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A CONTINUOUS GLUCOSE MONITORING SYSTEM (CGMS) – A PROMISING APPROACH FOR IMPROVING METABOLIC CONTROL IN PERSONS WITH TYPE 1 DIABETES MELLITUS TREATED BY INSULIN PUMPS

Petr Mlčák[a], Jana Fialová[a], Kateřina Trnková[a], Rudolf Chlup[a, b*]

[a] *Institute of Physiology, Faculty of Medicine, Palacký University, 775 15 Olomouc, Czech Republic*
[b] *II[nd] Department of Medicine, Teaching Hospital & Faculty of Medicine, Palacký University, I. P. Pavlova 6, 775 00 Olomouc, e-mail: rudolf.chlup@fnol.cz*

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This pilot study deals with the possibilities of a Continuous Glucose Monitoring System (CGMS, Minimed-Medtronic) to optimize insulin substitution. Ten persons with type 1 diabetes mellitus treated by means of an insulin pump entered the study and eight of them completed the protocol. CGMS was introduced for a period of 5 days. The standard dinner (60 g of carbohydrates) and overnight fasting were designed to ensure standard night conditions in all persons in the study while maintaining their usual daily eating routine, physical exercise and assessment of prandial insulin boluses. The only adaptation of basal rates of insulin pump was performed on day 3. Comparison of the mean plasma glucose concentration (0:00–24:00 hrs) between day 2 (before adaptation) and day 4 (following adaptation) was made. An independent comparison of the mean plasma glucose concentration between the night from day 2 till day 3 (22:00–6:00 hrs) and the night from day 4 till day 5 (22:00–6:00 hrs) was performed. The mean plasma glucose investigated by means of CGMS improved in the 24-hour period in 5 out of 8 persons and in the night fasting period (22:00 to 6 hrs) in 6 out of 8 persons. The CGMS is a useful means for assessment of the effectiveness of basal rate and prandial insulin doses in persons with type 1 diabetes treated by means of an insulin pump. However, further studies are necessary to improve the algorithm for insulin substitution.

INTRODUCTION

Continuous subcutaneous insulin infusion (CSII) by means of an insulin pump is a sophisticated method for insulin substitution in persons with type 1 diabetes mellitus. Adequate basal rates (BR) and prandial boluses (PB) of the insulin pump are the main assumptions for successful treatment. Routinely, both BR and PB have been applied according to the results of frequent self-monitoring of plasma glucose (SMPG) performed by means of a glucose meter (5–10 measurements per day). The Continuous Glucose Monitoring System (CGMS), registering 288 glucose concentrations per 24 hrs, seems to offer new ways for reaching optimum diabetes control[1–9, 11, 13, 15].

AIM

The aim of the present pilot study was to assess whether in persons with type 1 diabetes mellitus treated by means of an insulin pump, the CGMS would enable appropriate adaptation of the BR and/or PB in order to decrease mean plasma glucose (MPG) in the course of 24-hour period and/or in basal (fasting) conditions in the night period.

MATERIALS AND METHODS

The study was designed and performed from January to April 2003.

Ten persons with type 1 diabetes mellitus (see Table 1) gave their informed consent according to the Declaration of Helsinki and entered the study.

Investigation of glucose concentrations

Glucose concentrations were investigated in interstitial fluid (ISF-glucose) by means of the CGMS (Minimed-Medtronic) and in plasma (P-glucose) by means of a personal glucose meter Optium (Medisense-Abbot). The subcutaneously inserted sensor of the CGMS measured the electrical current that is related to interstitial glucose concentration. The assay method is based on electrochemical detection of glucose through its reaction with glucose oxidase. There is a good correlation between P-glucose (PG) and ISF-glucose[14]. Two CGMS monitors were used in the whole group. Each person was investigated by this means. The CGMS was calibrated every day according to PG values obtained from the glucose meter. Each person performed SMPG at least five times a day. In this study, the ISF-glucose (CGMS) correlated well with P-glucose (Optium) for the whole five-day period of investigation, i. e. not only for 3 days as stated in the literature[10].

