ORIGINAL ARTICLE

Association between hypoglycemia and the type of insulin in diabetic patients treated with multiple injections: an observational study

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KEY WORDS

diabetes, human insulin, hypoglycemia, insulin analogue

ABSTRACT

INTRODUCTION Hypoglycemia may have serious health consequences; therefore, it is important to expand knowledge on the factors that increase its prevalence.

OBJECTIVES The aim of the study was to evaluate the effect of the type of insulin—human vs. analogue—on the incidence of mild and severe hypoglycemia, body weight, and hemoglobin A_{1c} (HbA_{1c}) levels.

PATIENTS AND METHODS A total of 203 diabetic patients treated with intensive insulin therapy completed the questionnaire on hypoglycemia at baseline and at 3 and 6 months of the follow-up. Body weight and HbA_{1c} levels were measured at baseline and at 6 months. Incidence of mild and severe hypoglycemia, body weight, and HbA_{1c} levels were compared between patients treated with short-acting analogue and those treated with short-acting human insulin (regardless of the type of long-acting insulin used) and between patients receiving short- and long-acting analogue insulin and those receiving short- and long-acting human insulin. A multiple logistic regression analysis was used to find independent risk factors of severe hypoglycemia.

RESULTS At baseline, mild hypoglycemia was more common in patients receiving insulin analogue. There were no differences between the subgroups in the incidence of severe hypoglycemia, HbA_{1c} levels, and body weight. Male sex, older age, and the dose of long-acting insulin were independently associated with a higher incidence of severe hypoglycemia. Type 2 diabetes and higher body weight were associated with a lower risk of severe hypoglycemia.

CONCLUSIONS Our results suggest that use of insulin analogues may predispose to more frequent episodes of mild hypoglycemia, but it does not increase the incidence of severe hypoglycemia in patients on intensive insulin therapy. Insulin analogues are not different from human insulin in terms of the effects on HbA_{1c} levels and body mass.

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INTRODUCTION Strict glycemic control is crucial for reducing the risk of diabetic vascular complications. On the other hand, hypoglycemia remains the main limitation of diabetes treatment. For many years, this has been considered a major problem in type 1 diabetes and only a minor one in type 2 diabetes.[1] However, recent data has shown that, to a large extent, hypoglycemia affects also type 2 diabetic patients.[2] Moreover, with increasing use of insulin in type 2 diabetes, the prevalence of hypoglycemia is likely to escalate.

Iatrogenic hypoglycemia is the major factor precluding the maintenance of good glycemic control.[3] Many patients reporting hypoglycemic symptoms experience a reduced quality of life not only because of distressing acute symptoms, but also owing to concerns that these symptoms may recur. This anxiety often prevents them from taking insulin or oral hypoglycemic agents in appropriate doses. Some data suggest that the use of insulin analogues, both short- and long-acting, is associated with reduced risk of hypoglycemia compared with regular human insulin.[4,5]

TABLE 1 General characteristics of the patients at baseline

	All subjects, n = 203	Short-acting analogue insulin, n = 152	Short-acting human insulin, n = 51	Short- and long--acting analogue insulin, n = 80	Short- and long--acting human insulin, n = 44
age, y	46 ±15	44 ±14	51 ±15[a]	45 ±14	53 ±14[a]
men	79 (38.9)	59 (38.8)	20 (39.2)	23 (28.7)	19 (43.2)
type 1 diabetes	149 (73.4)	119 (78.3)	30 (58.8)[a]	63 (78.7)	23 (52.3)[a]
diabetes duration, y	17.7 ±11	17.4 ±11	18.6 ±9	18.7 ±11	18.7 ±8
body weight, kg	74 ±15	73.2 ±14	75.4 ±17	70.4 ±14	76.1 ±17
body mass index, kg/m^2	26 ±4.4	25.7 ±4.4	26.7 ±4.4	25.4 ±4.5	27 ±4.5[b]
short-acting insulin daily dose, U/24 h	37 ±15	36 ±15	42 ±16[b]	34 ±15	43 ±16[a]
long-acting insulin daily dose, U/24 h	19 ±8	18 ±7	20 ±9	17 ±6	21 ±9[b]
patients with glycemic threshold for hypoglycemic symptoms: ≤50 mg/dl	73 (36.7)	52 (35.1)	21 (41.2)	29 (36.7)	21 (47.7)

