Micro-needle Clinical Studies (Type-1 Diabetes)

Study Title

To compare the efficacy of the Micro-Needle based intradermal & epidermal drug delivery system with subcutaneous (s.c.) injection dose of human insulin after a standard meal at breakfast time in subjects with Type-1 diabetes.

Study Objective

Galaxy Technologies is going to investigate the efficacy and the reduction in injection pain of the novel micro-needle device in subjects with Type-1 diabetes in comparison with the s.c. injected insulin at the breakfast time. It is hypothesized that the drug delivery of insulin through this novel device may help regulate the blood glucose levels in patients during mealtimes and may improve quality of life (reduction in pain and trauma).

Investigational Plan

This was an open label randomized, cross over, comparative study of the Micro-Needle Device versus s.c. insulin injections involving 15 male or female volunteers with Type-1 diabetes. Any subject removed from the study because of inter-current illness, non-compliance with the protocol, or dropout, was replaced with another subject, fulfilling the inclusion criteria. Subjects were screened, and, after the initial screening visit, were asked to stay on their regular diabetes treatment regimen during the study period. The subjects were asked to check into the clinic one day prior to the start of the study. At this time, they were given a routine physical examination and their blood chemistry was checked.

Consent Process

The qualified study personnel, i.e., the study coordinator and/or investigator or other designee, explained the study procedure to all the subjects who were then each provided a copy of the consent form.

Source of Volunteers

The subjects were recruited through physicians' offices at St Joseph Hospital Toronto, Canada.

Characterization of Volunteers

The registered physician ruled all the subjects to be of good health following a physical examination, ECG and medical history. The physician also reviewed the pre-clinical test data from each subject. The latter included complete biochemical and hematological screens as well as urinalyses as follows:

1) Biochemical profile serum electrolytes (Na, K, and chloride, glucose, creatinine, HbA1c, liver enzymes (ALT, AST), etc.;
2) Hematology: Hemoglobin, total blood cell counts, and platelet count;

3) Urinalysis: Specific gravity, pH, glucose, ketone, and blood.

Inclusion Criteria

1) Type-1 diabetes;
2) Ages between 18-75 years;
3) Availability for the entire study period and willingness to adhere to protocol requirements as evidenced by a signed, written, informed consent;
4) Physical examination: without clinically significant abnormalities;
5) Vital signs and ECG: without clinically significant abnormalities;
6) BMI ≤ 28 (non-obese);
7) HbA1c ≤ 10.

Exclusion Criteria

1) Known history or presence of significant cardiac, gastrointestinal, endocrine, neurological, liver, kidney disease, or conditions known to interfere with the absorption, distribution, metabolism, or excretion of insulin;
2) Any clinically significant illness during the month prior to entry into this study;
3) Any subjects with a history of drug dependency or psychological disease;
4) Regular use of medication (other than the treatment of diabetes and cardiovascular disease or blood pressure) that interferes with the absorption, metabolism of insulin,
5) Abuse of alcohol, or participation in a clinical trial with investigational drugs within 30 days preceding this study, including MAO inhibitors;
6) Use of enzyme inducing and enzyme inhibiting drugs such as Phenobarbital, and carbamazepine within 30 days prior to entry into this study;
7) Pregnant or lactating mothers;
8) Have experienced more than one episode of severe hypoglycemia with seizure
or coma in the past year;
9) Have a history of ketoacidosis;
10) Have any acute illness within the 2 weeks prior to screening;
11) Have elevated liver enzymes ALT, AST, or alkaline phosphatase 1.5 times the upper limit of normal.

Medication

The medications prescribed by their doctor for good maintenance of health were allowed (anti-hypertensive, anti-cholesterol, etc).

Study Procedures

All subjects completed the following: one screening visit (visit 1), and two visits to the Clinical Research Centre scheduled 1 to 5 days apart. Participation in this study involved visiting the Clinical Research Centre for about six hours minimum (per study day), a one hour screen visit, and about one to two hours for travel, parking, and checkin time for each visit. Subjects were randomized according to

the schedule. Vital signs (blood pressure, weight, and pulse) were monitored during the day as follows 0 (baseline), 1.0, 2.0, 4.0 hours after pump insulin bolus dose.

All patients received the following two treatments in a randomized fashion on separate days:

1) Subjects were given a bolus dose of insulin (Humalog, Lilly) 7 units at time 0 minutes.
2) Subjects were given insulin dose (Humalog, Lilly) 7 units through the Micro-Needle Device at time 0 minutes.

