

## MULTIPLE INSULIN INJECTIONS USING A NEW DEVICE (PEN INJECTOR) IN DIABETIC PATIENTS

Metin ARSLAN\*, MD., Nuri ÇAKIR\*, M.D.,  
Göksun AYVAZ\*\*, M.D., Murat SUHER\*\*, M.D.

Gazi University, Faculty of Medicine, Department of Internal Medicine\*\*,  
Division of Endocrinology and Metabolism\*, Ankara, Turkey  
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**SUMMARY** : Seven patients with insulin dependent diabetes mellitus and five patients with non - insulin dependent diabetes mellitus were transferred to a new injection device (Insuject - X and Insuject - N) for usefulness and acceptability.

Patients were compared by evaluating the difference between multiple insulin and conventional insulin therapy. All of the patients reported a better well - being during pen injector therapy and preferred the new therapy to the conventional subcutaneous insulin therapy.

In conclusion, due to the physical discomfort during conventional subcutaneous insulin therapy, we can state that the insulin pen injector is a useful therapeutic device because of its easy usage.

**Key Words** : Diabetes Mellitus, Insulin Therapy, Insulin Pen Injector.

### INTRODUCTION

Although there are various considerations about whether the strict diabetic control prevents the development of vascular complications of diabetes (Grunwald et al. 1990), retinal, renal and nervous system functions are shown to be improved by the strict diabetic control (Dahl - Jorgensen et al. 1986; Frost - Lersen et al. 1983; Holman et al. 1983; Lauritzen et al. 1983; The Steno Study Group, 1982; White et al. 1982) with insulin injections.

In diabetic patients it is not possible to provide appropriate serum insulin concentrations as in non - diabetics by once or twice daily insulin injections (Schriffin and Belmonte, 1982; Tallroth et al. 1989) which results in basal hyperglycemia in most of these patients and this factor plays an important role in developing diabetic complications. Some methods such as insulin pumps and multiple insulin injecti-

ons are used to prevent the fluctuations of blood glucose and to keep the serum insulin concentration within the physiologic range. However, there are some questions about the safety of these pumps. Particularly ketoacidosis may be caused by the use of insulin pumps and thus a close follow up should be done by the physician. We, therefore, aimed to find out if the method of multiple pen injections was useful and acceptable in a group of diabetic patients who were administered conventional insulin treatment before.

### MATERIALS AND METHODS

The study was performed in Gazi University Medical Faculty between 1987 and 1990. Seven insulin-dependent diabetic and five non insulin-dependent diabetic patients were treated with the insulin pen injector. Of seven insulin dependent dia-

betic patients, 5 were female and 2 were male. Their ages ranged between 20 and 42 years (mean  $29,4 \pm 9,9$  years). Duration of diabetes mellitus in these patients were 2-15 years (mean  $8,9 \pm 5,2$  years). Three of the non-insulin dependent diabetics were male and 2 were female. They were 35 to 67 years of age (mean  $51,9 \pm 13,3$ ) and duration of their disease ranged from 8 to 15 years (mean  $10,6 \pm 4,6$  years).

Regular insulin was administered to Type I diabetic patients subcutaneously with a pen injector (Insuject - X) just before the meals (breakfast, lunch and dinner) and intermediate - acting insulin at bed - time with a conventional insulin injector.

Intermediate - acting insulin was administered to non-insulin dependent diabetic patients with pen injector (Insuject - N) twice a day (morning and evening). All the patients were within the  $\pm 20\%$  border of their ideal weight. None of them had any other disorder which might deteriorate the diabetic control.

Subjects were followed for 8-10 days in the hospital and glycemic profiles were figured by obtaining blood samples seven times a day : immediately before and 2 hours after the meals and bed time. Acceptability of the method was investigated by obtaining venous blood samples after mobilization. The effect on life quality of the patients was assessed by a series of interviews.

The blood glucose values were statistically analyzed with paired Student's t - test.

Informed consent was obtained form all patients.

## RESULTS

The mean blood glucose concentrations just before and after 3 months of the use of pen injector in Type I and Type II diabetics are shown in Table I and Table II respectively.

Hours	Before	After 3 months	p value
06	243±159	163± 47	p > 0,05
08	277±144	248±134	p > 0,05
12	236±111	217± 52	p > 0,05
14	302±156	242±105	p > 0,05
18	233±116	182± 72	p > 0,05
20	242 ± 82	181± 76	p < 0,05
22	258±100	196± 58	p > 0,05

Table - 1 : Mean blood glucose concentrations in Type I diabetics just before and after 3 months of the pen injector therapy.