Data are presented as means ± standard deviation or number (percentage); Mann–Whitney or χ^2 test.
To convert mg/dl to mmol/l, multiply by 18.

a $P < 0.01$
b $P < 0.05$: use of short-acting analogue vs. human insulin or short- and long-acting analogue vs. human insulin

This observational study was conducted to evaluate the frequency of mild and severe hypoglycemia according to the type of insulin (short- and long-acting analogue vs. human insulin), and to evaluate the effect of insulin type on body weight and hemoglobin A_{1c} (HbA_{1c}) levels.

PATIENTS AND METHODS A total of 203 consecutive adult subjects were recruited from the Provincial Outpatient Clinic for Diabetes in Zabrze, Poland. The inclusion criteria were as follows: diabetes (of any type) treated with at least 4 insulin injections per day in a regimen established at least 2 months prior to the beginning of the study and at least 1 episode of hypoglycemia within the preceding 3 months. All subjects monitored their blood glucose levels 4 times daily according to the instructions provided on admission to the clinic. The exclusion criteria were as follows: use of any oral hypoglycemic agents, no history of hypoglycemia, use of an insulin pump (continuous subcutaneous insulin infusion), and pregnancy. The scheme of insulin therapy on enrollment to the study remained unchanged during the follow-up period. No changes in insulin preparations (only changes in the dose of insulin as needed) and no new hypoglycemic drugs were allowed during the study.

Outcome measures At baseline, all patients were asked to answer the following questions: Do you feel the symptoms of hypoglycemia: always—sometimes—never? How often have you had mild hypoglycemia (defined as blood sugar below 63 mg/dl) during the last 3 months: once—1–2 times—once a month—more than once a month—once a week—more than once a week? Below what blood sugar level do you feel hypoglycemia symptoms? How often have you had severe hypoglycemia (defined as loss of consciousness or need of glucagon subcutaneous or glucose intravenous administration) during the last year? When did your hypoglycemia usually occur: during the day—at night—both? Who usually diagnosed hypoglycemia: yourself—other person? What was the cause of hypoglycemia: exercise—diet—alcohol—I do not know—other reasons?

Patients' demographic and clinical data including age, type and duration of diabetes, height, body weight, and type of insulin preparations and their regular daily dosages were collected. At 3 and 6 months of the follow-up, subjects were asked to answer the above questions with reference to the preceding 3 months.

Body weight and HbA_{1c} levels were measured twice: at baseline and after 6 months; the former with the same digital scale, and the latter with the use of high performance liquid chromatography (Variant Biorad, California, United States).

The primary outcome measure was: 1) the incidence of mild and severe hypoglycemia, 2) body weight, and 3) HbA_{1c} levels, in patients treated with short-acting human or short-acting analogue insulin (regardless of the long-acting insulin used) and in those receiving both short- and long-acting human or analogue insulin.

Statistical analysis Means ± standard deviations were calculated for all variables. The Shapiro–Wilk normality test was used to evaluate the distribution of the data. Given the non-normal distribution of most variables, nonparametric tests were used. The analyzed parameters were compared between the studied patient groups with the Mann–Whitney test. To assess the intragroup differences between the baseline and 3- and 6-month time points, the Wilcoxon test was used. The χ^2, McNemar's, or sign test was applied in the case of categorical variables. A logistic regression analysis was conducted to identify potential determinants of severe hypoglycemia. A P value of less than 0.05 was considered statistically significant.

