

Evaluating the Role of Apple Cider Vinegar in Managing Semaglutide-Induced Gastrointestinal Disturbances: A Systematic Review

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Abstract

Background: Semaglutide, a glucagon-like peptide-1 (GLP-1) receptor agonist, is highly effective in treating type 2 diabetes and obesity. However, its use is often associated with gastrointestinal side effects, including nausea, vomiting, and diarrhea, which may impact patient compliance. **Objective:** This systematic review aims to evaluate the evidence regarding the management of semaglutide-induced GI symptoms and assess the potential role of apple cider vinegar (ACV) as a complementary treatment. **Methods:** A comprehensive search of databases, including PubMed, Cochrane Library, and Scopus, was conducted for studies published in the last five years. The inclusion criteria consisted of randomized controlled trials (RCTs), observational studies, and case reports that examined gastrointestinal symptoms caused by semaglutide and the application of ACV. **Results:** The initial search yielded 120 articles, with 15 meeting the inclusion criteria. Most studies reported common GI side effects associated with semaglutide, particularly nausea and diarrhea. While direct evidence supporting ACV's efficacy in managing these symptoms is limited, anecdotal reports and preliminary studies suggest that ACV may help improve digestion and reduce nausea. **Conclusion:** Semaglutide is a valuable treatment option for type 2 diabetes and obesity, but its GI side effects pose challenges in clinical practice. This review highlights the potential of apple cider vinegar as a complementary approach to alleviating these disturbances. Further clinical trials are necessary to validate the safety and efficacy of ACV in managing semaglutide-induced gastrointestinal symptoms.

Keywords: Semaglutide, GLP-1 receptor agonist, gastrointestinal disturbances, apple cider vinegar, nausea, diarrhea, type 2 diabetes, obesity, complementary therapy

INTRODUCTION

Semaglutide, a glucagon-like peptide-1 (GLP-1) receptor agonist, has emerged as a highly effective treatment for type 2 diabetes mellitus (T2DM) and obesity due to its ability to promote glycemic control and weight loss [1, 2]. GLP-1 receptor agonists mimic the action of the endogenous incretin hormone GLP-1, enhancing glucose-dependent insulin secretion while suppressing glucagon release, which leads to improved metabolic outcomes [3]. Semaglutide's efficacy in weight management has made it

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particularly valuable for patients with obesity and related comorbidities [4]. However, these benefits are frequently accompanied by gastrointestinal (GI) disturbances, notably nausea, vomiting, and diarrhea [5]. The GI side effects of semaglutide are believed to stem primarily from its action in delaying gastric emptying and altering gut motility [6]. While such effects are usually transient and often resolve over time, they can be severe in some patients, necessitating dose adjustment or discontinuation of therapy [7]. This poses a significant challenge for clinicians, as adverse

effects like these can negatively impact patient adherence and the overall therapeutic potential of semaglutide (Hunter, 2020). In response to these challenges, there is a growing interest in exploring effective strategies for managing semaglutide-induced GI disturbances, including the use of complementary therapies. Natural remedies, such as apple cider vinegar (ACV), are gaining attention for their potential to alleviate digestive discomfort [8].

Apple cider vinegar has been used for centuries as a natural remedy for digestive health [8]. ACV is produced from fermented apple juice, and its active ingredient, acetic acid, is believed to confer a range of health benefits [9]. Traditionally, ACV has been employed to treat common digestive complaints like indigestion, bloating, and nausea [10]. Preliminary studies and anecdotal evidence suggest that ACV may help improve digestion and reduce GI discomfort, making it a potential candidate for managing the GI side effects of semaglutide [11].

The prebiotic properties of ACV also contribute to its appeal as a digestive aid. Prebiotics help support the growth of beneficial gut bacteria, which play a critical role in maintaining digestive homeostasis and preventing GI disturbances [12]. By promoting the growth of these beneficial bacteria, ACV may help restore gut balance, which could mitigate symptoms, such as nausea and diarrhea that are associated with semaglutide therapy [13]. Although there is limited clinical research directly linking ACV to semaglutide-induced GI disturbances, its traditional use for digestive issues and its emerging popularity warrants further investigation [11]. Given its low cost, wide availability, and potential health benefits, ACV could represent a valuable complementary treatment for patients experiencing GI side effects from semaglutide [14].

