ATTD7-0065

NASAL GLUCAGON FOR THE TREATMENT OF MODERATE TO SEVERE HYPOGLYCEMIC EPISODES IN CHILDREN AND ADOLESCENTS WITH TYPE 1 DIABETES

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ABSTRACT

Objectives: This multi-center, open-label study evaluated the effectiveness and ease of use of nasal glucagon (NG) in treating moderate or severe hypoglycemic (hypo) episodes in patients (pts) with type 1 diabetes (T1D), aged 4 to <18 yrs.
Methods: Pts and caregivers (CGs) were taught how to use NG. During naturally occurring symptomatic episodes of moderate or severe hypo in real world settings, CGs administered 3 mg NG and measured blood glucose (BG) levels over time. Adverse events (AEs), recovery of symptoms, and ease of use were solicited by questionnaires.
Results: Fourteen pts, who experienced 33 moderate hypo episodes with neuroglycopenic symptoms and a BG level ≤70 mg/dL, were included in the efficacy and main safety analyses. Mean number of episodes per pt was 2.4 (range 1 to 4). In all episodes, pts returned to normal status within 30 minutes after NG dose. No calls to 911 (emergency medical services) were needed. Mean baseline BG level was 56 (range 42-70) mg/dL. Within 15 minutes after NG dose, mean BG level increased to 114 (range 79-173) mg/dL, and continued to increase. No serious AEs occurred. For most episodes (61%), CGs administered NG in <30 seconds; in all cases, administration took <2 minutes. CGs were either satisfied or very satisfied with NG after most episodes (91%).
Conclusions: NG increased BG levels and resolved symptoms in all reported episodes of hypo among children and adolescents with T1D. The majority of CGs were highly satisfied with NG. Data suggest that NG is a viable alternative to currently available injectable recombinant glucagons.

BACKGROUND

- Use of injectable glucagon, the only commercially available glucagon formulation, may be challenging as it requires
  - Injection of diluent into a vial of dry glucagon
  - Swirling the solution to dissolve glucagon
  - Filling a syringe with the glucagon solution
  - Injecting the glucagon solution into the person experiencing hypoglycemia
- Conversely, nasal glucagon (currently under development) is
  - needle-free; absorbed passively through nasal mucosa
  - a nasal dry powder
  - ready to use; no reconstitution is needed
  - contained in a compact, portable, single-use nasal dosing device
  - effective even if the patient does not breathe deeply or inhale

INTRODUCTION

- Nasal glucagon is a promising alternative to injectable glucagon for the treatment of hypoglycemia in children and adolescents with type 1 diabetes[1]
- This open-label, prospective study evaluated the effectiveness and ease of use of nasal glucagon in home and school settings for treating naturally occurring episodes of moderate or severe hypoglycemia in children and adolescents with type 1 diabetes

METHODS

- Study participants were children and adolescents with type 1 diabetes aged 4 to <18 years
- If a naturally occurring severe or moderate hypoglycemic episode occurred, a single nasal glucagon dose (3 mg) was administered
  - Moderate hypoglycemia was defined as hypoglycemia (blood glucose ≤70 mg/dL) with neuroglycopenic symptoms such as poor concentration and dizziness[2]
  - Severe hypoglycemia was defined as hypoglycemia with severe neuroglycopenia (usually resulting in coma or seizure) and requiring parenteral therapy[2]
- Caregivers were instructed to seek emergency medical aid if nasal glucagon did not show an effect, per caregiver judgment, within 15 minutes
- Caregivers measured blood glucose just before or immediately after treatment and again at 15, 30, and 45 minutes after dosing
- Primary efficacy measure was percentage of participants awakening or returning to normal status (in the judgment of the caregiver) within 30 minutes of nasal glucagon administration
- Caregivers completed questionnaires to record symptoms, clinical response, and subjective evaluation of ease-of-use of nasal glucagon
- If possible, children and adolescents completed a questionnaire about nasal and non-nasal symptoms within 2 hours after complete recovery from the hypoglycemic episode