TABLE 2 Main clinical parameters of diabetes at baseline and at 6 months

		All subjects, n = 88	Short-acting analogue insulin, n = 63	Short-acting human insulin, n = 25	Short- and long--acting analogue insulin, n = 33	Short- and long-acting human insulin, n = 21
body weight, kg	baseline	74.0 ±16.4	71.6 ±14.7	78.5 ±19.6	70.4 ±14.0	79.1 ±19.4
	6 months	75.0 ±16.9[b]	72.8 ±15.1[b]	80.3 ±20.2	71.3 ±13.9[c]	80.3 ±19.5
	6 months minus baseline		1.17 ±2.81	1.78 ±4.57	0.98 ±2.23	1.20 ±4.30
hemoglobin A_{1c}, %	baseline	8.0 ±1.6	8.0 ±1.7	8.2 ±1.3	7.9 ±1.7	8.0 ±1.3
	6 months	7.9 ±1.4	7.9 ±1.5	7.9 ±1.1	7.9 ±1.7	7.9 ±1.2
short-acting insulin daily dose, U/24 h	baseline	38 ±15	36 ±14	44 ±17	36 ±15	45 ±17
	6 months	39 ±16	36 ±14	46 ±17[a]	34 ±15	46 ±16[a]
long-acting insulin daily dose, U/24 h	baseline	19 ±8	20 ±8	20 ±10	18 ±7	21 ±10
	6 months	20 ±8	19 ±8	20 ±9	17 ±7	21 ±9
patients with glycemic threshold for the diagnosis of hypoglycemia ≤50 mg/dl, %	baseline	27 (34.2)	22 (38.6)	5 (22.7)	12 (38.7)	5 (27.8)
	6 months	29 (36.7)	23 (40.4)	6 (27.3)	13 (41.9)	5 (27.8)

Data are presented as means ± standard deviation or number (percentage); Mann–Whitney, Wilcoxon, or χ^2 test.

a $P < 0.01$: use of short-acting analogue vs. human insulin or short- and long-acting analogue vs. human insulin

b $P < 0.01$

c $P < 0.05$: 6 months vs. baseline within the groups

RESULTS A total of 203 patients met the inclusion criteria, including 124 women and 79 men. Of the 203 patients, 178 presented at a follow-up visit at 3 months and 88 at 6 months. The other missed their control visits at 3 or 6 months and visited the clinic at other times. The baseline characteristics of the study participants are shown in TABLE 1. Patients treated with short-acting human (regular) insulin differed at baseline from those on analogue insulin in age and the total dose of short-acting insulin. Patients treated with both short- and long-acting human insulin were older and their doses of short- or long-acting insulin were higher compared with subjects on a short- and long-acting analogue (TABLE 1).

The mean HbA_{1c} level was comparable at baseline and after 6 months. We did not find any differences between the subgroups with regard to HbA_{1c} or body weight either at baseline or at the end of follow-up (TABLE 2). However, throughout the study, there was a slight increase in body weight in all subgroups, which was statistically significant in patients on analogue insulin. Still, the changes in body weight or HbA_{1c} did not differ significantly between the subgroups.

The incidence of mild hypoglycemia during the 3 months preceding the study period is shown in TABLE 3. At baseline, subjects on analogue insulin tended to experience mild blood glucose drops more often (TABLE 3), although this trend lost its statistical significance in the following 3 and 6 months (TABLE 3). Separate analyses for type 1 and type 2 diabetic patients did not reveal any significant differences (data not shown).

Regarding the question of whether patients felt the symptoms of hypoglycemia, 148 participants (72%) answered "I always feel", 48 patients (23%) "sometimes", and 7 patients (3.4%) "never". Of the patients feeling a drop in blood glucose level, 37% manifested symptoms when blood glucose was ≤50 mg/dl and 63% when blood glucose was >50 mg/dl. The mean hypoglycemic threshold was 59 mg/dl. As the main cause of hypoglycemia, 69 patients (34%) declared physical activity, 37 patients (18%) reported an error of estimation of premeal insulin dose, 49 patients (24%) claimed both, and 48 patients (12%) were unable to define the reason. Fifty-three percent (109 patients) experienced hypoglycemia mainly during the day, 12% (25 patients) at night, and in 34% (69 patients), hypoglycemia occurred irrespectively of the time of the day. Seven percent of the patients declared that they usually needed another person to diagnose hypoglycemia. These characteristics of hypoglycemia did not show any significant differences between the studied groups (data not shown).

