METABOLIC CONTROL AND BODY MASS INDEX IN PATIENTS WITH TYPE 1 DIABETES ON DIFFERENT INSULIN REGIMENS

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ABSTRACT

Introduction: Without sufficient insulin treatment, acceptable level of glycoregulation,
avoidance of dislipoproteinaemia and maintaince of body mass is difficult to achieve in patients with type 1 diabetes mellitus (DM). On the other hand sometimes it is difficult to prevent weight gain, endogenous hyperlipidemia and iatrogenic insulin resistance.

Aim: To compare metabolic control indicators in patients with type 1 DM in patients treated conventionally to those on intensified insulin regimen.

Material and methods: A sample of 52 persons with type 1 DM, without late complications and long duration of the disease, was selected. Among them 19 (36.5%) persons were treated with insulin in 4 or 5 doses, and 33 (63.5%) conventionally, in 2 doses. All the participants had biochemical indicators of metabolic control determined (glycosylated Hb , fasting and postprandial glycaemia, total cholesterol, triglycerides as well as lipoprotein fractions, HDLC and LDLC), body height (BH) and weight (BW) measured, body mass index calculated (BMI) and blood pressure measured (BP).

Results: In the group treated conventionally we found significantly higher mean values of BMI as compared to those on intensified insulin treatment (23.2 ± 2.0 kg/m^2, and 21.2 ± 1.2 kg/m^2 respectively, $p<0.01$) and proportion of those with overweight was as well significantly higher (27.3% versus 0%, $p = 0.012$). We noted higher mean values of systolic (134.2 ± 17.6 mmHg, versus 123.4 ± 12.7. $p<0.05$) and diastolic (83.2 ± 10.1, versus 74.0 ± 9.7, $p<0.01$) BP. Biohemical indicators of glycoregulation were significantly worse with, at the same time, higher total dose of applied insulin (55.9 ± 8.5 IU, versus 46.3 ± 10.0 IU, $p <0.01$), and insulin units per kg of body weight (0.84 ± 0.11 IU/kg versus 0.77 ± 0.15 IU/kg, $p<0.05$).

Conclusion: Results indicate that intensified insulin treatment is more favourable variant of treatment, by which the certain level of insulin resistance, which might be present in patients treated with two higher insulin doses, is probably reduced. Therefore it improves metabolic outputs, blood pressure values and body mass index but also may have beneficial impact to economic aspect of insulin treatment as well.

Key words: type 1 diabetes mellitus, insulin regimens, insulin resistance

INTRODUCTION

The management of type 1 diabetic patients remains continuous challenge to clinicians, particularly in regard to optimal insulin dosage which will adequately reduce hyperglycaemia, avoid hypoglycaemia, prevent lipolysis and maintain optimal muscle and adipose tissue mass and eventually prevent late complications of the disease(1, 2). Although subcutaneous application of insulin is per se non physiological because of the first by pass of the liver, for vast majority of patients, it remains the only available option for the time being (3). It can be delivered by so called intensified or conventional insulin regimen (4). The first one includes insulin administration 4 or 5 times daily, in the form of short- or rapid acting type before meals and intermediate or long-acting one at bedtime and if needed during the day. The other type of insulin regimen is standard or conventional one with two dosages of mixed insulin (short or rapid and intermediate acting) before breakfast and dinner. The insulin dosage in insulinopenic patients should be titrated cautiously and individually in order to prevent catabolic but as well hyperanabolic state, characterized by excessive weight gain, endogenous hyperlipidaemia and possibly iatrogenic insulin resistance (5, 6, 7).

The **main aim** of this cross-sectional study is to compare metabolic control and nutritional indicators in patients with type 1 diabetes mellitus treated conventionally to those on intensified insulin regimen.

MATERIAL AND METHODS

A sample of 52 persons with type 1 diabetes mellitus, with similar age and relatively short duration of the disease, who were treated on outpatient basis at the Department of Diabetes and Endocrinology of Clinical Centre University of Sarajevo, was selected. It did not include patients with other forms of autoimmune endocrine diseases, those with signs of diabetic or other forms of nephropathy and liver diseases. They did not have other kind of diabetic microvascular or macrovascular complications. All the participants were individual-

ly and carefully instructed about self management, with emphasis on dietary advices and physical exercise in the period prior to the beginning of the study. They did not experienced any acute deterioration of the disease, maior infection, surgery or severe stress in the period of at least 4 months.