Table 1. Characteristics of 10 persons with type 1 diabetes mellitus (sBP – systolic blood pressure, dBP – diastolic blood pressure).

Person No.	Sex m/f	Age [years]	Height [cm]	Weight [kg]	BMI [kg/m^2]	sBP [mmHg]	dBP [mmHg]	DM [years]	CSII [years]	Insulin pump	HbA_{1C} * [%]
1	m	31	180	60	19	100	75	6	4	MiniMed 507c	7.2
2	m	59	163	55	21	115	65	38	5	MiniMed 508	7.2
3	f	44	164	60	22	120	85	23	4	MiniMed 507c	6.5
4	m	27	176	79	26	150	100	14	4	MiniMed 507c	6.0
5	f	37	178	96	30	125	90	4	4	MiniMed 507c	8.9
6	f	39	164	69	26	110	70	13	3	MiniMed 507c	5.8
7	m	31	177	69	22	125	80	21	0.5	MiniMed 508	5.3
8	f	61	175	73	24	150	75	9	1	MiniMed 507c	5.6
9	f	30	176	65	21	120	70	16	10	H-TRONplus	5.6
10	f	22	176	64	21	120	90	7	0.5	MiniMed 508	8.7
mean	–	38	173	69	23	124	80	15	3.6	–	6.7
SD	–	12	6.2	11	3.2	15	10	9.7	2.6	–	1.2

* Values of HbA_{1c} are expressed according to the IFCC scale (normal range 2.8–4.0 %).
Converssion of HbA_{1c} values: NGSP = (0.915 * IFCC) + 2.15 [%]

Study design

The study design is shown in Fig. 1.

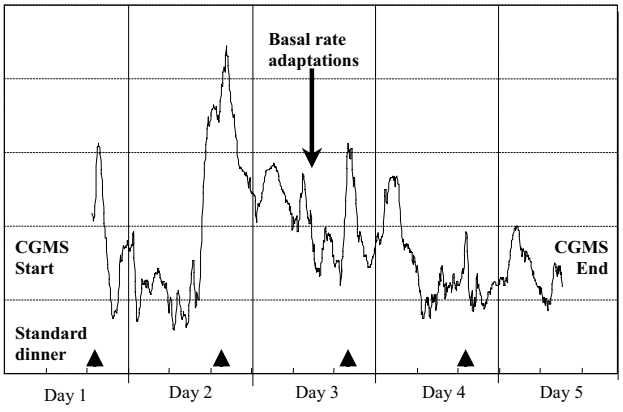

Fig. 1. Study design

Day 1:

a) Education of the tested person: on how to use the CGMS, how to keep to the study protocol (daily calibration of the sensor, alarms, frequency of SMPG at least five times a day, standard meals containing 60 g of carbohydrates between 18:00 and 19:00 hrs followed by overnight fasting up to breakfast between 8:00 and 9:00 hrs, usual meals and muscular exercise during the day, registration of prandial boluses, hypoglycaemias, combatting hypoglycaemia by means of 250 ml of juice, and others) and how to record the important events in a diary and/or monitor[12].
b) Checking the function of the monitor and connecting cable.
c) Insertion of the sensor into the subcutaneous tissue of the abdomen about 5 cm from the umbilicus and at least 10 cm from the insertion of the insulin pump (Fig. 2).
d) Sensor initialization.
e) Following the successful initialization the tested person used the CGMS at home while maintaining his/her normal daily routine.