Thirty-five patients (17%) experienced severe hypoglycemia at least once during the year preceding the study. We did not observe any differences between the subgroups in the frequency of severe hypoglycemia at any point of the follow--up (TABLE 4). Moreover, there were no statistically significant differences in the number of severe hypoglycemic episodes (TABLE 4). Likewise, the subgroups did not differ in the frequency or number of episodes of severe hypoglycemia when analyzed separately for type 1 or type 2 diabetic subjects (data not shown).

Using logistic regression, we found that male sex, older age, and the dose of long-acting insulin (irrespective of its type) were independently associated with the occurrence of severe hypoglycemia at baseline. On the other hand, type 2 diabetes (borderline significance) and higher body weight potentially decreased the risk of severe hypoglycemia (TABLE 5).

TABLE 3 Incidence of mild hypoglycemia in the study groups

Mild hypoglycemia[a]	Incidence	All subjects	Short-acting analogue insulin	Short-acting human insulin	Short- and long--acting analogue insulin	Short- and long--acting human insulin
baseline[b]	0/3 months	22 (10.8)	10 (6.6)	12 (23.5)	5 (6.3)	11 (25)
	1–2/3 months	50 (24.6)	41 (27)	9 (17.7)	24 (30)	9 (20.5)
	1/month	15 (7.4)	11 (7.2)	4 (7.8)	5 (6.3)	2 (4.6)
	>1/month	41 (20.2)	30 (19.7)	11 (21.6)	17 (21.2)	9 (20.4)
	1/week	32 (15.8)	25 (16.5)	7 (13.7)	10 (12.5)	7 (15.9)
	>1/week	43 (21.2)	35 (23)	8 (15.7)	19 (23.7)	6 (13.6)
	analogue vs. human		$P = 0.03$		$P = 0.06$	
mid-study[b]	0/3 months	25 (14)	15 (11.5)	10 (21.3)	8 (11.1)	9 (22.5)
	1–2/3 months	32 (18)	24 (18.3)	8 (17)	18 (25)	8 (20)
	1/month	18 (10.1)	11 (8.4)	7 (14.9)	9 (12.5)	5 (12.5)
	>1/month	43 (24.2)	33 (25.2)	10 (21.3)	13 (18.1)	9 (22.5)
	1/week	34 (19.1)	26 (19.9)	8 (17)	16 (22.2)	7 (17.5)
	>1/week	26 (14.6)	22 (16.8)	4 (8.5)	8 (11.1)	2 (5)
	analogue vs. human		$P = 0.32$		$P = 0.54$	
end-study[b]	0/3 months	12 (13.6)	9 (14.3)	3 (12)	6 (17.7)	3 (14.3)
	1–2/3 months	21 (23.9)	15 (23.8)	6 (24)	10 (29.4)	5 (23.8)
	1/month	9 (10.2)	6 (9.5)	3 (12)	4 (11.8)	3 (14.3)
	>1/month	18 (20.4)	10 (15.9)	8 (32)	4 (11.8)	6 (28.6)
	1/week	12 (13.6)	11 (17.5)	1 (4)	6 (17.7)	0
	>1/week	16 (18.2)	12 (19)	4 (16)	4 (11.8)	4 (19)
	analogue vs. human		$P = 0.46$		$P = 0.26$	

Data are presented as number (percentage).

a defined as blood glucose <63 mg/dl (3.5 mmol/l)
b at baseline: within the 3 months preceding the study; mid-study: within the first 3 months of the study; end-study: within the last 3 months of the study; χ^2 test

In the group of type 1 diabetic subjects, the logistic regression analysis showed the dose of long--acting insulin ($R^2 = 0.08$; $P = 0.005$) and older age ($R^2 = 0.04$; $P = 0.04$) to correlate independently with more frequent episodes of severe hypoglycemia. On the other hand, among type 2 diabetic patients, only higher body mass tended to be associated with the risk of severe hypoglycemia ($R^2 = -0.06$; $P = 0.08$).