The sample included 19 participants on intensified insulin treatment (IIT), with 4 or 5 insulin applications daily in the form of human, short-acting one before main meals and intermediate acting insulin at bedtime or in the morning . The other group consisted of 33 persons treated conventionally (CIT), by two dosages of mixed insulins (short and itermediate acting) before breakfast and dinner. There was not significant difference between the groups of participants in regard to the age and the duration of the disease (Table 1).

All the participants had biochemical indicators of metabolic control determined: glycosylated Hb (HbA1c), fasting glycaemia (FG), postprandial glycaemia (PG),total cholesterol (TCh), triglycerides (TGL), HDL-C and LDL-C. All analyses were carried out in the same venous blood samples collected from the fasting subjects except for the postprandial blood glucose values and HbA1c. The tests were carried out by Institute of Clinical Biochemistry, Clinical Centre University of Sarajevo.

Glucose levels were measured in venous blood samples using the automated glucose-oxidase reaction. Glycosylated Hb (HbA_1c) levels were measured using the BIO-RAD Micro Column Test. Total cholesterol as well as HDLC and LDLC and triglyceride levels were meaured enzymatically on an automated Abbot-Spectrum using Trace Cholesterol, HDLC , LDLC and Triglyceride commercial kits (PEG-6000 Method).

Nutritional status was assessed by measuring body weight (BW) and body height (BH) and calculating the body mass index (BMI) [/weight (kg)/height (m2)/] with a BMI of less than 18.5 indicating undernourishment and higher than 25 indicating being overweight. Individuals were weighed and measured using a Secca 770 digital scale and Secca 225 height statometer. All the participants have the blood pressure measured according to the country – wide integrated noncommunicable diseases intervention programme (CINDI) protocol (8) using a calibrated sphygmometer, Reister 600/306, Diplomat.

STATISTICAL ANALYSIS

The results were expressed as mean values with standard deviation or proportions expressed in percentages.The significance of the differences between the mean values among the groups was tested using the Student's unpaired t-test, while the difference between proportions was assessed using $\chi 2$ test. The differences were considered significant at the level of $p< 0.05$. Connection between variables was assessed by Pearson correlation coeficient with confidence limits of 95%.

RESULTS

We found significantly better indicators of glycoregulation and majority of lipid control indices in the intensivelly (IIT) treated group (Table 2 a). Although improvement in HDLC levels were noted this difference was not statistically significant.

Proportion of those who achieved more satisfactory glycaemic control was also significantly higher in the IIT group (Table 2 b), although the differences in lipid parameters were not significant.

Body weight, body mass index, systolic and diastolic blood pressure were significantly lower in the ITT group as well as proportion of overweight and hypertensive patient (Table 3 a, Table 3 b). There were no undernourished patients in both groups.

We noted significant negative correlation between the number of insulin injections with postprandial glycaemic levels (r= - 0.50), body mass index (r = -0.49) and glycosylated Hb (r = -0.44) (Table 4). The higher the number of insulin injections the lower lipid parameters were noted as well (Table 5). Negative correlation was found between the number of insulin injections and total IU, DBP, SBP and IU/kg (Table 6).

DISCUSSION

Although majority of previous studies indicated superiority of intensive insulin regimens in regard to prevention and delay of late microvascular complications (9, 10, 11) there has not been strong evidence that equal glycaemic control is significanlty less likely to be achieved with 2

Table 1. Characteristics of participants by the type of insulin regimen

	n	Age (y)	Males n (%)	Females n (%)	Duration (y)
IIT[1]	19	27.5 ± 7.6	8 (42.1%)	11 (57.9%)	5.1 ± 2.4
CIT[2]	33	31.8 ±10.2	15 (45.5%)	18 (54.5%)	5.5 ± 3.4
Student's *t* - test		1.714 p>0.05			0.250 p>0.05
$\chi 2$ test			3.13 p =0.077	3.38 p=0.067	

