

Insulin Buccal Spray (Oral-Lyn) efficacy in Type 1 Diabetes

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Abstract

Background: To determine efficacy and side effects of oral insulin spray (Oral-Lyn) in comparison to subcutaneously injected regular human insulin.

Methods: Fifteen patients with type 1 diabetes entered in this open-label single arm study with historical control of the same patients for 8 weeks conducted at the Endocrine and Metabolism Research Institute (EMRI). Some biochemical and hormonal lab tests were taken before and at the end of the study. All patients used Oral-Lyn spray instead of regular insulin in dinner time and peripheral glucose measurements were self-monitored by them via similar type glucometer in four different times included fasting, two hours after breakfast, before dinner and two hours post dinner time blood glucose measures.

Results: This study demonstrated that buccal spray had not serious complications and had the same effects on blood glucose control in comparison with regular insulin injections. Also, the rate of hypoglycemia was decreased to 33.3% at the end of the study from 50% at the beginning. Hemoglobin A1C (HbA1c) values did not show any significant changes throughout the study.

Conclusion: Oral-Lyn provides similar postprandial glucose control and caused lower hypoglycemic episodes when compared to regular insulin injections.

Keywords: Buccal Insulin Spray, Type 1 diabetes, Efficacy

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Introduction

Conventional injection insulin therapy is recognized to be inconvenient due to multiple daily injections. As we know, insulin is a large peptide molecule that might be absorbed from gastrointestinal tract, but it rapidly degraded in acidic gastric condition. Many efforts have been performed to deliver insulin via oral roots. So, a rapid-acting, orally administrated recombinant human insulin formulation (Oral-Lyn, Genex Biotechnology, Toronto, ON, Canada) has been identified to improve absorption properties in compare with subcutaneous injection of human regular insulin, but with an earlier maximum effect and a shorter duration of action (1, 2).

In the present study, buccal spray insulin was administrated to patients with type 1 diabetes to determine its efficacy in lowering blood glucose levels and evaluation of possible side effects in compare with subcutaneous regular insulin at mealtime.

Methods

This was an open-label single-arm study with historical control of the same patients for eight weeks since May to November 2009 which involved 15 patients with type 1 diabetes (12 males and 3 females). All the participants received information about the purpose of the study, procedures, and possible side effects of buccal spray, in detail. Screening evaluations included physical examinations and clinical and laboratory tests before study recruitment. Also, we questioned about the history of previous hypoglycemic episodes.

Inclusion criteria were at least 1-year history of type 1 diabetes mellitus, which is currently managed with daily insulin injections totaling 0.3 to 0.8 IU/kg of body weight. Their HbA1c should be greater than 6.5 % and less than or equal to 9.5%. Exclusion criteria were oral lesions and/or disease involving the oral cavity. They should not have history of severe hypoglycemia with seizure or coma within the past 6 months. All the participants underwent training about how to use an identical placebo spray device to avoid improper using of the device. Moreover, all the patients were given a certain glucometer device to check their blood glucose at different 4 times included fasting

blood sugar (FBS), 2 hours post breakfast (2hpp), and specially before dinner and 2 hours after throughout the study period. We assigned a visit session one week before the recruitment for adjusting the dose of regular insulin injection and Oral-Lyn spray puffs. Each puff was considered as one unit insulin. Oral-Lyn was considered in divided doses with 50% of the dose before the meal and the rest after the meal as recommended. We just substituted regular insulin in dinner time with Oral-Lyn and regular insulin in the morning and lunch times were unchanged. We assigned some visits to collect information about any new problem or side effect and results of self-monitored blood glucose values recorded by the patients. Before start and at the end of the study, the participants were evaluated for some laboratory tests included: cell blood count (CBC), HbA1c, lipid profile, liver enzymes, blood urea nitrogen (BUN) and serum Creatinine (Cr), 24 hours urine protein and microalbumin values. The study protocol was approved by the Ethics Committee of Endocrine and Metabolism Research Institute of Tehran University of Medical Sciences and all the participants signed informed consent.

