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Contents

Monthly Volume 16 Number 5 May 16, 2024

EDITORIAL

ORIGINAL ARTICLE

Retrospective Study

Prospective Study

World Journal of Gastrointestinal Endoscopy

Monthly Volume 16 Number 5 May 16, 2024

Contents

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EDITORIAL

Has Coca-Cola treatment become the first-line therapy for gastric bezoars, both in general and specifically for western countries?

Maria Delgado Galan, Luis Ramon Rabago

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Abstract

Phytobezoars is a rare disease and less common in Western countries. The stomach is the primary site for these formations, and endoscopic treatment involving fragmentation and extraction has traditionally been the most effective approach. However, medical treatments using enzymatic and chemical agents, such as cellulase and Coca-Cola, aimed at dissolving the bezoars, have also been utilized, showing varying degrees of resolution success. Notably, the oral dissolution treatment with Coca-Cola has emerged as a promising, simpler, and more cost-effective method. The study by Liu *et al* represents an important step in clinical research on this topic, despite some limitations that need addressing for a more comprehensive understanding of its findings. Key considerations for future research include sample size calculation, endoscopic procedure details, outpatient vs. inpatient treatment, and detailed cost calculations. The study's exclusions, such as patients with upper gastric surgery, phytobezoars older than 14 d, and cases of gastroparesis, limit its applicability to broader populations, especially in Western countries. Given the promising outcomes of the Coca-Cola treatment, it's advocated as a first-line therapy for phytobezoars. Nonetheless, further research is essential to overcome these limitations. However special situations such as perforation or small bowel obstruction will require surgical treatment.

Key Words: Phytobezoars; Endoscopic treatment; Oral dissolution treatment with Coca-Cola; Randomized study; Editorial

Core Tip: The study by Liu *et al*, is a prospective randomized study about the treatment of gastric phytobezoars through daily intake of Coca-Cola *vs* endoscopic treatment, and represents an important step in clinical research on this topic. Given the promising outcomes of the Coca-Cola treatment observed in this study, which demonstrated a 100% success rate in dissolving phytobezoars and showed reduced costs and occurrence of gastric ulcers, it is recommended as a primary treatment option for phytobezoars. The study's exclusions, such as patients with upper gastric surgery, phytobezoars older than 14 d, and cases of gastroparesis, limit its applicability to broader populations, especially in Western countries.

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INTRODUCTION

Before delving into the discussion of this topic, we must first review some fundamental aspects of gastric bezoars, as shared by many authors previously. This includes understanding the concept of bezoars, the types of bezoars, and some epidemiological data. Gastric bezoars are accumulations of non-digestible material in the foregut that can form a large mass of residue, potentially obstructing the passage of the alimentary bolus[1].

The knowledge of animal bezoars has ancient roots, with the latest insights into human bezoars often traced back to Oriental medicine. The term "bezoar" originates from the Arabic word "badzher" or the Persian word "padzher", both translating to "antidote." Throughout history, bezoars have been associated with protective, anti-poisoning, and even mystical qualities.

Related to their composition, we can differentiate five types of bezoars[2]. The most common type of bezoar is the phytobezoar, primarily composed of residual non-digestible fibers, especially cellulose. A unique subtype of phytobezoar is the diospirobezoar, formed from the residue of consumed persimmons. The high concentration of tannins in the fruit's skin polymerizes upon contact with gastric acid and mucous, resulting in the formation of a bezoar from leftover food particles. These bezoars are characterized by their extreme hardness, making them difficult to treat.

The trichobezoar is composed of hair and is a rare condition typically found in patients, often women, with psychiatric disorders such as trichotillomania and trichophagia[3]. In some cases, the hair mass extends beyond the stomach into the small intestine or even the colon, a condition known as Rapunzel syndrome.

The pharmacobezoar forms from the accumulation of non-digestible drug excipients or substances used to transport drugs. The lactobezoar is made from milk products and is exclusively found in premature infants fed with various lactose-based formulas. The polybezoar is made up of various non-digestible materials such as plastics, paper, and other foreign substances. It often occurs in individuals with behavior alterations, such as psychiatric patients or those exhibiting pica behavior[4].

