.53 ± 9.83 years) and 157 female (mean age: 84.87 ± 8.58 years, $P < 0.0001$). Diabetes was diagnosed prior to the admission in most cases and the duration of diabetes was not available.

Geriatric assessment (table 1):

The majority of residents with diabetes had high levels of co-morbidities, polypharmacy, dementia or impaired cognitive performance and reduced mobility . They had a high degree of dependency proven by the percentage of residents with an 1-2 AGGIR score (55.5%). 202 residents (85.6%) were exposed to polypharmacy. No resident was able to measure capillary glucose, to inject insulin or to take OAA on his own.

Diabetes treatment:

24.1 % of the residents were treated with a single daily long-acting insulin analog and 23.3 % with complex insulin treatment schemes 41.9% with OAA alone and 10,6 % did not receive any anti-diabetic treatment (table 2). Restrictive diabetic diet with limited access to sugar was prescribed to 60.8 % of patients; food texture was normal in 74.2 % , grounded in 14.6 % and blended in 10,4 %. Platelets antiagregants and statins were given to 46.6% and 30.7% of residents, 17.9% of them being treated by both medications.

Glycemic control:

A tight glycemic control was observed in 140 (59.3 %) residents with diabetes. The mean blood glucose was 137 ± 24 mg/dl. The glycemic control was fair and acceptable in 45 (19.1%) residents with a mean blood glucose of 173 ± 11 mg/dl. Exposure to moderate or severe chronic hyperglycemia was observed in 28 (11.9%) and 23 (9.7 %) of the residents, respectively (table 3). The mean glucose was 200 ± 21 and 230 ± 26 mg/dl, respectively.

In the majority of residents treated with OAA, glycemic control was tight (80/99; 80.8 %) or fair (13/99; 13.1%), while chronic hyperglycemia was observed in 6 residents. In more than half of the insulin-treated residents (67/112) glycemic control was tight or fair, 40/57 (70.2 %) and 27/55 (19.1 %) being treated with one daily injection of long-acting insulin or with complex insulin schemes, respectively (table 4).

HbA1c was significantly higher in residents with moderate or severe chronic hyperglycemia (8.24 ± 1.10 and 8.50 ± 1.03 %, respectively) than in residents with tight or fair glycemic control (6.50 ± 0.77 and 7.74 ± 1.03 %, respectively).

Hypoglycemia

Population characteristics were not significantly different between residents with or without hypoglycemia (Table 5). Hypoglycemia classified as mild or severe have been detected in 17.8 % of the residents. No case of major hypoglycemia that requires admission in emergency room or parenteral injection of 30 % glucose or glucagon was collected. The majority of the hypoglycemia was observed before breakfast (65.9%). Hypoglycemia events were noticed in 18 out of 140 (12.9 %) residents with tight glucose control, in 9 out of 45 (20.0 %) residents with fair glucose control, in 10 out of 28 (35.7 %) residents with moderate

chronic hyperglycemia, in 5 out of 23 (21.7 %) residents with severe chronic hypoglycemia and in 27 out of 185 (14.6 %) residents with tight or fair glucose control (table 6).

There was no significant association between hypoglycemia and low HbA1c values. Mean HbA1c tended to be higher in residents with hypoglycemia (table 6). The relative risk of hypoglycemia was not different across various HbA1c values compared with the 7-7.9 % HbA1c interval (table 7). Sensitivity and specificity of HbA1c were 33.3 % and 47.6 % and for a 6,5% cutoff and 47.6 % and 70.3 % for a 7.0 % cutoff, respectively . The relative risk of hypoglycemia was significantly ($P = 0.0095$) higher (2.78, 95% CI 1.44-5.36) for patients with moderate chronic hyperglycemia compared to those with tight glucose control (figure 1).

Patients who needed insulin treatment were difficult to manage. Management was even more difficult with complex insulin regimens than with basal insulin injection with a high percentage of chronic hyperglycemia and hypoglycemia episodes (table 4 and 6).

DISCUSSION

Our results show that diabetes of half residents is well-controlled with tight glucose control, low HbA1c and without hypoglycemia event or blood glucose at 70 mg/dl or less. There was no risk of hypoglycemia in 56/122 residents, 23 without treatment and 33 treated with metformin alone. The risk of hypoglycemia was low in 2 residents treated with gliptine. As expected, HbA1c was within the 7 % (90/122) and 8 % (120/122) targets in this group.