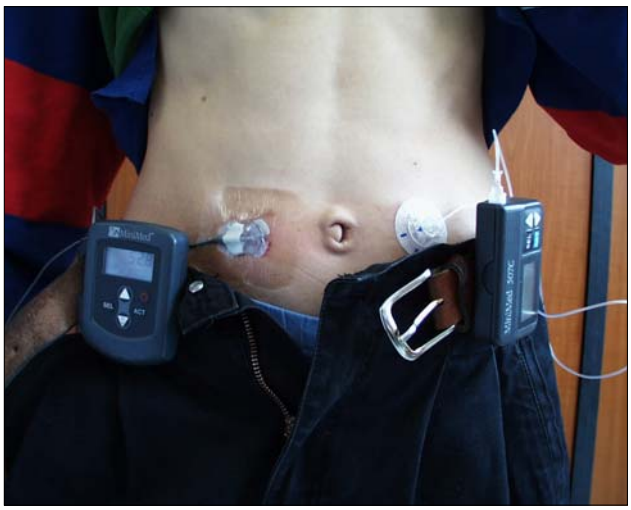

Fig. 2. Continuous Glucose Monitoring System (Minimed-Medtronic): monitor, connecting cable, and sensor inserted into the subcutaneous tissue (right handside from the umbilicus) together with an insulin pump Minimed 507c with infusion set inserted into the subcutaneous tisue (left handside from the umbilicus)

Table 2. Insulin doses (BR, PB), MPG (288 values/d) and carbohydrates in meals before (day 2) and after (day 4) adaptation of BR and PB. Persons 4 and 7 were excluded from calculations of means (stars). Decrease of values is marked (grey field) in evaluated persons only.

Person No.	BR [IU/d]		PB [IU/d]		BR + PB [IU/d]		MPG [mmol/l]		carbohydrates p.o. [g/d]	
	day 2	day 4	day 2	day 4	day 2	day 4	day 2	day 4	day 2	day 4
1	18.8	19.1	11.0	11.0	29.8	30.1	6.6	**4.6**	185	200
2	34.5	**33.7**	14.5	**14.0**	49.0	**47.7**	8.0	**6.7**	167	**142**
3	14.9	15.2	19.5	21.2	34.4	36.4	7.1	**6.2**	235	270
* 4 *	* 20.0 *	* 20.6 *	* 28.0 *	* 16.0 *	* 48.0 *	* 36.6 *	* 9.6 *	* 4.8 *	* 261 *	* 220 *
5	12.9	16.8	24.5	**18.0**	37.4	**34.8**	10.3	11.8	180	**170**
6	18.9	19.5	12.9	**9.0**	31.8	**28.5**	9.5	10.8	153	200
* 7 *	* 18.1 *	* 17.7 *	* 12.0 *	* 13.5 *	* 30.1 *	* 31.2 *	* 5.7 *	* 6.0 *	* 219 *	* 246 *
8	17.0	**16.7**	11.5	**10.5**	28.5	**26.7**	5.3	7.3	218	220
9	18.2	**17.7**	14.0	**13.0**	32.2	**30.7**	5.6	**4.8**	186	250
10	18.6	18.9	15.0	15.0	33.6	33.9	9.8	**7.3**	195	230
mean	19.2	19.7	15.4	**14.0**	34.6	**33.6**	7.8	**7.4**	190	210
SD	6.1	5.5	4.2	**3.8**	6.0	6.1	1.8	2.4	25	39

Table 3. Insulin doses (BR, PB), MPG (96 values/d) and carbohydrates in meals before (the night from day 2 till day 3) and after (the night from day 4 till day 5) adaptation of BR and PB. Persons 4 and 5 were excluded from calculations of means (stars). Decrease of values is marked (grey field) in evaluated persons only.

Person No.	BR [IU/d]		PB [IU/d]		BR + PB [IU/d]		MPG [mmol/l]		carbohydrates p.o. [g/d]	
	night 2/3	night 4/5	night 2/3	night 4/5	night 2/3	night 4/5	night 2/3	night 4/5	night 2/3	night 4/5
1	6.0	6.3	0.0	0.0	6.0	6.3	6.1	**5.0**	0	0
2	6.5	6.5	0.0	0.0	6.5	6.5	10.2	**8.5**	0	0
3	5.0	5.6	0.0	0.0	5.0	5.6	9.3	**9.1**	0	0
* 4 *	* 6.8 *	* 6.8 *	* 0.0 *	* 0.0 *	* 6.8 *	* 6.8 *	*4.7 *	* 2.5 *	* 30 *	* 25 *
* 5 *	* 4.8 *	* 5.6 *	* 0.0 *	* 1.0 *	* 4.8 *	* 6.6 *	* 8.9 *	* 8.9 *	* 0 *	* 0 *
6	5.7	5.8	0.0	0.0	5.7	5.8	16.1	**14.6**	0	0
7	4.8	4.8	0.0	0.0	4.8	4.8	3.9	10.1	0	0
8	4.8	4.8	0.0	0.0	4.8	4.8	8.8	**6.9**	13	**0**
9	5.3	**5.2**	0.0	0.0	5.3	**5.2**	7.4	7.6	0	0
10	5.6	5.8	0.0	0.0	5.6	5.8	13.2	**7.1**	0	0
mean	5.5	5.6	0.0	0.0	5.5	5.6	9.4	**8.6**	1.6	**0**
SD	0.57	0.59	0.0	0.0	0.57	0.59	3.6	**2.7**	4.3	**0**

