Local Heating at the Insulin Injection Site by Use of the InsuPad is able to Reduce Postprandial Glucose Excursion in Daily Life

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Background and Aims: The insulin action profiles of subcutaneously injected short acting insulin analogues are still slow compared to physiologically released human insulin. Thus postprandial glucose excursions cannot be avoided. InsuPad is a medical device designed to accelerate insulin delivery rate by applying local heat at the insulin injection site. Whenever an insulin injection is given, the skin surface temperature is heated up locally to 38.5 C° for 30 minutes. This pilot-study examines the impact of the InsuPad use on postprandial glucose excursion after breakfast and dinner in daily life conditions.

Methods: Diabetic patients with high insulin resistance were instructed to use the InsuPad when injecting insulin bolus prior to breakfast and dinner in one study phase for one month and to measure their blood glucose at least five times per day (pre- and post-breakfast, pre-lunch and pre- and post-dinner). In the other study phase patients were instructed to maintain the same blood glucose measurement schedule for one month without using the InsuPad device. The order of the phases was randomized. All blood glucose data were transmitted to a central computer using the DIASEND System. A valid pre-post-prandial measurement time difference was 75 - 135 minutes. An ANOVA, controlling for order of study phase, patient and meal (breakfast vs. dinner) was used to analyse the effect of the InsuPad on postprandial glucose excursions. 10 diabetic patients were using short acting insulin analogues. Participants had considerable overweight and were rather insulin resistant. Two thirds of the sample were type 2 diabetic patients, receiving oral anti-diabetic medication in addition to a multiple daily injection insulin therapy (see table 1).

Results: In the two 4 week periods there were 283 vs. 257 valid pre-post-measurements with and without using the InsuPad after breakfast and dinner. Also the time differences, mean carbohydrate intake and insulin doses between pre-meal and postprandial glucose values were very similar in the study phases with and without InsuPad (see table 2). Preprandial blood glucose levels were similar before breakfast and dinner in both phases and decreased by 0.05 ± 59.1 mg/dl if InsuPad was used, whereas the postprandial glucose levels significantly increased by 11.3 ± 56.3 mg/dl if the InsuPad was not used (see figure 1). After breakfast the InsuPad was able to reduce the pre-post-prandial blood glucose difference by 9 mg/dl (see figure 2), whereas after dinner the pre-post-prandial difference was significantly reduced by 15 mg/dl (see figure 3). The overall glycaemic control (mean total blood glucose values) was significantly better when using the InsuPad compared to the no-use-phase (149.7 ± 54.5 mg/dl vs. 158.7 ± 57.7 mg/dl; p=.016; see figure 4). Percentage of hypoglycaemic (< 60 mg/dl) or hyperglycaemic (> 300 mg/dl) blood glucose measurements were slightly decreased when using the InsuPad but the difference was not statistically significant (% hypoglycaemic values 1.5% vs. 1.8%, p=.496; % hyperglycaemic values 1.6% vs. 2.1%, p=.250). Also the numbers of biochemically defined hypoglycaemic or hyperglycaemic episodes per week were not substantially different during the phases with and without InsuPad use (see figure 5 and 6).

Conclusion: This pilot-study indicates that local heating of the insulin injection site by use of the InsuPad is able to reduce postprandial blood glucose excursions as well as mean glucose values significantly in daily life in diabetic patients with a high insulin resistance. Safety parameters like the prevalence of hypoglycaemic and hyperglycaemic glucose measurements were not affected by the use of InsuPad.

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Table 1: Sample characterstics

Characteristics	
N	10
Mean age ± SD (yrs)	51.1 ± 7.7
Mean diabetes duration ± SD (yrs)	15.7 ± 7.7
Mean BMI ± SD (kg/m²)	34.4 ± 5.7
% Type 2	70% (7)
Mean HbA1c ± SD (%)	8.2 ± 0.9
Mean daily insulin dose ± SD (IU/Kg)	0.92 ± 0.33
Mean daily prandial dose ± SD (IU)	51.7 ± 22.2