DISCUSSION Our results suggest that the type of insulin preparation (regular or analogue) does not affect the incidence of severe hypoglycemic episodes in diabetic patients treated with multiple insulin injections, regardless of the diabetes type. On the other hand, we found that the occurrence of severe hypoglycemia is more likely with higher doses of long-acting insulin, regardless of the preparation type. Furthermore, the risk of severe hypoglycemia appears to increase with age and is higher in men. On the contrary, type 2 diabetic patients (vs. type 1) and subjects with higher body mass seem to be less prone to severe hypoglycemic episodes.

In type 1 diabetes, intensive insulin therapy is the treatment of choice. However, there is new data suggesting that adding metformin may be a good support regarding reduction of insulin resistance and better glycemic and lipid profile in type 1 obese patients.[6] Owing to total insulin dependence, this type of diabetes is associated with higher risk of hypoglycemia than type 2 diabetes. However, progression of β-cell failure in type 2 diabetic patients requires initiation of insulin therapy and then its intensification in the course of the disease. With time, owing to diminished counterregulation response, those patients tend to be more prone not only to mild but also severe hypoglycemia.[7]

The current guidelines for the treatment of diabetes stress the importance of tight glycemic control to avoid long-term complications.[8] Strict glycemic control is also crucial to reduce the risk of congenital abnormalities in pregnancy complicated by diabetes.[9] On the other hand, a strict approach to maintaining normal glycemia increases the risk of hypoglycemia, which can in fact be caused by virtually all exogenous insulin preparations. There have been reports that the use of short-acting insulin analogues (premeal) may be associated with a lower risk of nocturnal hypoglycemia as opposed to human (regular) preparations— it was supposed that their use may eliminate the relatively long hypoglycemic effect of the human insulin evening dose (premeal) during the first part of the night.[10] Likewise, reduction of

TABLE 4 Incidence of severe hypoglycemia in the study groups

Severe hypoglycemia[a]	Incidence	All subjects	Short-acting analogue insulin	Short-acting human insulin	Analogue vs. human	Short- and long-acting analogue insulin	Short- and long-acting human insulin	Analogue vs. human
baseline[b]	number of episodes	0.31 ±0.97	0.30 ±0.99	0.33 ±0.93	$P = 0.88$	0.22 ±0.59	0.36 ±0.99	$P = 0.95$
	patients with ≥1 episodes	35 (17.2)	27 (17.8)	8 (15.7)	$P = 0.73$	13 (16.3)	7 (15.9)	$P = 0.96$
mid-study[b]	number of episodes	0.19 ±0.57	0.17 ±0.50	0.24 ±0.74	$P = 0.96$	0.14 ±0.45	0.28 ±0.79	$P = 0.73$
	patients with ≥1 episodes	21 (11.8)	16 (12.1)	5 (10.9)	$P = 0.97$	7(9.6)	5 (12.8)	$P = 0.84$
end-study[b]	number of episodes	0.09 ±0.39	0.09 ±0.38	0.08 ±0.41	$P = 0.90$	0.12 ±0.41	0.1 ±0.45	$P = 0.83$
	patients with ≥1 episodes	5 (5.6)	4 (6)	1 (4.2)	$P = 0.86$	3 (7.9)	2 (3.9)	$P = 0.72$

Data are presented as mean ± standard deviation or number (percentage).

a defined as loss of consciousness or need of glucagon subcutaneous or glucose intravenous administration;
b at baseline: within the 3 months preceding the study; mid-study: within the first 3 months of the study; end-study: within the last 3 months of the study; χ^2 test

nocturnal hypoglycemia was confirmed for long-acting analogues with a flatter absorption profile in comparison with human bedtime insulin, either in type 1[4,11] or type 2 diabetic patients.[12] On the other hand, a Cochrane review of 49 randomized controlled studies showed no difference between short-acting insulin analogues and regular human insulin in the frequency of either mild or severe hypoglycemic episodes.[13]