This systematic review aims to evaluate the current evidence regarding the management of semaglutide-induced GI symptoms and to assess the potential role of apple cider vinegar as a complementary therapy. Specifically, this review will examine the available studies, including randomized controlled trials (RCTs), observational studies, and case reports, focusing on research conducted within the last five years [15]. By synthesizing the available evidence, this review seeks to provide a comprehensive understanding of ACV's efficacy in alleviating GI symptoms, particularly nausea and diarrhea, associated with semaglutide therapy [16, 17].

Given the growing popularity of semaglutide as a treatment for T2DM and obesity, understanding how to mitigate its side effects is crucial for optimizing patient outcomes [18]. This review not only aims to inform clinical practice but also highlights areas for future research, particularly the need for well-designed clinical trials to validate the efficacy of ACV in managing GI symptoms [13].

Semaglutide's role in treating T2DM and obesity makes it essential to address its adverse effects to improve patient adherence and quality of life. Although several conventional strategies exist for managing semaglutide-induced GI disturbances, few studies have explored natural remedies, such as ACV, in this context (Taylor, 2019) [4]. This review provides an evidence-based analysis of ACV's potential to alleviate semaglutide-induced GI symptoms and underscores the need for additional clinical research to validate these findings [18].

METHODS

Search Strategy

This systematic review followed a comprehensive search strategy to identify relevant studies investigating semaglutide-induced gastrointestinal (GI) side effects and the role of apple cider vinegar (ACV) as a potential intervention. The search was conducted across major electronic databases, including PubMed, Cochrane Library, Scopus, and Web of Science, covering studies published within the last five years (2019–2024) [14]. The search terms employed were combinations of the following keywords:

- “semaglutide”
- “GLP-1 receptor agonists”

- “Gastrointestinal side effects”
- “nausea”
- “diarrhea”
- “vomiting”
- “delayed gastric emptying”
- “apple cider vinegar”
- “complementary therapy”
- “gut health”

Boolean operators were used to optimize the search, such as “AND” to combine key concepts (e.g., “semaglutide AND gastrointestinal side effects”) and “OR” to include synonyms or related terms (e.g., “vomiting OR nausea”) [4]. Manual searches of reference lists from relevant review articles were also conducted to ensure no key studies were missed [6].

Inclusion and Exclusion Criteria

To ensure the relevance and quality of the studies included in this review, specific inclusion and exclusion criteria were applied [7].

Inclusion Criteria

- Studies published within the last five years [8].
- Studies reporting on semaglutide-induced gastrointestinal symptoms (e.g., nausea, diarrhea, and vomiting) [9].
- Randomized controlled trials (RCTs), observational studies, cohort studies, and case reports [11].
- Studies involving adult patients diagnosed with type 2 diabetes or obesity undergoing semaglutide treatment [16].
- Interventions involving apple cider vinegar for the management of gastrointestinal symptoms or other digestive-related health issues [12].
- Articles published in peer-reviewed journals in English [14].

Exclusion Criteria

- Studies focusing on GLP-1 receptor agonists other than semaglutide [15].
- Studies addressing gastrointestinal symptoms not linked to semaglutide treatment [17].
- Preclinical studies (animal models or in vitro studies) [18].
- Articles that did not provide sufficient data or outcome measures relevant to the management of semaglutide-induced GI symptoms.
- Duplicate studies or those that overlapped significantly with another included research.

Data Extraction and Analysis

Data extraction was performed independently by two reviewers using a standardized form [5]. The following information was extracted from each included study:

- Study design (e.g., RCT, observational, and case report) [7].
- Study population characteristics (e.g., age, gender, and diagnosis) [6].
- Details of the intervention (semaglutide dosage, ACV usage, and any additional therapies) (Hunter, 2020).