RESULTS

- This study was conducted at 3 sites in USA
  - One site was discontinued for repeated protocol deviations and GCP non-compliance
  - All participants from this site (N=11) were excluded from these analyses
- A total of 15 participants, aged 5 to 17 years, enrolled at the two GCP-compliant sites
- Out of these, 14 participants experienced ≥1 moderate hypoglycemic episode
- These participants were white (100%), predominantly male (64%), with a mean duration of diabetes 6.3 years (range 2.5 to 14.3 years)
- 21% of participants had reduced awareness of hypoglycemia at baseline (Clarke Hypoglycemia Unawareness Survey[3])
- There were 33 episodes of moderate hypoglycemia (mean=2.4 per participant)
  - No episodes of severe hypoglycemia (per protocol definitions)
  - One participant experienced neither moderate nor severe hypoglycemia
- Common hypoglycemia symptoms were hunger, tiredness, and trembling (Figure 1)
- In 61% of episodes, caregivers administered nasal glucagon in <30 seconds (Figure 2)
- In 100% of episodes (for 100% of participants), hypoglycemia symptoms resolved and participants returned to normal status in <30 minutes after nasal glucagon administration (Figure 3)
- Blood glucose levels increased within 15 minutes after nasal glucagon administration in all participants and continued to increase over 45 minutes (Figure 4)
- Adverse events, predominantly nasal discomfort and watery eyes, were experienced by all participants; many adverse events resolved within 1 hour of administration (Figure 5)
- Most caregivers were satisfied or very satisfied with nasal glucagon (Figure 6)