Table 2: Treatment Data

	Without InsuPad	With InsuPad	p
# of valid pairs	257	283	.263
Ø amount of KE ± SD	4.0 ± 1.0	3.9 ± 0.8	.822
Ø dose of bolus insulin ± SD (IU)	18.8 ± 9.1	17.9 ± 8.9	.405
Ø time difference ± SD (min)	102 ± 16	103 ± 19.0	.777
# of valid pairs (breakfast)	127	147	.227
Ø amount of breakfast KE ± SD	3.7 ± 0.9	3.7 ± 0.9	.976
Ø dose of breakfast bolus insulin ± SD (IU)	19.0 ± 9.0	18.1 ± 11.1	.603
# of valid pairs (dinner)	130	136	.713
Ø amount of breakfast KE ± SD	4.2 ± 1.3	4.1 ± 0.7	.787
Ø dose of breakfast bolus insulin ± SD (IU)	18.7 ± 9.8	16.9 ± 6.4	.543

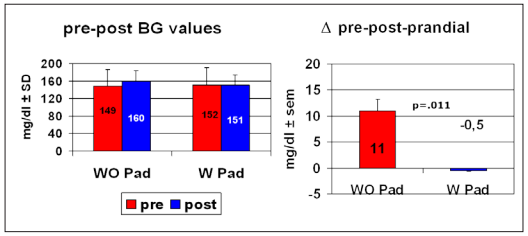

Figure 1: Effect of InsuPad on breakfast and dinner postprandial control (effect controlled for subjects and order)

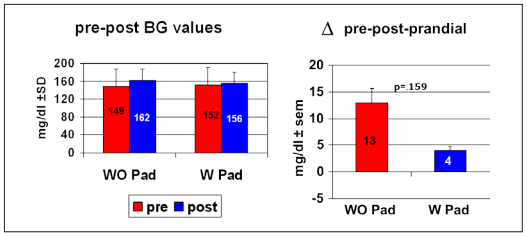

Figure 2: Effect of InsuPad on breakfast postprandial glucose control (effect controlled for subjects and order)

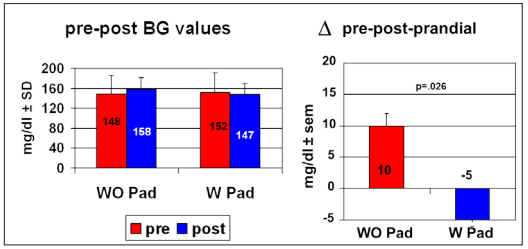

Figure 3: Effect of InsuPad on dinner postprandial glucose control (effect controlled for subjects and order)

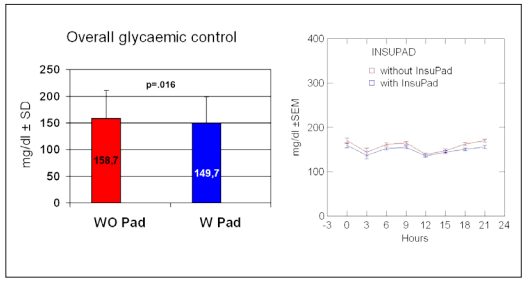

Figure 4: Overall-effect of InsuPad on glycaemic control (effect controlled for subjects and order)

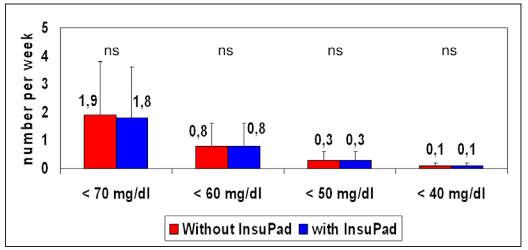

Figure 5: Number of biochemical hypoglycaemic episodes per week

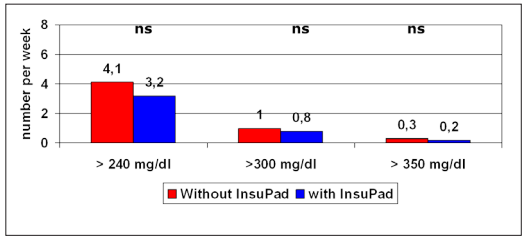

Figure 6: Number of biochemical hyperglycaemic episodes per week