Guidelines for diabetes management in frail elderly have been established both on the fear of hypoglycemia and on the few benefit of good glycemetic control on vascular complications due to limited life expectancy. Relaxing glycemetic control and HbA1c up to 8, 8.5 or even 9 % are considered acceptable. Therefore, older patients with HbA1c lower than 6,5 or 7 % have been said overtreated with hypoglycemia episodes or risk (22). The

prevalence of hypoglycemia events in older varies according to the different definitions that have been used. Vajen et al. have reported a 21,2 % of residents with diabetes experienced hypoglycemia events, one fifth of them being considered severe with blood glucose lower than 50 mg/dl (23). In the study of Newton et al. the prevalence of hypoglycemia defined by a cutoff of 70 mg/dl was 42% (24). Andreassen et al have defined hypoglycemia as blood glucose lower than 4 mmol/l and hypoglycemia risk as glucose range between 4 and 6 mmol/l (73 and 109 mg/dl, respectively25). In other reports, the criteria are not defined (22). In our study, we have classified hypoglycemia into two categories based on clinical records and capillary glucose levels. The cutoff blood glucose levels were selected because they approximate levels at which symptoms appear along with neuroendocrine activation (70 mg/dl) and cognitive dysfunction with neuroglucopenia (50 mg/dl, 20, 21). Residents with only blood glucose below 70 mg/dl were included in the hypoglycemia group. LBGI in the hypoglycemia risk range was noticed in only 16/42. These residents with diabetes have several blood glucose values below 70 mg/dl unlike the others 26 that show very few low glucose. The majority of low blood glucose were observed at the regular periods of capillary blood sampling. In older with cognitive impairment, the prevalence of hypoglycemia may be underestimated due to the unawareness of warning symptoms (5, 26). Indeed, it has been shown that the number of glucose levels lower than 70 mg/dl were significantly higher when measured by continuous glucose monitoring rather than by 4 capillary glucose determinations (27). The prevalence of hypoglycemia in nursing home may be lower than in elderly living at home (medication intake and meals may not be secure inthe later, 28). Therefore, guidelines for glucose control in geriatric institution should be different from guidelines for dependant persons with diabetes living at home.

Hypoglycemia episodes have been found in all categories of glucose control: tight, fair, moderate and severe chronic hyperglycemia. The risk of hypoglycemia was significantly

higher in the residents with moderate chronic hyperglycemia. These residents show glucose variability likely due to difficulties in treatment adaptation and to irregular meals intakes. Hypoglycemia as well as chronic hyperglycemia were more frequent in residents treated with complex insulin protocols than in those under one daily long-acting insulin analog. Our results indicate that HbA1c is not the appropriate index for detection of hypoglycemia risk. Indeed, there was no association between the risk of hypoglycemia and HbA1c. HbA1c measure may not be adequate to insure safety and effectiveness of anti-diabetic treatment as previously reported (28, 29).

Patients with similar HbA1c and mean glucose values can have markedly different daily glucose excursions and rates of hypoglycemia and hyperglycemia episodes. The more relaxing objectives on diabetes management of frail elderly are based on the limited benefit of tight glucose control on cardiovascular complications which declines with rising co-morbidities and functional impairment (3, 30-32). However, they do not take into account the acute deleterious effects of chronic hyperglycemia on the central and peripheral nervous system including osmotic complications with increased urine volume and worsening incontinence. Lethargy or neuropathy aggravation may facilitate recurrent falls, skeletal muscle decline (33, 34). The influence of hyperglycemia on cognitive function and neurodegenerative diseases is suspected on several epidemiological studies (35, 36).

Chronic hyperglycemia as well as hypoglycemia episodes were more frequent in insulin-treated residents, especially in those under other insulin regimens. Diabetes management in the above-mentioned patients could be improved by a better control of meal intake and by staff education.

Studies on the influence of good and poor glucose control on functional capacities, infections sensitivity and quality of life are necessary for evidence-based guideline on blood glucose and HbA1c levels in this population. The high percentage of chronic hyperglycemia

in insulin-treated residents indicates that this treatment procedures should re-evaluated for alternative therapeutic modalities.

In conclusion, our data show that diabetes was well-controlled in half residents in nursing homes. Glycemic control was poor in 40% of insulin-treated residents. Our data suggest that HbA1c is not the adequate marker for the detection of hypoglycemia risk. Indeed, in 60 % of patients with hypoglycemia, there is evidence for intermittent chronic hyperglycemia. Therefore, blood glucose follow up should be recommended.

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C.O researched data, contributed to discussion and wrote the manuscript; M.G analysed the data and contributed to discussion; F.R initiated the study, contributed to discussion and edited the manuscript.

C.O, M.G, and F.R declare no conflict of interest.

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Table 1. Population characteristics in diabetic residents.

	n (%)
Age at survey, mean $\pm$ SD	82.75 $\pm$ 9.48
Female	157 (66.5)
Comorbidity	
Charlson comorbidity index, mean $\pm$ SD	3.69 $\pm$ 1.60
Renal insufficiency	17 (7.2)
Heart disease	100 (42.4)
Hypertension	147 (62.3)
Stroke	38 (16.1)
Functional status	
Heavy dependence	131 (55.5)
Mild dependence	85 (36.0)
Polypharmacy (more than four medications)	202 (85.6)

All data are presented as numbers (%) except when indicated otherwise

Table 2. Diabetes treatment in diabetic residents.

Diabetes treatment	n (%)
Insulin	112 (47.5)
Basal daily injection (BDI)	57 (24.1)
Other insulin regimens	55 (23.3)
Basal-Bolus	20
BDI + OAA	25
2-3 premixed	10
Oral antidiabetic agents	99 (41.9)
Metformin	38
Sulphonylurea	19
Glinide	8
Gliptine	2
Combination with metformin	28
Other OAA combinations	4
Nonpharmacological controlled	25 (10.6)

All data are presented as numbers (%) except when indicated otherwise. OAA: oral antidiabetic agents.