Day 3:

a) In about 48 hours after the sensor insertion the data were transferred from the monitor and from the insulin pump (Minimed only) into the computer (Figures 3–7).
b) According to the evaluation of the whole protocol (including glucose concentrations, BR, PB of the insulin pump and amount of ingested carbohydrates), the basal rates were modified (mostly in the range ± 0.1 IU/h, only if the PG concentration exceeded the target limits, i.e. fPG 4.0–6.0 mmol/l and/or prae- and postprandial PG 6.0–10.0 mmol/l) and/or adaptations of prandial boluses were recommended.

Fig. 3. Data transfer from the insulin pump Minimed 508 to the PC by means of Comstation and Minimed Solution Software

Fig. 4. CGMS Monitor and Comstation

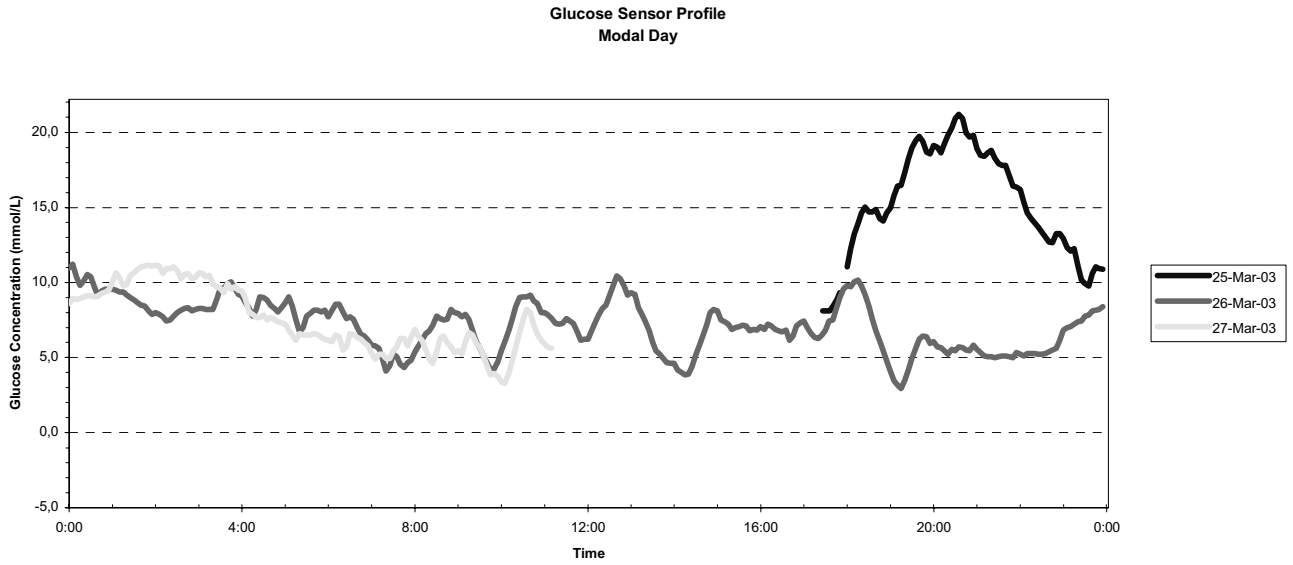

Fig. 5. Data downloaded from the CGMS-monitor into the PC and printed: Modal day – each day is drawn in different colour

c) Subsequently, the tested person continued in this adapted routine at home.