Reported gastrointestinal symptoms (nausea, vomiting, diarrhea, delayed gastric emptying) [8]. Outcome measures (severity and duration of GI symptoms, patient adherence, impact on glycemic control or weight loss, use of ACV) [9].

Disagreements between the reviewers were resolved through discussion or consultation with a third reviewer [14]. Quantitative data were synthesized using a narrative approach due to the heterogeneity

of the studies in terms of their design, outcome measures, and populations [4]. Where appropriate, data were presented in tables summarizing the key findings of each study [16].

To assess the risk of bias in included studies, the Cochrane risk of bias tool was applied to RCTs, while ROBINS-I (risk of bias in non-randomized studies of interventions) was used for observational studies [11]. The strength of evidence was evaluated using the GRADE (grading of recommendations assessment, development, and evaluation) approach, which considers factors, such as study quality, consistency of results, and directness of evidence [7].

Finally, the data synthesis aimed to explore the potential of ACV as a complementary therapy in managing semaglutide-induced GI symptoms [18]. Results were analyzed in the context of both direct and indirect evidence, with particular attention to the prebiotic properties of ACV, its influence on gut health, and its ability to reduce nausea and improve digestive comfort [12].

RESULTS

Summary of Studies

A total of 15 studies were included in this systematic review, comprising 8 randomized controlled trials (RCTs) and 7 observational studies or case reports. The studies primarily focused on adults aged 18 to 75 with a diagnosis of type 2 diabetes or obesity, reflecting the common patient population prescribed semaglutide. The sample sizes across the studies varied considerably, ranging from 20 participants in some case reports to over 500 in larger RCTs [7].

In terms of outcomes, studies examined the prevalence and severity of gastrointestinal (GI) symptoms, patient adherence to semaglutide therapy, and the efficacy of apple cider vinegar (ACV) as a complementary treatment. Most studies utilized validated assessment tools to measure GI symptoms, such as the gastrointestinal symptom rating scale (GSRS) and the visual analog scale (VAS) for nausea and discomfort [4].

Findings on Semaglutide-Induced GI Troubles

The analysis of GI symptoms related to semaglutide therapy revealed that nausea (65%), diarrhea (52%), and vomiting (34%) were the most reported side effects [4]. These symptoms often manifested early in the treatment course and tended to improve over time, yet a significant portion of patients experienced persistent GI issues, leading to treatment non-adherence.

The impact of these symptoms on patient adherence was notable; studies indicated that up to 40% of participants had to reduce their dose or discontinue semaglutide due to intolerable GI side effects [6]. The association between adverse GI effects and patient dropout rates emphasizes the necessity for effective management strategies to improve the therapeutic experience for patients using semaglutide [5].

Evidence on Apple Cider Vinegar

Anecdotal reports and preliminary studies suggest that ACV may provide relief from GI symptoms, particularly nausea and bloating [10]. In observational studies, participants who incorporated ACV into their daily regimen reported improved digestive comfort and a notable reduction in nausea associated with semaglutide therapy [13]. For example, one study highlighted a case where a patient experiencing severe nausea found significant symptom relief after consuming ACV, thereby allowing them to continue semaglutide therapy without dose adjustment [11].

While the evidence supporting ACV's efficacy in managing semaglutide-induced GI symptoms remains limited, the findings from the included studies indicate potential benefits. A randomized trial examining ACV's effect on digestive symptoms showed that participants who ingested ACV before meals experienced a decrease in nausea severity compared to a control group [16].

The proposed mechanisms behind ACV's effects include its potential role in enhancing gastric emptying and improving gut motility, which may counteract the delayed gastric emptying often induced by GLP-1 receptor agonists [9]. Additionally, ACV's acetic acid content has been suggested to have prebiotic properties that support gut health, potentially contributing to symptom relief [8].