The standard definition of severe hypoglycemia involves the need of other people's assistance to treat it.[14,15] This definition includes patients who can treat hypoglycemia unaided but receive unnecessary assistance of others. We used a more robust definition of severe hypoglycemia as an "injection of glucose or glucagon by another person". To assess the incidence of severe hypoglycemia, the number of patients with at least 1 such hypoglycemic episode per year was estimated—17% of the patients experienced severe hypoglycemia at least once a year. In total, there were 0.31 episodes per person per year, which is within the range observed in the Diabetes Control and Complications Trial (DCCT).[15]

As stated above, our results negate the role of insulin type in the incidence of severe hypoglycemia, which is in line with the results of the above Cochrane meta-analysis.[13] Proper education and high level of self-control are crucial factors to minimize the risk of hypoglycemia in diabetes.[16] The increased incidence of severe hypoglycemia with larger doses of long-acting insulin, especially among type 1 diabetic patients, suggests that an extensive whole-day insulin background is the key contributor to hypoglycemic episodes, and not the short-acting insulin shots. Total insulin-dependence in type 1 diabetes seems to explain why this factor predominates among these patients, contrary to type 2 diabetic patients with varied preservation of insulin release. This also imposes greater caution in establishing the regimens of night-time injections, and arguably speaks in favor of a more intensive day-time treatment, especially in type 1 diabetes.

The whole-group analysis, as well as that limited to type 1 diabetic patients, revealed older age of patients as another potential determinant of severe hypoglycemia. This is presumably due to the fact that less intense and atypical symptoms of hypoglycemia are associated with an increased age.[17] The stronger relationship between age and hypoglycemia in type 1 diabetes may be due to a larger age span of the affected patients, as compared with type 2 diabetic patients, and hence, more apparent manifestation of the association in the statistical analysis. Our observation is in line with some other studies,[18,19] but not all.[20]

There is evidence that, in type 2 diabetic patients, hypoglycemia-induced counterregulatory hormonal release occurs at higher blood glucose levels than in nondiabetic subjects[21,22] or patients with type 1 diabetes.[23] The trend to a lower risk of severe hypoglycemia with type 2 diabetes shown in our study can be explained by these phenomena. Furthermore, the analyses showed that higher body mass is somewhat protective against severe hypoglycemia, especially among type 2 diabetic patients. This finding might be explained by higher insulin resistance among more obese patients and type 2 diabetics as well as larger distribution volume of insulin in larger patients.

Male sex was another contributory factor to the increased risk of hypoglycemia in our study. Trials performed in type 1 diabetic patients have shown that women have lower counterregulatory responses to hypoglycemia than men and thus a higher risk of hypoglycemia.[24,25] However, no such data are available for type 2 diabetes. On the contrary, other researchers[26] have implied that antecedent hypoglycemia in women has a less

TABLE 5 Potential determinants of severe hypoglycemia in the study population (multiple logistic regression)

Adjusted $R^2 = 0.09$	Wald Z-value	Odds ratio	Wald probability level
daily dose of long-acting insulin	2.437	1.065	0.015
body weight	–2.300	0.959	0.021
male sex	2.564	3.459	0.010
type 2 diabetes	–1.873	0.323	0.061
age	2.310	1.042	0.021

blunting effect on counterregulatory response during a subsequent hypoglycemic episode than in men, which would corroborate our results.

The results suggest that the studied insulin types have similar effect on HbA_{1c} levels and body mass. Slight increases in body weight observed throughout the study period in all subgroups (but significant only in those on analogues) may be explained by weight gain during autumn and winter seasons owing to lack of exercise and diet rich in calories. The mean baseline HbA_{1c} level in our study was 8.25%, which is in line with reports regarding glycemic control from other countries.[27,28]

The study showed a higher incidence of mild hypoglycemic episodes at baseline with the use of analogue insulin preparations. This may result from a quicker action of the analogues than regular insulin; however, a higher percentage of type 1 diabetic patients in the fast-acting analogue group, who are prone to labile glycemia and have greater tendency to hypoglycemia, may underlie this observation. As stated above, the existing literature data do not confirm an increased risk of mild hypoglycemia with analogues.[13] The difference observed at baseline in our study lost its statistical significance during the study period, which might have been caused by a smaller number of subjects during follow-up visits and possibly more cautious glycemic control associated with participation in the study (trial effect). The latter would point to a reversibility of more frequent mild hypoglycemic episodes with better treatment compliance.