1 - intensified insulin treatment
2 - conventional insulin treatment

Table 2. Parameters of glyco- and liporegulation by the type of insulin regimen

a) mean values

	HbA_1c[3] (%)	FG[4] (mmol/l)	PG[5] (mmol/l)	TCh[6] (mmol/l)	LDLC[7] (mmol/l)	HDLC[8] (mmol/l)	TGL[9] (mmol/l)
IIT[1]	6.9 ± 0.8	7.1 ± 1.4	10.1 ± 2.1	4.9 ± 0.4	2.9 ± 0.5	1.20 ± 0.27	1.65 ± 0.79
CIT[2]	7.9 ± 1.2	8.3 ± 1.1	12.2 ± 1.7	5.4 ± 0.9	3.4 ± 0.9	1.09 ± 0.25	2.12 ± 0.71
***t*-test**	3.257	3.152	3.954	2.564	2.590	1.430	2.227
p-value	p<0.01	p<0.01	p<0 01	p<0.05	p<0.05	p>0.05	P<0.05

[1] - intensified insulin treatment
[2] - conventional insulin treatment
[3] - glycosylated haemoglobin
[4] - fasting glycaemia
[5] - postprandial glycaemia
[6] - total cholesterol
[7] - low density lipoprotein cholesterol
[8] - high density lipoprotein cholesterol
[9] - triglycerides

b) proportions

	HbA_1c[3] ≤ 7.0 n (%)	FG[4] ≤ 7.0 n (%)	PG[5] ≤ 10.0 n (%)	TCh[6] ≤ 4.8 n (%)	LDLC[7] ≤ 3.0 n (%)	HDLC[8] ≥ 1.0 n (%)	TGL[9] ≤ 1.7 n (%)
IIT[1]	14 (73.7)	12 (63.2)	12 (63.2)	9 (47.4)	12 (63.2)	16 (84.2)	9 (47.4)
CIT[2]	6 (18.2)	5 (15.2)	2 (6.1)	10 (30.3)	14 (42.2)	24 (72.7)	8 (24.2)
χ^2-test	15.7	12.6	19.9	1.51	2.07	0.9	2.93
p-value	p<0.001	p<0.001	p<0.001	p=0.218	p=0.149	p=0.343	P=0.087

[1] - intensified insulin treatment
[2] - conventional insulin treatment
[3] - glycosylated haemoglobin
[4] - fasting glycaemia
[5] - postprandial glycaemia
[6] - total cholesterol
[7] - low density lipoprotein cholesterol
[8] - high density lipoprotein cholesterol
[9] - triglycerides

dosages of appropriate mixtures of short and intermediate acting human insulins (12, 13). In addition , majority of above mentioned studies noted significant weight gain and hypoglycaemic episodes with intensified insulin regimes. In that regard, the question of developing the syndrome of insuline resistance as seen as an underlying disorder in type 2 diabetes related to overweight has been raising a lot of concern recently (14, 15, 16).

Our results indicates that majority of metabolic indicators were improved with intensified insulin regimen. At the same time the total number of applied daily insulin units and moreover insulin units per kg of body weight, were significantly less in this group. This indicates improved insulin sensitivity with IIT, so that the smaller amounts of exogenous insulin was sufficient to achieve satisfactory glyco and lyporegulation (Table 2 a, Table 3 a). The finding of higher proportion of hypertensive patients can also be attributed to higher level of insulin resistance in CIT group (Table 3 b).

It is very likely that 2 higher daily insulin dosages promote to some extent weight gain and compromise patients' adherense to dietary recommendations.

In addition to achieving more favourable metabolic outputs, it is interesting that the cost of insulin treatment was decreased, as we noted 16.3% of reduction of total daily insulin requirements from 56 to 47 IU (Table 3 a) and 9.4% in regard to IU/kg (0.85 to 0.77IU/kg). Although investments in self-monitoring can initally increase the costs of IIT, as was shown in DCCT (10, 18, 19), in future we can expect lower rate of micro and macrovascular complications which would contribute to the lower cost in long term period (17, 20).