Table 3. Glycemic control in diabetic residents

Glycemic control	
Tight	140 (59.3)
Fair	45 (19.1)
Chronic hyperglycemia	
Moderate	28 (11.9)
Severe	23 (9.7)
HbA1c (%)	
Mean $\pm$ SD	7.13 $\pm$ 1.20
$\leq$ 6.5	78 (33.1)
6-6.7	41 (17.4)
7.1-8	70 (29.7)
8.1-9	32 (13.6)
$>$ 9	15 (6.4)

All data are presented as numbers (%) except when indicated otherwise.

Table 4. Antidiabetic treatment and glycemic control

Glucose control	Basal daily injection (n = 57)	n (%)		
		Other insulin regimens (n = 55)	OAA (n = 99)	Nonpharmacological controlled (n = 25)
Tight	20 (35.1)	17 (30.9)	80 (80.8)	23 (92.0)
Fair	20 (35.1)	10 (18.2)	13 (13.1)	2 (8.0)
Chronic hyperglycemia				
Moderate	7 (12.3)	16 (29.1)	5 (5.1)	0
Severe	10 (17.5)	12 (21.8)	1 (1.0)	0

All data are presented as numbers (%). OAA: oral antidiabetic agents.

Table 5. Population characteristics in residents with or without hypoglycemia

	n (%) ^a		
	Nonhypoglycemia (n = 194)	Hypoglycemia (n = 42)	<i>P</i> Value ^b
Age at survey, mean ± SD	82.55 ± 9.39	83.69 ± 9.95	0.354 ^c
Female	128 (66.0)	29 (69.0)	0.7024
Comorbidity			
Charlson index, mean ± SD	3.6 ± 1.6	4.07 ± 1.42	0.0701 ^c
Renal insufficiency	13 (6.7)	4 (9.5)	0.5212
Heart disease	84 (43.3)	16 (38.1)	0.5361
Hypertension	119 (61.3)	28 (66.7)	0.5184
Stroke	31 (16.0)	7 (16.7)	0.9125
Functional status			
Heavy dependence	112 (57.7)	19 (45.2)	0.2663
Mild dependence	68 (35.1)	17 (40.5)	0.5067
Polypharmacy (more than four medications)	167 (86.0)	35 (83.3)	0.6455

^aAll data are presented as numbers (%) except when indicated otherwise

^b*P* values for differences between nonhypoglycemia and hypoglycemia were calculated using the χ^2 test except when indicated otherwise

^c*P* value for differences between nonhypoglycemia and hypoglycemia was calculated using the Mann-Whitney U test.

Table 6. Diabetes, glucose control and HbA1c in residents with or without hypoglycemia.

	n (%) ^a		<i>P</i> value ^b
	Nonhypoglycemia (n = 194)	Hypoglycemia (n = 42)	
Diabetes treatment			
Basal daily injection	43 (22.2)	14 (33.3)	0.1252
Other insulin regimens	31 (16.0)	24 (57.1)	< 0.0001
OAA	95 (49.0)	4 (9.5)	< 0.0001
Nonpharmacological controlled	25 (12.9)	0	0.0139
Glucose control			
Tight	122 (62.9)	18 (42.9)	0.0166
Fair	36 (18.6)	9 (21.4)	0.6675
Chronic hyperglycemia			
Moderate	18 (9.3)	10 (23.8)	0.0152
Severe	18 (9.3)	5 (11.9)	0.6028
HbA1c (%)			
Mean ± SD	7.06 ± 1.14	7.46 ± 1.40	0.0931 ^c
≤ 6.5	66 (34.0)	12 (28.5)	0.4961
6.6-7	35 (18.0)	6 (14.3)	0.5603
7.1-8	58 (29.9)	12 (28.5)	0.8646
8.1-9	25 (12.9)	7 (16.7)	0.4209
> 9	10 (5.2)	5 (11.9)	0.104

^a All data are presented as numbers (%) except when indicated otherwise

^b *P* values for differences between nonhypoglycemia and hypoglycemia were calculated using the χ^2 test except when indicated otherwise

^c *P* value for differences between nonhypoglycemia and hypoglycemia was calculated using the Mann-Whitney U test

Table 7. RR of hypoglycemia in HbA1c categories (reference: HbA1c 7.1-8%)

HbA1c (%)	RR	95% CI	<i>P</i> value
≤ 6.5	0.8974	0.4315-1.867	0.8256
6.6-7	0.8537	0.3466-2.102	0.7956
7.1-8	1		
8.1-9	1.276	0.5546-2.936	0.591
> 9	1.944	0.805-4.697	0.1681

Figure 1. Relative risk of hypoglycemia in residents with diabetes (reference tight control). *P* values of relative risk of hypoglycemia in fair glucose control, moderate or severe chronic hyperglycemia were 0.235, 0.0095, and 0.328, respectively.