Bezoars are indeed uncommon occurrences, especially in Western countries[5], perhaps because persimmon consumption is less popular compared to Eastern[6], resulting in a scarcity of large-scale, comprehensive studies on the condition. Most of the available literature consists of small case investigations, with a notable absence of retrospective, multicentric series, and even fewer prospective studies. The reported incidence of bezoars varies, with a 0.5% occurrence among patients undergoing gastroscopies and a range of 0.4% to 4.8% among those investigated for bowel obstruction [1]. This variability highlights the infrequent nature of bezoars while also indicating a potentially higher prevalence within smaller populations characterized by specific risk factors or underlying conditions predisposing them to gastrointestinal obstructions.

Despite the lack of precise data regarding its prevalence in the general population, various events and circumstances are known to favor the development of bezoars[7]. Generally, any condition or disease that alters stomach anatomy or function, or delays gastric emptying, can promote bezoar formation. Therefore, gastric surgeries (especially partial gastrectomy and vagotomy) are significant risk factors. Other predisposing factors include gastric ulcers, Crohn's disease, gastric cancer, hypothyroidism, diabetes with gastroparesis[8], or medications that delay gastric emptying.

Symptoms and diagnosis

Although many affected individuals are asymptomatic, bezoars can produce a wide variety of symptoms, some of which can be severe. These symptoms may include dyspepsia, such as epigastric pain, epigastric fullness, abdominal discomfort, and early satiety. Sometimes, the mass can cause ulcers in the upper digestive tract, leading to bleeding with symptoms such as hematemesis, hematochezia, or melena, along with anemia. Additionally, the mass in contact with the digestive wall can result in necrosis and perforation, leading to the development of an acute abdomen with symptoms like fever, hypotension, sepsis, or gastrointestinal obstruction[1,6,9].

Iwamuro *et al*[6] described abdominal pain in 35% of patients in a series of 31 patients, with the most frequent complication being gastric ulcer, occurring in 64.5% of patients. Lee *et al*[10] reported a gastric ulcer rate of 41.2%. However, the incidence of gastric ulcers in Western series appears to be lower. For instance, Gökbulut *et al*[11] in a series of 66 patients reported a gastric ulcer rate of 27%. along with 11% of duodenal ulcers. Similarly, Ladas *et al*[12] reported a gastric ulcer rate of 21.7%.

Diagnosis relies on imaging studies such as endoscopic or radiologic examinations, with gastroscopy being particularly useful for diagnosing gastric bezoars. They typically appear as a single mass in the gastric fundus space, exhibiting variable coloration depending on their composition. In rare situations, multiple organic masses may be observed, and exceptionally rarely, impacted fiber food might be discernible in the esophagus. Computed tomography (CT) stands out as the favored radiologic method for assessing bezoars, offering a comprehensive visualization of their location, differentiation between singular or multiple masses, and detection of any potential complications. On a CT scan, bezoars may appear as ovoid or rounded masses, sometimes with air bubbles inside and a mottled pattern.

Treatments

Various treatment options are available for phytobezoars, including medical management, endoscopic intervention, and surgical procedures. The choice of treatment should be based on several factors, including the size, composition, and location of the phytobezoar, as well as any underlying conditions present in the patient.

Endoscopic treatments: Endoscopic treatments are widely recognized as the primary approach for managing phytobezoars and hold a significant role in the treatment of gastric bezoars around the globe are the most frequently and worldwide used treatment for fitobezoars. Its objective is to achieve mechanical fragmentation using various tools such as forceps, snare polypectomy, Dormie basket, or Roth net rescue net. Wang *et al*[13] reported a study involving 15 patients with bezoars measuring up to 10 cm in size. The initial intervention involved fragmentation using either a monopolar diathermy knife equipped with a 15 mm needle (bezotome) for trichobezoars, or a mechanical lithotripter. Successful resolution of the issue was achieved in all cases within a timeframe of 3 d.

In 2014, Kurt *et al*[14] Reported the first successful treatment of a large bezoar using a specially designed bezoaratom oval polyfilament snare, although this tool is not currently commercially available. Recently, in 2021, Toka *et al*[15] published a series involving 37 patients treated with a homemade bezoaratom, utilizing a 0.025 guidewire and an endoscopic retrograde cholangiopancreatography lithotripter. Their approach involved initial fragmentation of phytobezoars, followed by the addition of 2500 mL of Coca-Cola *per* day for 5 d, resulting in a 100% success rate in resolving all cases with a maximum of three endoscopic procedures. Ten patients with phytobezoars smaller than those in the Hu *et al*[16] cohort were published in 2022[16]. They were treated with another homemade mechanical lithotripsy method and the fragments were retrieved endoscopically.