Results

Insulin which administered via the buccal root was well-tolerated in all the patients. No serious complication was observed among the patients; nonetheless just one patient had bleeding gum that was in case of dropouts. Two patients had mouth numbness and one of them reported vertigo which lasted no longer and had no serious sequel (Table 1). More than 50% of the patients at the beginning of the study reported hypoglycemia episodes and this rate decreased to 33.3% at the end of the study (Table 2).

Mean glucose values before dinner and 2 hours after the dinner at start and at the end of the study has shown in Table 2. Also, this Table shows that the mean values of patients' weight were not changed throughout the study. Mean values of HbA1c did not significantly change throughout the study period. There were no changes in hormonal and biochemical lab test values except Creatinine which was raised in patients at the end of the study (Table 3).

Table 1- Characteristics of the patients

Characteristics	Age (Years)	Wt (kg)	BMI (Kg/m ²)	Diabetes Duration (Years)	Regular Insulin (unit)	Side effect
1	34	70	25.4	5	14	Bleeding gum
2	30	65	24.1	7	12	-
3	26	71	22.4	1.5	10	-
4	22	80	28.3	12	6	-
5	18	66	23.1	5	12	Mouth Numbness
6	24	66	27.8	5	6	-
7	24	71	21.6	1	8	Mouth & lip numbness
8	22	83	30.4	8	28	-
9	20	88	22.1	7	4	-
10	25	110	31	6	8	-
11	21	51	19.9	3	17	-
12	22	95	30.6	6	18	-
13	22	65	23.5	19	8	Vertigo
14	32	66	22.5	6	6	-
15	44	88	26.2	7	18	-

Table 2- Comparison between some parameters related to blood glucose before and after the study*

Variables	Before study	After study
Previous Hypoglycemic Episodes (%)	58.3%	33.3 %
FBS (mg/dl)	172.6±76.9	167.2±67.3
BS before dinner (mg/dl)	146.9±44.6	131.9±28.4
BS after dinner (mg/dl)	182.9±57.6	170.7±64.6
HbA1c (%)	8.4±1.8	8.7±2.0
Weight(kg)	77.5±15.9	77.4±16.3

*In comparison, no significant differences were seen (P>0.05)

Table 3- Effects of Oral-Lyn on some laboratory parameters before and after the study *

Variables	Before study Mean±SD	After study Mean±SD
WBC count (×1000)	6.7±1.2	6.7±1.5
Hb (mg/dl)	15.1±1.6	15.7±1.7
Platelets (×1000)	233±46.6	244.7±52.5
TG (mg/dl)	116.1±65.5	140.5±94
Total Cholesterol (mg/dl)	163.6±33.6	166.6±28.7
ALT (mg/dl)	11.5±6.9	13.6±5.4
AST (mg/dl)	17.9±5.	19±5.6
BUN (mg/dl)	11.5±2.5	12.3±2.5
Creatinine (mg/dl)	0.9±0.1	1.03±0.1
Uric Acid (mg/dl)	4.9±1.5	4.9±1.5
24 hours urine protein (gr)	8.7±4.1	7.1±2.3

*In comparison, no significant differences were seen (P>0.05)

Discussion

Our study showed that Oral-Lyn provided similar postprandial glucose control in patients with type 1 diabetes comparing with regular insulin. Also, it caused lower hypoglycemic episodes when compared to regular insulin injections. Hypoglycemia rates decreased from 54% to 33% as evidenced by our results which suggest that lesser risk of hypoglycemia is expected by using this route of insulin delivery; although it was not statistically significant due to low sample size, it seems clinically meaningful. As we know, the pharmacokinetic properties of Oral-Lyn have been found to be similar to that of rapid-acting regular insulin in patients with type 1 and type 2 diabetes (1-4). The Oral-Lyn peptide has some advantages

such as rapid absorption, no need for injection, and decrease postprandial hyperglycemia. Also, this formulation causes no major complication or discomfort in the mouth as we observed in our study and is rapidly absorbed within 5-10 min which is faster than subcutaneous injected regular insulin. Although, our results derived from a small number of patients, which considered our study limitation, it was revealed that insulin delivered via oral route at mealtime could be considered as an acceptable substitute for regular insulin injections.

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