Day 5:

a) In about 96 hours after the sensor insertion the second (final) transfer of data from the CGMS monitor and from the insulin pump into the computer was performed. The correlation coefficient of the sensors and meter values never decreased below 90 %.
b) This second evaluation resulted in final individual recommendations for BR and/or PB (to be evaluated in the near future).
c) The sensor was removed.

Evaluation of the results

Comparisons of the obtained data (MPG, BR, PB and amount of carbohydrates in meals) were performed for the following periods of time:

1) Day 2 (00:00–24:00 hrs) versus day 4 (00:00–24:00 hrs).
2) The night from day 2 till day 3 (22:00–6:00 hrs) versus the night from day 4 till day 5 (22:00–6:00 hrs).

RESULTS

An overview of investigated parameters is shown in Table 2 and Table 3.

Adaptations of insulin pump basal rates and prandial boluses based on two-day period of evaluation by means of the CGMS resulted in a decrease of MPG:

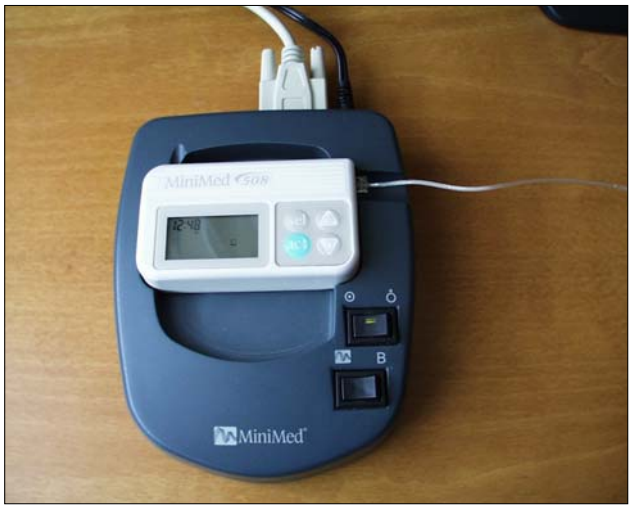

Fig. 6. Insulin pump Minimed 508 and Comstation ready to data transfer to the PC

1) when evaluating the 24-hour period in 5 out of 8 persons,
2) when evaluating the fasting night period (22:00 to 6:00 hrs) in 6 out of 8 persons.

An increase of MPG was found:

1) In 3 out of 8 persons during the assessment of the 24-hour period. This was probably related to the increased amount of ingested carbohydrates and/or to contraregulation after hypoglycaemia which occurred even though insulin doses had been decreased.
2) In 2 out of 8 persons during the assessment of the night fasting period while continuing the intake of the same insulin doses.

Excluded persons:

1) During the assessment of the 24-hour period persons 4 and 7 were excluded due to transient disconnection of the cable on day 4.
2) During the assessment of the night fasting person 4 was excluded due to prolonged hypoglycaemia. Person 5 was excluded due to disconnection of the cable on day 5.