Hours	Before	After 3 months	p value
06	191±61	126±36	p < 0,05
14	221±40	180±24	p > 0,05

Table - 2 : Mean blood glucose concentrations in Type II diabetics just before and after 3 months of the pen injector therapy.

In Type I diabetics, blood glucose levels measured 3 months after starting the pen injector therapy were found to be lower than the values obtained before the pen injector. However, decreases in glycemia were not statistically significant with the exception of the values measured at 8 o'clock p.m. (p < 0,05).

In Type II diabetics, significant decreases were observed at fasting blood glucose concentrations obtained 3 months after the use of pen injector when compared with the values before treatment. The decreases observed at postprandial blood glucose levels were not significant.

The meal hours of the subjects gained regularity with the use of pen injector. The patients mentioned that they had to have their meal within 15 minutes after the insulin pen injections. Otherwise signs of hypoglycemia (palpitation and sweating) would occur which had not been happening while they were using conventional insulin therapy.

Improvement in menstrual disorders observed in 5 Type I female diabetics prior to the therapy was another important point. A female subject who had secondary amenorrhea for 5 years and the other one for 8 months before pen injector therapy begun having normal cycles on the 3rd and 2nd month of the treatment respectively and regular menstrual cycles continued there after. The other 3 female subjects who had oligohypomenorrhea became normal after pen injection therapy.

Pain localized to feet disappeared on the first month of therapy and paresthesia was reduced in a male patient. In a female diabetic patient there had been visual complaints and diarrhea frequent postprandially and all of these symptoms improved after treatment. A diabetic foot ulcer which had been present for one month in a female subject healed up. A male patient mentioned that the involuntary contractions in toes had disappeared after the therapy.

The problems which might have been due to the use of pen injector were as follows : Hypoglycemia signs occurred at the beginning of therapy in 3 subjects. They solved this problem by arranging their

meal hours. Two of them had difficulties to be accustomed to the new feeding order. However both got used to it later.

The questions asked and the answers received from 7 Type I diabetic patients are listed in Table 3.

## DISCUSSION

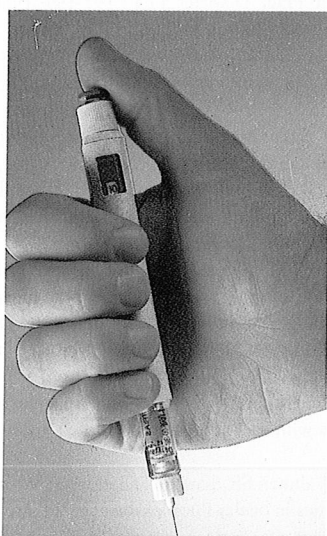
In the present study, blood glucose levels were found to be decreased after the treatment when compared with the values at the beginning in either Type I or Type II diabetic patients. It is difficult to

1- Feel better with the new device?	7 Yes
2- Easy to use it?	7 Yes(no need, even cotton)
3- How to keep it while working?	2 with them 5 in their beg
4- Difficult to use it while working or out door?	7 No (too easy)
5- Frequency of the change of the needles?	3 times a week
6- Feel sure injecting all the insulin?	7 Yes
7- Want to continue the insulin treatment with the new device?	7 Yes
8- Made any change in feeding times while the treatment?	7 No

Table - 3 : The list of the questions and the answers received from 7 Type I diabetic patients.



Fig . 1 : The types of insulin pen



a



b

Fig . 2 : Application of insulin pen.

make a decision about HbA<sub>1c</sub> and fructosamine values because these parameters could not be measured in all our patients. The decrease in glycemia with the use of insulin pen injector is considered to be the result of a close follow up during the therapy. Because the patients had conventional insulin therapy prior to this study, the decrease in blood glucose levels during or after the use of new device suggests superiority of the new technique to the other methods (Schriffin and Belmonte, 1982; Talroth et al. 1989).