Figure 1. Symptoms of Hypoglycemia

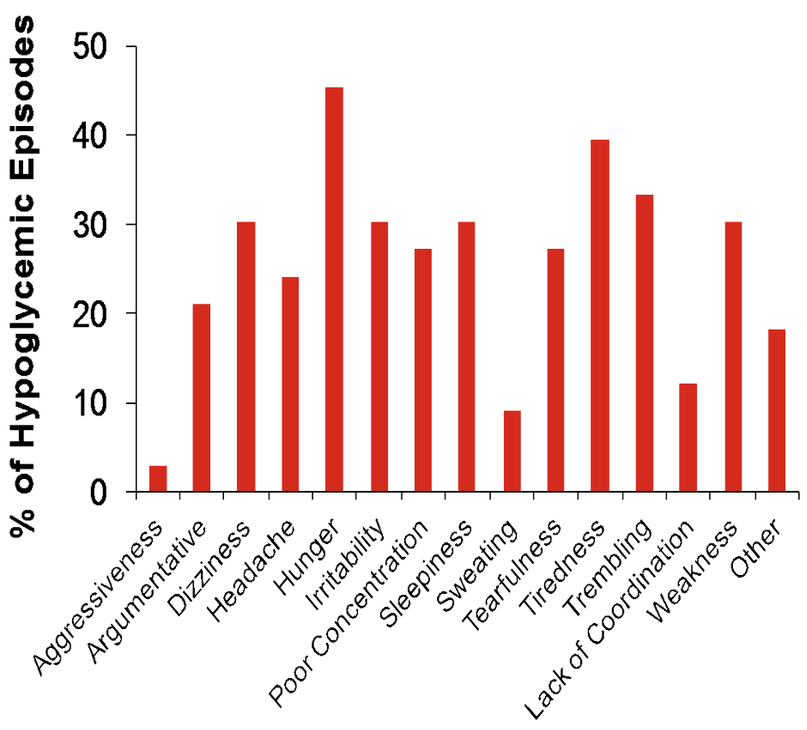


Figure 2. Time Taken to Administer Nasal Glucagon

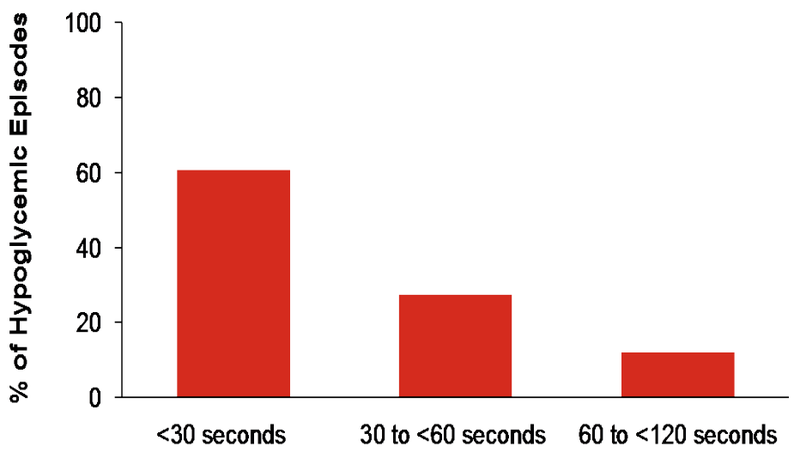


Figure 3. Time Taken to Return to Normal Status After a Hypoglycemic Episode

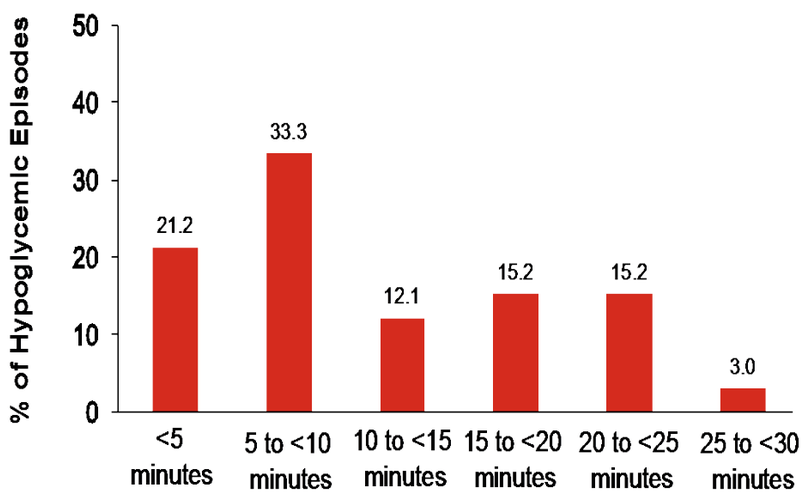
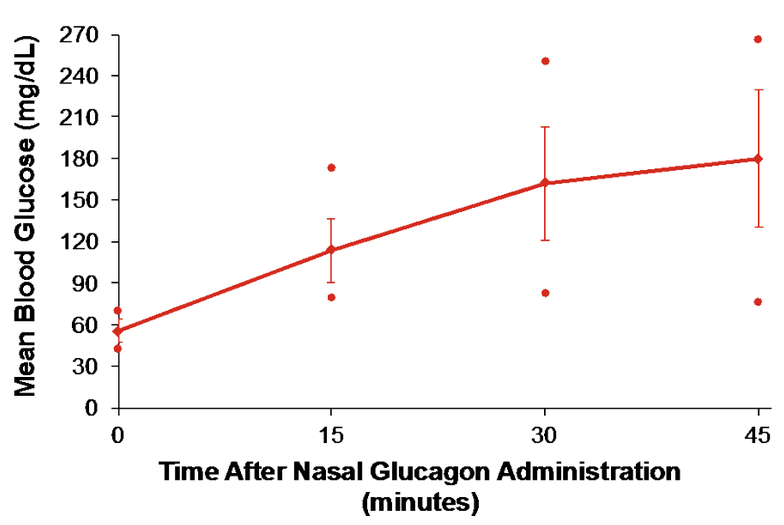
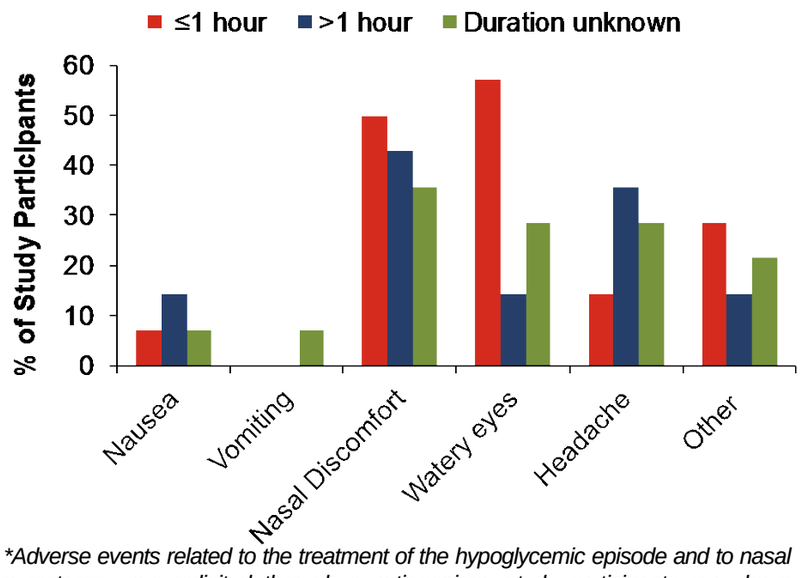