The study has several limitations. First, it should be acknowledged that the number of the studied subjects was relatively small and further decreased during the follow-up. Furthermore, the study group was heterogeneous in terms of age, sex, and type of diabetes, so any definite conclusions have to be drawn with caution. Finally, a period of 6 months is too short to assess the effect of therapy on body weight.

In conclusion, the risk of severe hypoglycemia is independent of the type of insulin preparation (analogue or human). The education of patients with emphasis on good self-control of diabetes, and better knowledge on long-acting insulin dosing, remains the main modifiable factor that may reduce the risk of hypoglycemia in patients treated with intensive insulin therapy.

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ARTYKUŁ ORYGINALNY

Występowanie hipoglikemii w zależności od rodzaju stosowanej insuliny u chorych na cukrzycę leczonych wielokrotnymi wstrzyknięciami – badanie obserwacyjne

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SŁOWA KLUCZOWE

analogi insuliny, cukrzyca, hipoglikemia, insulina ludzka

STRESZCZENIE

WPROWADZENIE Hipoglikemia może prowadzić do poważnych konsekwencji dla zdrowia, toteż ważne jest stałe poszerzanie wiedzy na temat czynników zwiększających ryzyko jej wystąpienia.

CELE Celem pracy była ocena wpływu stosowanej insuliny – ludzkiej lub analogowej – na częstość występowania łagodnej i ciężkiej hipoglikemii, masę ciała i wartość hemoglobiny A_{1c} (HbA_{1c}).

PACJENCI I METODY 203 chorych na cukrzycę leczonych intensywną insulinoterapią wypełniło kwestionariusz dotyczący hipoglikemii wyjściowo oraz po 3 i 6 miesiącach obserwacji. Masę ciała i wartość HbA_{1c} mierzono wyjściowo i po 6 miesiącach. Porównywano występowanie łagodnych i ciężkich hipoglikemii, masę ciała oraz wartość HbA_{1c} u chorych leczonych szybko działającymi analogami insuliny ludzkiej w porównaniu do chorych leczonych ludzką insuliną krótkodziałającą (niezależnie od rodzaju stosowanej insuliny o przedłużonym czasie działania) oraz u chorych leczonych tylko analogami insuliny ludzkiej (szybko i długo działającej) lub tylko insuliną ludzką (krótko i długo działającą). Zastosowano model wieloczynnikowej regresji logistycznej aby zidentyfikować niezależne czynniki ryzyka wystąpienia ciężkiej hipoglikemii.

WYNIKI Stwierdzono częstsze występowanie łagodnej hipoglikemii w grupie leczonej analogiem insuliny ludzkiej wyjściowo. Nie stwierdzono różnic między analizowanymi podgrupami w częstości występowania ciężkiej hipoglikemii, wartości HbA_{1c} i masie ciała. Płeć męska, starszy wiek oraz dawka stosowanej insuliny o przedłużonym czasie działania były niezależnie związane z częstszym występowaniem ciężkiej hipoglikemii. Cukrzyca typu 2 i zwiększona masa ciała wiązały się z mniejszym ryzykiem wystąpienia ciężkiej hipoglikemii.

WNIOSKI Nasze wyniki sugerują, że stosowanie insulin analogowych może predysponować do częstszych epizodów łagodnej hipoglikemii, przy czym nie zwiększa częstości ciężkiej hipoglikemii u pacjentów stosujących intensywną insulinoterapię. Analogi insuliny ludzkiej nie różnią się od insuliny ludzkiej odnośnie wpływu na wartość HbA_{1c} i masę ciała.

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