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*Clinical Trials Study*

**Coca-Cola Consumption vs Fragmentation in the Management of Patients with Phytobezoars: A Prospective Randomized Controlled Trial**

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**Abstract**

BACKGROUND

Gastric phytobezoars (GPBs) are very common in northern China. Combined therapy involving carbonated beverage consumption and endoscopic lithotripsy has been shown to be effective and safe. Existing studies on this subject are often case reports highlighting the successful dissolution of phytobezoars through Coca-Cola consumption. Consequently, large-scale prospective investigations in this domain remain scarce. Therefore, we conducted a randomized controlled trial to examine the effects of Coca-Cola consumption on GPBs.

AIM

To evaluate the impact of Coca-Cola on GPBs, including the dissolution rate, medical expenses, ulcer rate, and operation time.

METHODS

A total of 160 consecutive patients diagnosed with GPBs were allocated into two groups (a control group and an intervention group) through computer-generated randomization. Patients in the intervention group received a Coca-Cola-based regimen

(Coca-Cola 2000-4000 mL per day for 7 days), while those in the control group underwent emergency fragmentation.

## RESULTS

Complete dissolution of GPBs was achieved in 100% of the patients in the intervention group. The disparity in expenses between the control group and intervention group ( $t=25.791$ ,  $P=0.000$ ) was statistically significant, and the difference in gastric ulcer occurrence between the control group and intervention group ( $X^2=6.181$ ,  $P=0.013$ ) was also statistically significant.

## CONCLUSION

Timely ingestion of Coca-Cola yields significant benefits, including a complete dissolution rate of 100%, a low incidence of gastric ulcers, no need for fragmentation and reduced expenses.

## INTRODUCTION

Gastric bezoars (GBs) are defined as foreign objects that develop within the gastrointestinal tract due to the accumulation of ingested material<sup>[1]</sup>. Specifically, GPBs were consisted of indigestible cellulose, tannin, and lignin derived from the consumption of persimmons, hawthorn fruits, or date plum persimmons. Tannin undergoes polymerization, resulting in a coagulum that includes protein, pepsins, cellulose, and hemicellulose, forming bezoars<sup>[2]</sup>. In recent years, a combined therapy approach involving litholysis with carbonated beverages and endoscopic lithotripsy has emerged as an effective and safe treatment for GPBs<sup>[3]</sup>. However, despite the excellent outcomes, this therapeutic approach causes significant discomfort and has high costs and a prolonged operation time<sup>[4]</sup>. Notably, in 2013, S. D. Ladas proposed the consumption of Coca-Cola as a first-line treatment option, highlighting its ability to effectively dissolve GPBs<sup>[5]</sup>. Coca-Cola consumption has been recognized as a

particularly safe, cost-effective, and well-tolerated intervention <sup>[6]</sup>. While case reports documenting the successful dissolution of phytobezoars exist, large-scale clinical studies in this domain are scarce. Therefore, we conducted a randomized controlled trial to evaluate the impact of Coca-Cola consumption on GPBs, including the dissolution rate, medical expenses, ulcer rate, and operation time.

## **MATERIALS AND METHODS**

### ***Study design and sample estimation***

This meticulously designed study followed a prospective, single-blinded approach with balanced randomization at a 1:1 ratio. Ethical approval for the study was obtained from the Institutional Review Board of the Affiliated Hospital of Qingdao University (QYFYWZLL 26293), and the study was registered in the ClinicalTrial.gov Protocol Registration System with the registration number NCT05645263. The study was conducted at the Affiliated Hospital of Qingdao University from January 1st, 2018, to December 1st, 2022. All participants who expressed willingness to take part in the study provided digital informed consent. The study strictly adhered to the principles outlined in the World Medical Association Declaration of Helsinki.

The sample size was calculated using the following website: <http://riskcalc.org:3838/samplesize/>. Ultimately, a total of 160 patients (2 arms) were enrolled in the study and randomly allocated to the control or intervention group at a 1:1 ratio.

### ***Participants***

The study employed specific inclusion and exclusion criteria to ensure the selection of appropriate participants. The inclusion criteria encompassed the absence of contraindications (such as severe heart diseases, suspected shock, or digestive tract perforation), suspected mental diseases, or infectious diseases of the digestive tract that could hinder gastroscopy. Additionally, participants were required to have a bezoar history of no more than 14 days, no history of peptic ulcer diseases and an age range between 14 and 80 years. The exclusion criteria comprised individuals who had history

of upper GI surgery, underwent previous therapies before enrollment or individuals who did not consent to random allocation.

#### *Equipment and consumables*

The following instruments and materials were used in this study: CV-290 (Olympus Co. Ltd), GIF-Q260J (Olympus Co. Ltd), the WF-DTH fragmentation kit (Wilson Shanghai Co. Ltd), disposable snares (Micro-Tech Nanjing Co. Ltd), and Coca-Cola.