In a study performed previously to compare the metabolic control ability of insulin pump and insulin pen injector in insulin dependent diabetic subjects showed that some level of metabolic control could be provided by both methods. Since 80 % of insulin pump users complained about the physical discomfort of the device, insulin pen injector is reported to be preferred (Bak et al. 1987). In the present study all of 7 Type I and 5 Type II diabetic patients also preferred the pen injector to the conventional insulin therapy because of its easier usage. The increased number of injections were considered a negligible problem by the patients. On the other hand getting used to having the meals in exact time to avoid the hypoglycemia risk was a problem. However, the patients overcame this difficulty in time. Because of feeling themselves safer with the easy-to-use pen injector, patients may not pay proper attention to keeping the glucose concentrations in optimum ranges. Thus, it may be assumed that metabolic control can not be provided by insulin injector therapy.

In Type I diabetics, blood glucose decreases were not statistically significant. It might be due to the insufficient number of subjects.

In 5 Type I female diabetics, menstrual disorders improved. After this observation, we have started evaluating FSH, LH, E2 and PRL levels in our new insulin pen users. But, we could not get these hormone values in all 5 Type I female diabetics.

Although some side effects due to the use of insulin pen, such as deterioration of visual disorders (Hyer et al. 1988) and development of diabetic ketoacidosis (Mc Rury et al. 1988) had been reported, no such side effects were observed in our patients. In addition, none of patients complained about any technical problems of the device.

In conclusion, this new device was widely accepted by our patients. Therefore it may be offered as an alternative therapeutical method to the conventional treatment, particularly for Type I diabetics.

We believe that the value of the device will be accepted with the widening usage and technical improvements.

Correspondance to : Dr.Metin ARSLAN  
Gazi Üniversitesi Tıp Fakültesi  
İç Hastahkları Anabilim Dalı  
Endokrinoloji ve Metabolizma  
Bilim Dalı  
Beşevler  
06510 ANKARA - TURKEY  
Phone : 4 - 212 48 31

#### REFERENCES

1. Bak JF, Nielsen OH, Pedersson O and Beck-Nielsen H : Multiple insulin injections using a pen injector versus insulin pump treatment in young diabetic patients. *Diabetic Res* 6 / 8 : 155 - 158, 1987
2. Dahl - Jorgensen K, Brinchmann - Hansen D, Hansen KF : Effect of near normoglycemia for two years of progression of early diabetic retinopathy, nephropathy and neuropathy : The Oslo Study. *Br Med J* 293 : 1195-1199, 1986
3. Frost - Larsen K, Sandahl Christiansen J, Parving HH : The effect of strict short - term metabolic control on rational nervous system abnormalities in newly diagnosed type I (insulin - dependent) diabetic patients. *Diabetologia* 24 : 207-209, 1983
4. Grunwald JE, Brucker AJ, Schwartz SS, Braunstein SN, Baker L, Petrig BL and Rica CE : Diabetic glycemic control and retinal blood flow. *Diabetes* 39 : 602-607, 1990
5. Holmann RR, Mayon - White V, Orde - Peckar C, Steemson J, Smith B, Mc Pherson K, Rizza C, Knoght AH, Dorman TL, Howard - Williams J : Prevention of deterioration of renal and sensory - nerve function by more intensive management of insulin dependent diabetic patients. *Lancet* 1 : 204-208, 1983
6. Hyer SL, Froyd HE, Kohner EM : Effect of Novopen on glycemic control and patient independence in diabetic visual impairment. *Pract. Diabetes* 5 / 5 : 197-199, 1988
7. Lauritzen T, Frost - Larsen K, Larsen HW, Dekert T : The Steno Group : Effect of 1 year - normal blood glucose levels on retinopathy in insulin dependent diabetics. *Lancet* 1 : 200-204, 1983
8. Mc Rury SM, Small M, Boal A : Diabetic ketoacidosis during Novopen therapy. *Diabetic Med.* 5 / 1 : 87-88, 1988
9. Schriffin A and Belmonte MM : Treatment of insulin - dependent diabetes with multiple subcutaneous insulin injections. *Med. Clin. Amer.* 66 : 1251-1267, 1982
10. Talroth G, Karlson B, Nilsson A and Agardh CD : The influence of different insulin regimes on quality of life and metabolic control in insulin - dependent diabetics. *Diabetes Res Clin Pract* 6 / 1 : 37-43, 1989
11. The Steno Study Group : Effect of 6 months of strict metabolic control on eye and kidney function in insulin - dependent diabetics with background retinopathy. *Lancet* 1 : 121-124, 1982
12. White NH, Waltman SR, Krupin T, Santiago JV : Reversal of abnormalities in ocular fluorophotometry in insulin - dependent diabetes after five to nine months of improved control. *Diabetes* 31 : 80-85, 1982