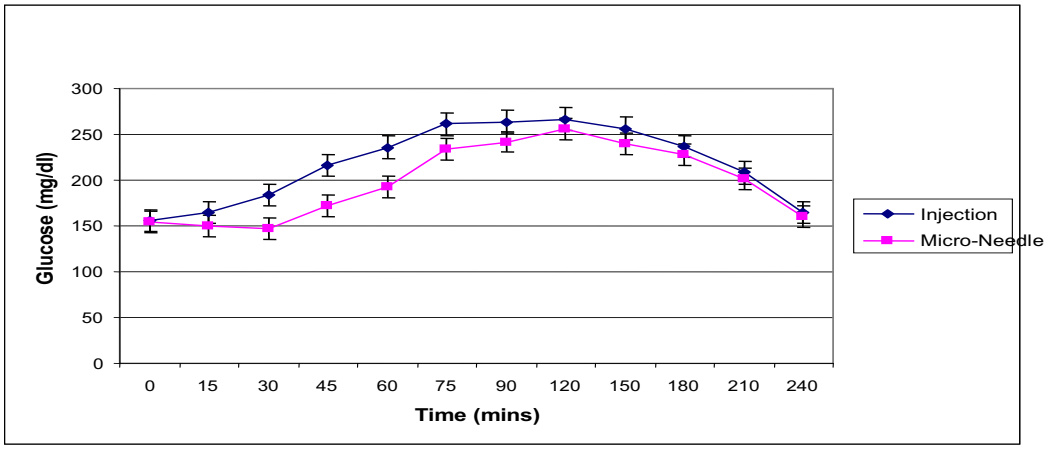
Ten minutes later the dose subjects were asked to consume 360 calories from Boost or Ensure Plus liquid meals. Blood samples for plasma glucose and insulin was taken 30 minutes before the liquid meal (-30 minutes); directly after (0 minutes); and four times per hour for four hours after the meal (15, 30, 60, 90, 120, 180, 240 and 300 minutes). At the end of the study period, the catheter was removed and subjects were permitted to leave the clinic after examination by the physician who declared them safe to leave the clinic.

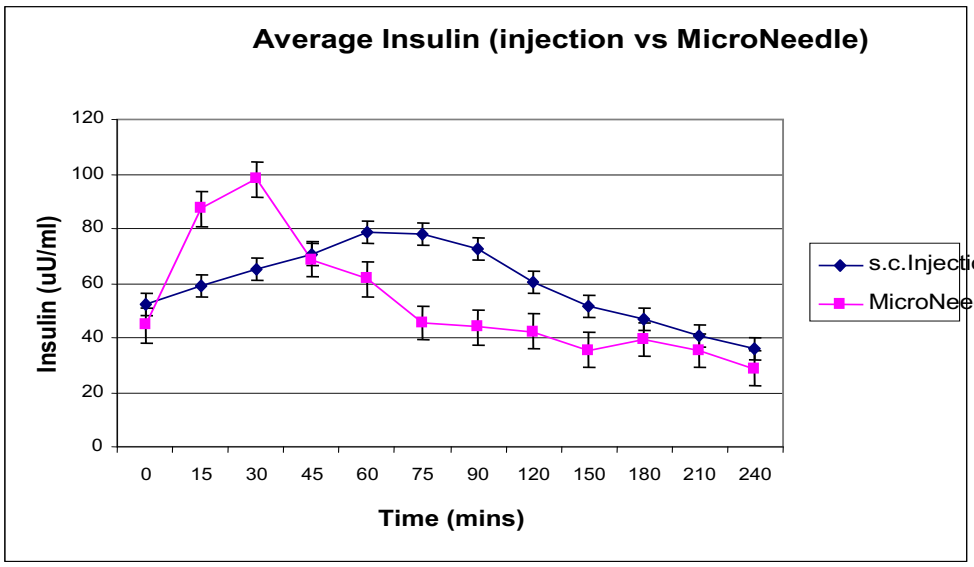
Results

There was a significant difference in the glucose excursions at 30 and 60 minutes after a standard meal challenge as derived from the values of lower glucose levels in the Micro-Needle Device injection treatments when compared to the standard injection treatments. The 30 minutes and 60 minutes post-prandial glucose levels were significantly lowered with the Micro-Needle Device versus the injection group (146 ± 5 mg/dL Micro-Needle Device versus 184 ± 7 mg/dL injection: 21% lower at 30 minutes and 192 ± 6 mg/dL Micro-Needle Device versus 236 ± 9 mg/dL injection: 19% lower at 60 minutes $p<0.003$). The rises in serum insulin levels were significantly higher (Cmax = 98 ± 6 uU/ml for Micro-Needle Device at 30 minutes versus 65 ± 3 uU/ml injection treatment, 35% higher, $P<0.001$). The absorption of insulin through the skin layers was significantly faster when compared to the s.c. injected rapid acting insulin (Humalog). The insulin delivered through the Micro-Needle Device was effective in lowering glucose when compared to the regular s.c. insulin injection. This was attributed to the much more rapid absorption of insulin through the skin layers (Tmax = 30 ± 5 minutes for Micro-Needle Device versus Tmax = 60 ± 10 minutes injection). There was no statistical difference in the variability of the absorption of insulin in the Micro-Needle Device versus s.c. injection as estimated from the individual data of each treatment and both treatments were comparable to each other in absorption characteristics ($p>0.751$).

The absolute bioavailability of this preparation injected through the Micro-Needle Device was estimated to be closely identical to the average data of the 23 subjects in comparison with the s.c. bolus injection dose. These results are shown in the following graph.

Average Glucose (Micro-Needle Injection vs s.c. Injection





Pain Assessment

There was no pain associated with the Micro-Needle Device injection as patients never felt the pricking pain associated with the regular injection

Actual Device Picture