Nasal glucagon: a viable alternative to treat insulin-induced hypoglycaemia in adults with type 1 diabetes

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Background and aims:

Any insulin-treated individual with diabetes is at risk of severe hypoglycaemia (SH). Glucagon is available as a rescue medication in these instances. Currently available commercial glucagon products require reconstitution and injection, which are cumbersome during an emergency situation. Nasal glucagon (NG) is a nasally administered, drug-device combination product that consists of a dry powder spray formulation with 3-mg synthetic glucagon contained within a single-use device.

This study in adults with type 1 diabetes (T1D) aimed to demonstrate non-inferiority between intramuscular glucagon (IMG) and NG as treatment for insulin-induced hypoglycaemia.

Materials and methods:

This randomised, two-period, crossover trial was conducted at two clinical sites and used a NG drug product manufactured at commercial scale. The comparator was glucagon [rDNA origin] injection. Hypoglycaemia (plasma glucose [PG] <3.3 mmol/L) was induced by an intravenous insulin infusion. Five minutes after stopping insulin, either 3-mg NG or 1-mg IMG was administered followed by multiple PG measurements up to 90 min.Treatment success was defined as an increase in PG to ≥3.9 mmol/L or an increase of ≥1.1 mmol/L from the PG nadir within 30 min of receiving glucagon. Non-inferiority of NG was declared if the upper limit of the two-sided 95% CI of the difference in percentage of patients achieving treatment success (IMG-NG) was <10%. Besides spontaneously reported adverse events (AEs), a Nasal and Non-Nasal Symptom Questionnaire (NNSQ) assessed local tolerability of NG.

Results:

Of the 66 participants included in the primary efficacy analysis who received both NG and IMG, 100% achieved treatment success. The study demonstrated non-inferiority of NG to IMG. All participants achieved treatment success by 25 min with the mean time to treatment success of 11.4 min (NG) and 9.8 min (IMG). Similar glucose responses were observed with NG and IMG within 40 min post glucagon administration.

No deaths or other serious AEs occurred. Forty-eight AEs occurred after NG and 51 after IMG. Most AEs were mild and transient, and the frequency was similar between IMG and NG. Transient nasal and ocular symptoms were common after NG.

Conclusion:

Nasal glucagon was as efficacious and safe as intramuscular glucagon for the treatment of insulin–induced hypoglycaemia in adults, thus supporting the use of nasal glucagon as a rescue treatment for severe hypoglycaemia.