In 1986, Naveau *et al*[17] published two cases of phytobezoars that failed to respond to enzymatic treatment with cellulase and were subsequently treated by Nd: YAG laser therapy. Both cases were successful, with the disappearance of the bezoar occurring in one case after a single session and in the other after three sessions.

Blam and Lichtenstein[18] published a report on three patients treated by direct aspiration of a bezoar using an endoscope with a large working channel of 6 mm (GIFT-XT30 Olympus). The procedure resulted in complete success, with the extraction of the bezoar accomplished in a single procedure, each lasting 20 min. The volumes of the bezoars extracted were 500, 700, and 1000 mL, respectively, and no complications were reported. Another longstanding endoscopic therapeutic approach, widely employed with notable success, is endoscopic Electrohydraulic Lithotripsy, such as the series which was published by Kuo *et al*[19] in 1999 with a 100% rate of success in one unique session and without complications.

Enzymatical and other solubilization treatments: Lastly, alternative therapeutic options involve solubilization treatments with various enzymatic compounds such as cellulase, papain, and N-acetylcysteine, or chemical substances like Coca-Cola, bicarbonate, physiological fluids, or pineapple juice. These treatments aim to dissolve phytobezoars.

The chemical compound most frequently used is Coca-Cola. Its use for the dissolution of phytobezoars is based on its acidic properties and the presence of carbonic and phosphoric acids, which can help break down the fibrous material in phytobezoars.

Several authors have shared their findings on the efficacy of Coca-Cola in treating phytobezoars, employing varying doses and durations of treatment. Despite differences in methodology, comparable outcomes have been consistently reported across the studies.

Ladas *et al*[20] in 2002 were the first to report a successful treatment with Coca-Cola. The same author conducted a literature review in 2012[12], covering 24 published articles from 2002 to 2012, which included a total of 46 patients. They found a 50% rate of dissolution of phytobezoars and subsequent resolution with fragmentation in 41.3% of cases, resulting in a successful treatment outcome for 91.3% of patients.

Interestingly, two patients who experienced complete chemical dissolution of their bezoars developed bowel obstruction within the first to sixth week of treatment, requiring surgical intervention[21].

This severe complication should be considered when using this type of treatment. Mihai *et al*[22] published a cohort study of 12 patients treated with 4.8 Liters of Coca-Cola ingested over 12 h, reporting a similar success rate. They observed complete dissolution in 42% of cases and resolution after endoscopic fragmentation in another 42% of cases.

In recent years, researchers like Ota *et al*[23] in 2022 have introduced a novel method for treating bezoars through chemical intervention, which involves directly injecting Coca-Cola into the phytobezoar. This approach presents several advantages compared to traditional methods such as oral intake or nasogastric administration, as it requires smaller amounts of Coca-Cola and shorter treatment durations. Consequently, it offers a viable option for patients who may be intolerant to Coca-Cola ingestion or those with obstructive small bowel syndromes. Following this line of treatment, Ota *et al*[23] later reported a case of successful treatment in a patient with pyloric obstruction using this technique, followed by endoscopic fragmentation and extraction of the fragments.

N-acetylcysteine, cellulase, and papain are other drugs with enzymatic properties used to dissolve phytobezoars. While adverse effects haven't been documented with the former two, instances of esophageal perforation, gastric

ulceration, and hypernatremia have been associated with papain. Cellulase offers a good safety profile; however, its availability is limited as it is not commercially available in all countries, thereby restricting its use.

Finally, some authors have proposed combined treatments with various chemical substances. Cerezo Ruiz *et al*[24] published two cases of bezoars treated with cellulase (1 capsule of 300 mg twice a day), pancreatin, ursodeoxycholic acid, omeprazole, levosulpiride, and Coca-Cola (660 mL/d) for 4 d. Recently, Shah *et al*[25] reported a case of gastric bezoar treated with 2 Liters of Coca-Cola *per* day and metoclopramide 10 mg three times a day for 3 d. In both cases, complete dissolution of the bezoar was achieved by the end of treatment.

