

Investigation of Ginger to Decrease Nausea Associated with GLP-1 Therapy

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INTRODUCTION

Gastrointestinal side effects are common among patients treated with glucagon-like peptide-1 (GLP-1) receptor agonists and may limit therapy in up to 6% of patients.[1] Nausea occurs in 15%-50% of patients treated with GLP-1s and may lead to drug discontinuation.[1,2]

Ginger (*Zingiber officinale*) has been traditionally used to treat stomach upset and nausea, and a clinically tested treatment for nausea during pregnancy, motion sickness, and chemotherapy. This placebo-controlled pilot study is the first to investigate the effectiveness of a commercially available dietary supplement ginger chew to decrease nausea associated with GLP-1 therapy.

MATERIALS & METHODS

This double-blind study enrolled patients who were newly prescribed a GLP-1, or who were commencing step-up therapy and had a history of nausea with lower GLP-1 doses. Qualified participants were randomized to receive a Ginger chew or Placebo (caramel candy) for nausea management.

Participants self-monitored for *de novo* development of nausea after initiation or step-up GLP-1 use and recorded symptom severity before and after dosing (two chews per dose) in a daily Product Use Diary. Nausea was graded using a 10-point Likert scale (0=none; 1-3=mild; 4-6=moderate; 7-9=severe; 10=vomiting). Change in nausea severity was calculated per total dose and per nausea event.

Analysis populations included modified Per-Protocol (mPP) and modified Intent-to-Treat (mITT). Mean change in nausea severity between groups was performed using a paired t-test. Comparison of reduction in nausea events per group was performed using a Fisher's exact test.

RESULTS

The mITT population included 78 participants (Ginger = 39, 5 male/34 female; mean age 50.3 years. Placebo = 39, 5 male/34 female, mean age 50.6 years).

Descriptive statistics for nausea associated with GLP-1 medications does not suggest the severity and frequency of nausea was dose-dependent or dependent on duration of GLP-1 use (Table 1).

Table 1. Characteristics of Nausea Associated with GLP-1 Use

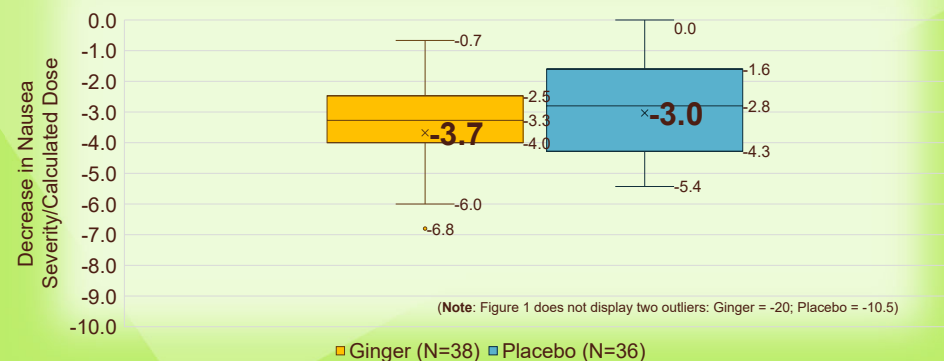
GLP-1	# Nausea Events*	Mean Severity (STD)	Minimum Severity	Maximum Severity
Semaglutide				
0.2 – 0.5 mg	70	5.4 (2.1)	1	10
1.0 – 1.7 mg	104	6.2 (1.5)	2	9
2.0 – 5.0 mg	130	5.9 (2.0)	1	10
Tirzepatide				
0.75 – 2.5 mg	35	4.5 (1.9)	1	10
5.0 – 10.0 mg	106	5.3 (2.0)	1	9
12.0 – 17.0 mg	131	4.7 (1.9)	1	10
Dulaglutide				
3.0 – 4.5 mg	18	4.2 (2.8)	1	10

10-point Likert scale (0=none; 1-3=mild; 4-6=moderate; 7-9=severe; 10=vomiting)

* mITT Population; GLP-1 dosing unclear for 39 nausea events (semaglutide=13 events; tirzepatide=26 events) thus could not be included

Post-dose nausea severity declined 3.7 points in the Ginger group vs. 3.0 points in the Placebo group (Figure 1); however, this did not reach statistical significance (p=0.286).

Figure 1. Mean Decrease in Nausea per Calculated Total Dose (mITT Population)



(Note: Figure 1 does not display two outliers: Ginger = -20; Placebo = -10.5)

RESULTS (cont.)

Any reduction in nausea severity was observed in 96.2% of Ginger participants vs. only 83.0% in the Placebo group (p<0.001, Table 2).

Mild to Moderate reduction in nausea severity was observed in 92.3% of Ginger participants vs. only 81.6% in the Placebo group (p<0.001, Table 2).

Table 2. Reduction in Nausea Severity after Ginger and Placebo

2 x 2 Contingency	Any Reduction (Δ = -10 to -1)	No Change/ Worsening Nausea (Δ = 0 to +2)	P Value	
Ginger	300/312 (96.2%)	12/312 (3.8%)	<0.001	
Placebo	282/321 (88.0%)	39/321 (12.1%)		
2 x 3 Contingency	Maximum Reduction (Δ = -10 to -7)	Mild-Moderate Reduction (Δ = -6 to -1)	No Change/ Worsening Nausea (Δ = 0 to +2)	P Value
Ginger	12/312 (3.8%)	288/312 (92.3%)	12/312 (3.8%)	<0.001
Placebo	20/321 (6.2%)	262/321 (81.6%)	39/321 (12.1%)	

No drug-related adverse events were identified in either group.

CONCLUSIONS

- The Ginger supplement was statistically superior in achieving **Any** nausea reduction and **Mild/Moderate** nausea reduction following GLP-1 dosing compared to Placebo
- Ginger therapy was associated with a greater numerical reduction in nausea severity compared to placebo, though it did not reach statistical significance in this pilot trial

References

- Husain M, Birkenfeld AL, Donsmark M, *et al.* GLP-1s and cardiovascular outcomes in patients with Type 2 diabetes. *N Engl J Med.* 2019;381:841-851.
- Gorgojo-Martinez JJ, Mezquita-Raya P, Carretero-Gomez J, *et al.* Clinical recommendations to manage gastrointestinal adverse events in patients treated with GLP-1 receptor agonists: a multidisciplinary expert consensus. *J Clin Med.* 2023, 12: 145.