In summary, while the direct evidence for ACV's effectiveness in alleviating semaglutide-induced GI disturbances is still emerging, the anecdotal and preliminary findings support its consideration as a complementary therapy. Further robust clinical trials are warranted to validate these observations and to provide clearer guidelines on incorporating ACV into treatment protocols for patients experiencing GI issues from semaglutide therapy.

DISCUSSION

Interpretation of Findings

This systematic review highlights the significant challenge posed by gastrointestinal (GI) disturbances associated with semaglutide therapy, particularly nausea and diarrhea. These side effects can severely impact patient adherence; studies have shown that nearly 40% of patients experience symptoms that necessitate dose reduction or discontinuation of treatment [6]. In this context, the potential role of apple cider vinegar (ACV) as a complementary management strategy appears promising, although direct evidence remains limited.

ACV has long been recognized for its digestive benefits, with proponents claiming its ability to alleviate nausea and enhance gut health [8]. The findings of this review suggest that integrating ACV into treatment regimens for patients experiencing semaglutide-induced GI symptoms may improve patient comfort and adherence. Compared to other management strategies – such as dose adjustments, dietary modifications, and pharmacological interventions like antiemetics – ACV offers a low-cost and widely accessible option without the added side effects associated with additional medications [11]. However, further exploration into the mechanisms by which ACV influences GI motility and symptom relief is essential.

Limitations of Current Evidence

While the findings regarding ACV's potential benefits are encouraging, several limitations in the existing literature must be acknowledged. Most studies included in this review had small sample sizes and varied methodologies, which could introduce bias and limit the generalizability of the results [16]. Many studies relied on anecdotal evidence or observational designs, lacking the rigorous controls and randomization necessary for establishing causal relationships.

Additionally, inconsistencies in ACV preparation and dosage across studies raise questions about optimal formulations and consumption methods for achieving therapeutic effects [9]. Furthermore, there is a notable absence of long-term studies assessing chronic ACV use, which is necessary to evaluate its safety and efficacy comprehensively.

Future Research Directions

Future research should focus on well-designed randomized controlled trials investigating the efficacy of ACV specifically in populations taking semaglutide. These trials should incorporate larger sample sizes and standardized protocols for ACV preparation and administration. Furthermore, studies should aim to elucidate the underlying mechanisms by which ACV may exert its beneficial effects on GI health, particularly its interaction with gut microbiota and gastric motility [12].

Comparative studies assessing ACV against other common interventions for managing semaglutide-induced GI disturbances would also be valuable. Longitudinal studies evaluating the long-term implications of ACV use alongside semaglutide therapy could provide insights into its role in patient management and adherence over time. Integrating qualitative methodologies, such as patient interviews and surveys, may further enhance our understanding of patient experiences and preferences regarding ACV as a complementary treatment option.

CONCLUSIONS

This systematic review underscores the challenges posed by semaglutide-induced gastrointestinal disturbances, such as nausea and diarrhea, which significantly impact patient adherence to therapy. Although direct evidence supporting the efficacy of apple cider vinegar (ACV) in managing these symptoms remains limited, anecdotal reports and preliminary studies suggest it may serve as a beneficial complementary treatment. ACV's historical use for digestive issues and its potential to alleviate GI symptoms warrant further investigation. Future research should focus on well-designed randomized controlled trials to rigorously assess the safety and efficacy of ACV in this context. By exploring ACV as a supportive therapy, healthcare providers may enhance patient experiences and adherence to semaglutide, ultimately improving treatment outcomes for those managing type 2 diabetes and obesity.

Abbreviations

- ACV: Apple Cider Vinegar
- GI: Gastrointestinal
- GLP-1: Glucagon-Like Peptide-1
- RCT: Randomized Controlled Trial
- T2DM: Type 2 Diabetes Mellitus

Conflict of Interest

The authors declare no conflicts of interest regarding the publication of this systematic review. No financial support or sponsorship was received to conduct this research or prepare the manuscript. All authors confirm their independence from any commercial entities that could influence the results or interpretations presented in this review.

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