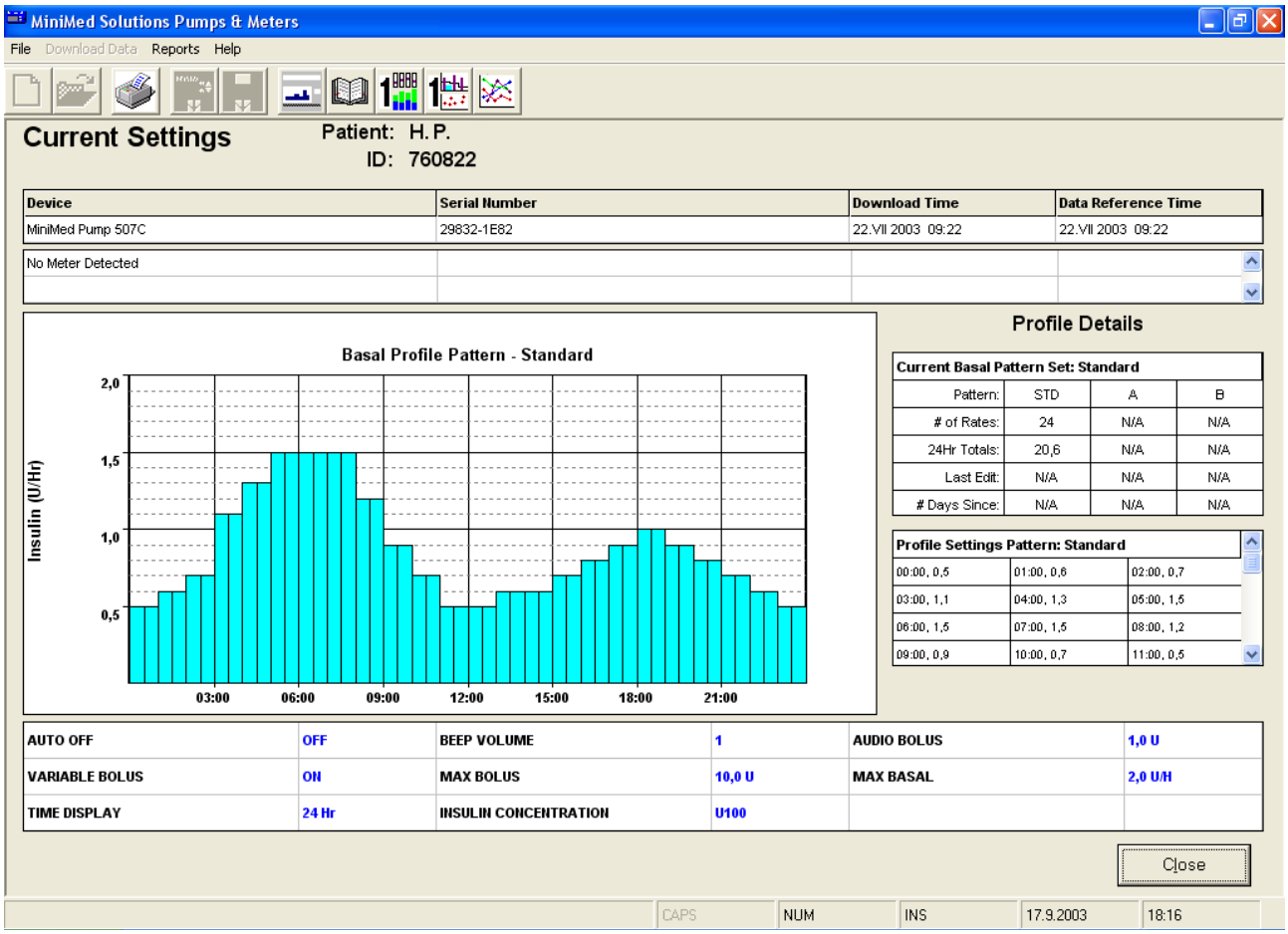

Fig. 7. Current settings of basal rates – data were downloaded from an insulin pump Minimed 508 into the PC by means of Minimed Solution Software and printed

DISCUSSION

In the course of the last thirty years continuous attempts have been made to develop an external closed-loop system to enable adequate substitution of insulin in persons with type 1 diabetes mellitus. There are few problems with insulin pumps and, on the other hand, quality and lifetime of the glucose sensor and appropriate algorithm for insulin administration are the limiting factors. For this reason, we have tried to use the present devices (CGMS and insulin pumps), PC with respective software and our own experience as a "fair means" to improve diabetes control.

The limited number of patients does not allow us to do a statistical analysis. However, the presented case reports yield important information for further studies.

CONCLUSIONS

The CGMS is a useful means for assessment of effectiveness of basal rate and prandial boluses in persons with type 1 diabetes melittus treated by means of an insulin pump. Using the CGMS with an adaptation BR and PB based on two-day PG measurement resulted in MPG decrease in 5 out of 8 persons when assessing the 24-hour period, and in 6 out of 8 persons when assessing the night fasting period. MPG increased in 3 out of 8 persons when assessing the 24-hour period, and in 2 out of 8 persons when assessing the night fasting period. In these persons a final correction of BR and PB was carried out. The effects will be monitored later on.

Further studies are necessary to adjust the algorithms for insulin substitution.

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