Surgical treatments. Traditionally, surgical treatment has been the primary approach for managing bezoars. Despite the development of medical and endoscopic treatments, surgical intervention remains the preferred option in specific situations and circumstances. These include cases where the bezoar presents as an ileo-obstructive or small bowel obstruction, perforation, or when its location is inaccessible to other techniques. Moreover, surgical intervention might be warranted if prior attempts with medical or endoscopic methods have proven ineffective.

A noteworthy Korean study[26] published in 2021 examined 51 patients who received either endoscopic or surgical treatments for phytobezoars. The study aimed to uncover factors influencing treatment outcomes stressed the significance of timely diagnosis and intervention to avoid surgery and its potential complications. Findings revealed that patients over 65 and those with small bowel phytobezoars were more likely to require surgical intervention. Surprisingly, a history of gastric surgery didn't dictate the type of surgical treatment needed but was linked to a higher rate of complications.

DISCUSSION

The study by Liu *et al*[27] represents a significant contribution to the understanding and management of gastric phytobezoars, particularly given the rarity of the condition and the lack of large-scale studies comparing different treatment modalities. By conducting the first prospective clinical randomized single-blinded study to compare the efficacy of Coca-Cola ingestion with endoscopic treatment, the authors provide valuable evidence and information that may influence clinical practice, especially in Western contexts where this condition is less common.

It is highly surprising to note the number of patients with bezoars included in a unicentric study, which is something relatively rare in Western countries. Indeed, this study represents a significant contribution in the field, and recognizing its limitations is essential for a thorough interpretation of its impact. Although we will address specific limitations subsequently, it is imperative to note that they do not detract from the study's overarching significance.

Despite being a randomized trial, the article lacks a clear description of objectives and goals. Additionally, it fails to outline specific variables for analysis, which are crucial for determining the necessary sample size. lack of detail impedes the ability to perform a straightforward sample size calculation. Consequently, readers are referred to an external website for specifics regarding the calculation of the sample size, a direction that may not fully compensate for the lack of detailed methodology within the article itself. This oversight could potentially affect the robustness of the study's conclusions and its overall contribution to the field.

Furthermore, the article omits details on the conditions of the endoscopic procedures, specifically whether they were conducted under conscious sedation or general anesthesia. It also fails to clarify if the treatments were carried out on an outpatient basis. This lack of information could significantly impact the interpretation of the study's feasibility and applicability in different clinical settings.

Additionally, the article does not provide insights into the methodology used for cost calculation. This omission leaves readers without a clear understanding of how costs were computed, including what specific items were included in the cost analysis. Such information is crucial for evaluating the economic aspect of the treatments under investigation, making its absence a notable gap in the article's comprehensive reporting.

The etiology of phytobezoars in the Asian population[9], as demonstrated in this article, seems to diverge from the commonly observed trends in Western countries[1,5,7]. This could explain the large number of patients included in the study, which would typically be impossible in Western countries without a multicentric collaboration.

In Western societies, factors such as gastric surgery, vagotomy, and gastroparesis are recognized as significant contributors to the formation of phytobezoars[7]. On the other hand, the evaluation of the size of the phytobezoar is not sufficiently objective, especially when more reliable radiologic methods are available for this purpose.

The article provides important information regarding the treatment of phytobezoars with Coca-Cola, revealing a notably high success rate in phytobezoar dissolution. This outcome, surpassing previous reports in the literature[12,22] may be linked to the substantial volume of Coca-Cola ingested over the course of 7 d. Nonetheless, the practicality of this treatment approach raises questions, particularly concerning its suitability for patients who have undergone gastric surgery. The tolerance of such patients to the prescribed volume of Coca-Cola warrants careful consideration, given that their altered gastric anatomy might influence both the efficacy of the treatment and the patient's ability to consume the beverage without adverse effects.

Furthermore, the authors' decision to exclude patients with gastric surgeries undermines the reader's confidence in the efficacy of the dissolution treatment for this subgroup. Coupled with the lack of explanation for this exclusion, the absence of information about this issue not only diminishes the study's generalizability but also raises doubts about the tolerability and safety of consuming the required amount of Coca-Cola in individuals with gastric remnants. Consequently, readers are left without assurance regarding the effectiveness and safety of the dissolution treatment in patients who have undergone gastric surgeries. Clarifying the rationale behind this exclusion would have provided valuable insights into the applicability of the treatment across different patient populations and improved the interpretation of the study's findings.