Figure 4. Blood Glucose Levels After Nasal Glucagon Administration, Mean (SD)



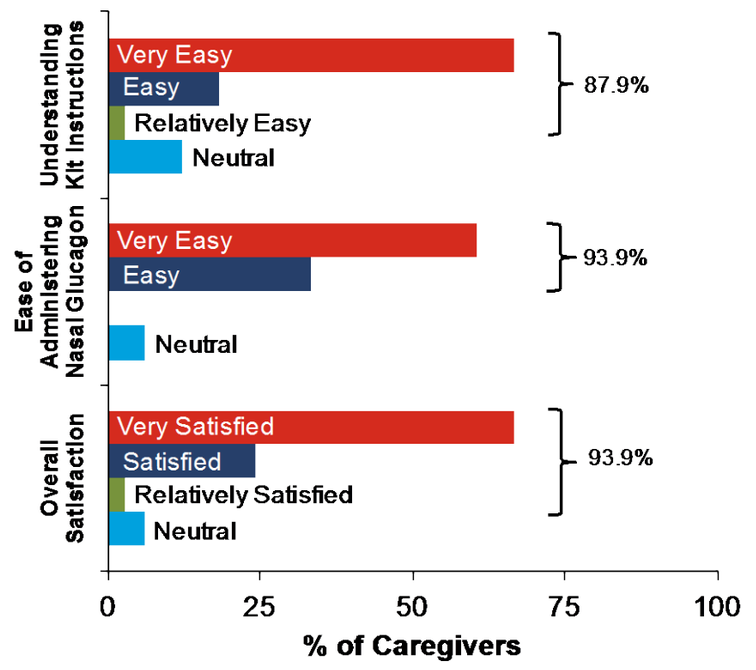
Dots represent maximum and minimum values
Mean blood glucose at time 0 was 56 mg/dL

Figure 5. Duration of Adverse Events After Nasal Glucagon Administration*



**Adverse events related to the treatment of the hypoglycemic episode and to nasal symptoms were solicited through questionnaires; study participants may have experienced multiple moderate hypoglycemic episodes and reported adverse events after each episode. For example, a study participant may have experienced nasal discomfort lasting ≤1 hour after one episode and nasal discomfort lasting >1 hour after another. Hence, the total of the above bars could be greater than 100% for a single adverse event.*

Figure 6. Caregiver Satisfaction



CONCLUSIONS

- Nasal glucagon
  - enabled all participants to return to normal status within 30 minutes
  - increased blood glucose levels within 15 minutes in all participants
  - was rated satisfactory or very satisfactory by most caregivers
  - had safety data that were consistent with previous studies
  - can be a viable alternative to injectable glucagon in pediatric patients with type 1 diabetes

References:

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3. Clarke WL, et al. *Diabetes Care* 1995;18:517-522

Acknowledgments

1. The authors would like to thank the healthcare professionals, study participants, and caregivers for making the study possible.
2. The authors would also like to thank Dr. Sheetal Pradhan of Eli Lilly and Company for her assistance in preparation of this poster.

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ATTD7-0065