Although overall metabolic control was closer to optimal in IIT group, it could be even better, which would possibly be achieved with currently available rapid and long acting insulin analogues with superior pharmacokinetic properties (21).

Table 3. Nutritional status indicators, blood pressure values, and insulin units by the type of insulin regimen

a) mean values

	BW[3] (kg)	BMI[4] (kg/m^2)	SBP[5] (mmHg)	DBP[6] (mmHg)	IU[7]	IU/kg[8]
IIT[1]	60.7 ± 7.4	21.2 ± 1.2	123 ± 13	74 ± 10	46.8 ± 10.3	0.77 ± 0.16
CIT[2]	67.7 ± 9.8	23.2 ± 2.0	134 ± 18	83 ± 10	55.9 ± 8.5	0.85 ± 0.11
t-test	2.707	4.000	2.352	3.255	3.473	2.162
p-value	p<0.01	p<0.01	p<0.05	p<0.01	p<0.01	p<0.05

[1] - intensified insulin treatment
[2] - conventional insulin treatment
[3] - body weight
[4] - body mass index
[5] - systolic blood pressure
[6] - diastolic blod pressure
[7] - total daily insulin units
[8] - insulin units per kg of body weight

b) proportions

	BMI[3] >25.0 kg/m^2 n (%)	BMI <18.5 kg/m^2 n (%)	SBP[4] >140 mmHg n (%)	DBP[5] >90 mmHg n (%)
IIT[1]	0 (%)	0 (0)	2 (10.5)	0 (0)
CIT[2]	9 (27.3)	0 (0)	15 (45.4)	11 (33.3)
χ^2-test	6.25		6.69	8.03
p value	0.012		0.009	0.004

[1] - intensified insulin treatment
[2] - conventional insulin treatment
[3] - body mass index
[4] - systolic blood pressure
[5] - diastolic blod pressure

CONCLUSION

Intensified insulin regimen in type 1 diabetic patients is more favourable variant of treatment by which the certain level of insulin resistance, which might be present in patients treated with two higher daily dosages, is probably reduced. Therefore it improves metabolic outputs, body mass index and blood pressure values and in longer terms may have beneficial impact to development of late complications as well as to economic aspects of insulin treatment.

Table 4. Correlation coefficients (with 95% confidence limit) between the number of insulin applications (NIA) and glycaemic parameters and body mass index (BMI)

	FG[1]	HbA_1c[2]	PG[3]	BMI
NIA	**r = - 0.37**	**r = - 0.44**	**r = - 0.50**	**r = - 0.49**
	(-0.37< r^2 <0.63)	(-0.29< r^2 <0.66)	(-0.14< r^2 <0.70)	(-0.19< r^2 <0.60)

[1] - fasting glycaemia
[2] - glycosylated Hb
[3] - postprandial glycaemia

Table 5. Correlation coefficients (with 95% confidence limit) between the number of insulin applications (NIA) and main lipid parameters

	LDLC[1]	TCh[2]	TGL[3]	HDLC[4]
NIA	**r = - 0.34**	**r = - 0.32**	**r = - 0.24**	**r = + 0.20**
	(-0.37< r^2 <0.63)	(-0.42< r^2 <0.60)	(-0.47< r^2 <0.57)	(-0.24< r^2 <0.31)

[1] - low density lipoprotein cholesterol
[2] - total cholesterol
[3] - triglycerides
[4] - high density lipoprotein cholesterol

Table 6. Correlation coefficients (with 95% confidence limits) between the number of insulin applications (NIA) and blood pressure values and insulin requirements

	SBP[1]	DBP[2]	IU[3]	IU/kg[4]
NIA	**r = - 0.32**	**r = - 0.42**	**r = - 0.44**	**r = - 0.22**
	(-0.42< r^2 <0.60)	(-0.32< r^2 <0.65)	(-0.29< r^2 <0.66)	(-0.48 < r^2 <0.56)

[1] - low density lipoprotein cholesterol
[2] - total cholesterol
[3] - total daily insulin units
[4] - insulin units per kg of body weight

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