01 ORAL SPRAY INSULIN IN PATIENTS WITH TYPE 1 DIABETES: COMPARISON WITH SUBCUTANEOUS INSULIN

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Objective: Insulin therapy by subcutaneous injection is the standard treatment for patients with Type 1 diabetes. Recently, a viable alternative has been developed in the form of an insulin-ejecting aerosol spray for oral insulin delivery. With this system insulin is delivered into the mouth at high speed and is absorbed through the oropharyngeal mucosa into the circulation. ***Methods:*** In the present study we aimed to evaluate the metabolic effect of oral spray insulin compared to subcutaneous insulin in patients affected by Type 1 diabetes. The study protocol was designed to compare blood glucose, insulin and C-peptide levels in 9 patients treated with subcutaneous or oral insulin on two consecutive study mornings. On day 1 patients were treated with their usual subcutaneous regular insulin regimen. On day 2 patients received oral spray insulin. In both mornings of days 1 and 2 patients received 125 mL of a standard meal. Patients were sampled up to 4 hours to evaluate blood glucose, plasma insulin and C-peptide. No basal insulin was administered to patients in the morning of the test. In 3 male patients affected by Type 1 diabetes (aged 28, 34, 35 years) pre-meal oral insulin treatment was prolonged for two consecutive days. In these patients we blood glucose levels were monitored throughout the day for three consecutive days by the recently developed glucose sensor monitoring system. ***Results:*** There were no significant differences in the blood glucose, insulin and C-peptide levels measured after treatment with subcutaneous insulin or oral insulin. In the 3 patients who received oral insulin for two days and who were monitored using the glucose sensor, no significant differences were observed in blood glucose levels with either oral or subcutaneous insulin.
Conclusions: We conclude that insulin via the buccal spray formulation is effective as the subcutaneous route in lowering blood glucose levels.

02 MUTATIONS IN THE HEPATOCYTE NUCLEAR FACTOR-1α GENE IN CHINESE MODY FAMILIES: PREVALENCE AND FUNCTIONAL ANALYSIS

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Maturity-onset diabetes of the young (MODY) is an autosomal dominant form of diabetes characterized by an early age of onset (usually <25 years). We screened for mutations in the hepatocyte nuclear factor (HNF)-1α (MODY 3) gene in 50 unrelated Southern Chinese families, which fulfilled the minimum criteria for MODY: two generations of type 2 DM with at least one member diagnosed under the age of 25 years. The 10 exons, flanking introns and promoter region of the HNF-1α gene were amplified by polymerase chain reaction and sequenced directly. Functional properties of the mutant proteins were investigated using site-directed mutagenesis and luciferase reporter assay. Six of the 50 (12%) subjects were found to have mutations, including one novel nonsense mutation Q176X, one novel intronic mutation IVS7-6 G→A and 4 reported mutations (frameshift mutation P379fsdelCT, nonsense mutation R171X, missense mutation G20R and P112L). The expression levels of wild type and mutant proteins in HeLa cells were similar except for R171X and Q176X which were not detected with the C-terminal antibody. The mutations locating in the coding region were found to have decreased trans-activating activity. The intronic mutation cosegregated with diabetes in the family, created a potential splice acceptor site and might alter the splicing of the HNF-1α mRNA. In conclusion, mutations in the HNF-1α gene appear to be an important cause of MODY in Southern Chinese. The mutations may affect normal islet function by altering the expression of the target genes.