Additionally, it should be noted that the study did not encompass patients with phytobezoar diagnoses lasting beyond 14 d, yet no rationale was offered for this exclusion criterion. This absence of explanation warrants attention as it potentially excludes patients with more matured phytobezoars, which might present greater challenges in terms of fragmentation and dissolution using Coca-Cola.

Despite limitations in the methodology, which could have been rectified, the written paper remains informative and valuable. This study represents a pioneering randomized single-blinded trial that evaluates two treatment modalities, shedding light on their efficacy. The findings not only corroborate the viability of this treatment approach with a notable success rate and without necessitating endoscopic intervention but also yield insights into an inexplicable reduction in gastric ulcer incidence and substantial cost savings.

The remarkable dissolution rate of phytobezoars, notably higher than previously documented in the literature, may be attributed to the prolonged consumption of Coca-Cola in significant quantities. However, a key consideration is whether patients who have undergone gastric surgery would exhibit similar tolerance to such quantities of the beverage.

The lower rate of ulcers observed in the group treated with Coca-Cola compared to the control group is noteworthy. However, the underlying reasons for this disparity remain unclear, as it is not clearly established whether the confirmation of the existence of gastric ulcers occurred at the time of diagnosis or when the final treatment concluded. Nevertheless, this observation merits additional investigation due to its profound implications.

One aspect that warrants further investigation is the potential impact of the duration of the dissolution treatment on ulcer formation. The significance of the treatment duration in influencing this outcome remains uncertain and merits further exploration. Understanding the relationship between treatment duration and ulcer development could provide valuable insights into optimizing the therapeutic approach for phytobezoar dissolution.

Regarding the lesser costs of the dissolution treatment, we will have to believe it, but we do not have enough data to analyze, and for sure it another important data to support this treatment option.

Indeed, the purported lower costs associated with the dissolution treatment present an intriguing aspect of this study. However, due to insufficient data provided, conducting a thorough cost analysis proves challenging. Therefore, obtaining comprehensive data on the costs associated with dissolution treatment would be valuable for supporting its adoption as a viable treatment option for phytobezoars.

Finally, when considering management options for other types of gastric bezoars, several approaches can be explored. Endoscopic interventions utilizing mechanical fragmentation techniques such as dormie basket lithotripsy, snare polypectomy, or improvised lithotripters employing a 0.0035 guidewire to round the phytobezoar are viable options contingent upon the bezoar's dimensions. Alternatively, the injection of Coca-Cola into these bezoars using a large Injection Needle Catheter, akin to those employed in deflating intragastric balloons, or employing electrohydraulic lithotripsy or laser lithotripsy may be viable alternatives. However, vigilant patient monitoring is imperative until all phytobezoar fragments have passed through fecal matter, particularly if they were not eliminated through endoscopic means.

CONCLUSION

In summary, the utilization of a chemical dissolution treatment, particularly through the application of Coca-Cola over a week-long period, presents itself as a viable primary treatment approach for gastric phytobezoars. This method aims to effectively promote their expulsion *via* fecal matter. This approach seems to reduce the occurrence of gastric ulcers, lower expenses and might circumvent the need for potentially risky endoscopic procedures. However, additional investigation is required to evaluate the effectiveness of this approach in patients with a history of gastric surgery, vagotomy, gastroparesis, or other conditions that might impact gastric motility or anatomy. Despite these constraints, this assay offers valuable clinical insights for medical practice. It's essential for future research to expand on this groundwork, possibly addressing these limitations and delving deeper into the comparative effectiveness of diverse treatments for gastric or intestinal bezoars. Such efforts could advance our comprehension and handling of this rare yet complex condition.

All in all, the article offers valuable insights into the issue at hand. However, Western readers might view it as preliminary rather than definitive. Moving forward, it would be beneficial to conduct additional multicenter studies exploring the efficacy of Coca-Cola treatments in populations excluded from this paper within Western countries.

FOOTNOTES

Author contributions: Delgado Galan M conducted the literature review on the topic, while Rabago LR concentrated on the critical analysis of the randomized trial's discussion and conclusion.

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