#### **METHOD**

A total of 160 consecutive patients were enrolled in the study by doctors in the outpatient department and randomly assigned at a 1:1 ratio to either the control group, which underwent emergency fragmentation with gastroscopy, or the intervention group, which consumed Coca-Cola in the endoscopy center. The enrollment period spanned from January 1st, 2018, to December 1st, 2022. Randomization was conducted by the investigator using a web-based computer-generated random number system ([www.randomization.com](http://www.randomization.com)). In the intervention group, patients consumed Coca-Cola to treat GPBs. The amount consumed was 250 mL-500 mL every 2 h until bedtime, tailored to individual health conditions and lifestyle habits. Close attention was given to the patients' bowel movements to assess the excretion of bezoars (which are usually harder than normal stool and not scattered by flushing water). The duration of Coca-Cola ingestion was 7 days for the intervention group. Upon completion of the Coca-Cola therapy, patients underwent another endoscopy because endoscopy can observe the mucosa of the stomach directly and further intervention if fragmentation was necessary. The endoscopist recorded all images for every patient. The volume of GPBs was estimated under endoscopy and the evaluation for gastric ulcer was performed in the first endoscopy. Prior to endoscopy, all patients provided digital informed consent.

Statistical analysis was performed using SPSS version 22 (IBM, Inc. Armonk, NY, USA). Continuous variables are presented as the mean and standard deviation (SD). Independent samples t test was utilized for continuous variable analysis. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. A significance level of  $P < 0.05$  was considered statistically meaningful.

## **RESULTS**

*The CONSORT 2010 Flow Diagram is illustrated in Figure 1.*

*Atypical images pertaining to the study findings are shown in Figures 2 and 3*

The images of Figure 2 and Figure 3 are all from the intervention group. The patient in Figure 2 has a GPB history of 7 days and the patient in Figure 3 has a GPBs history of 14 days. The former 2 images of Figure 2 shows the GPBs in the stomach and an ulcer which is shallow and bleeding located in the angulus in the first endoscopy and the last image shows nothing anomaly except the ulcer in the second endoscopy after Coca-Cola therapy. The former 2 images of Figure 3 shows the GPBs in the stomach and a deep ulcer located in the angulus in the first endoscopy and the last image shows nothing anomaly except the shallower ulcer in the second endoscopy after Coca-Cola therapy.

**Figure 2** Image of GPBs in a patient with a GPBs history of 7 days. The gastric ulcer, which is shallow and bleeding located in the angulus of the stomach; no GPBs or bleeding in the stomach was observed after Coca-Cola therapy.

**Figure 3** Image of GPBs in another patient with a GPBs history of 14 days. A deep gastric ulcer is located in the angulus of the stomach; no GPBs was observed and the gastric ulcer became smaller and shallower after Coca-Cola therapy.

### ***General data***

Data on age, bezoar volume and medical expenses are presented in Table 1. There were no statistically significant differences in age or bezoar volume between the 2 groups, but there was a significant difference in medical expenses.

### ***Dissolution rate***

Remarkably, a complete dissolution rate of 100% was achieved in the intervention group, highlighting the effectiveness of the intervention in treating GPBs.

### ***Medical expenses***

Table 1 provides information regarding the medical expenses incurred during the study. The statistical analysis revealed significant differences in the medical expenses



between the control and intervention groups. ( $1540.01 \pm 250.81$  RMB vs.  $27.59 \pm 7.96$  RMB,  $t=25.971$ ,  $P = 0.000$ ).

### ***Operation time***

The gastric fragmentation time of the control group was  $31.23 \pm 9.62$  min; however, no patients had gastric fragmentation in the intervention group.

### ***Gastric ulcer rate***

Information on the occurrence of gastric ulcers between the control and intervention groups is presented in Table 2. The rate of gastric ulcer occurrence was 86.25% in the control group and 70.0% in the intervention group. Notably, a statistically significant difference was observed between the control group and intervention group in terms of gastric ulcer occurrence ( $\chi^2=6.181$ ,  $P = 0.021$ ). The results shed light on the varying rates of gastric ulcer occurrence associated with different treatment approaches.

## **DISCUSSION**

GPBs often arise from the ingestion of persimmons, hawthorn fruits, or date plums on an empty stomach. They can also be associated with conditions such as diabetic gastroparesis<sup>[7]</sup> and endoscopic sclerotherapy, which can lead to delayed gastric emptying<sup>[8, 9]</sup>. In the present study<sup>[10]</sup>, patients were successfully treated using a combination of endoscopic fragmentation and pharmacotherapy. While this combined therapy has been indicated to be effective, it involves high costs, discomfort, and long operation time.

A significant milestone in the use of Coca-Cola for phytobezoar treatment was the publication of the article "Gastric phytobezoars may be treated by nasogastric cola lavage" in 2002 by S. D. Ladas, *et al*<sup>[11]</sup>. This study documented complete success in the treatment of five phytobezoar patients using Coca-Cola lavage. In a systematic review conducted by S. D. Ladas in 2013, it was concluded that Coca-Cola can effectively dissolve GPBs and could be considered a first-line treatment option, with a complete dissolution rate of 50% and a favorable outcome observed in 91.3% of patients<sup>[5]</sup>. It has been reported that the consumption of 3 Liters of Coca-Cola every 12 h has a

satisfactory effect on bezoar lysis<sup>[5, 12, 13]</sup>. Our study demonstrated a complete phytobezoar dissolution rate of 100%, which aligns with previous findings.

The article "In Vitro Analysis of Gastric Phytobezoar Dissolubility by Cola, Cola Zero, Cellulose and Papain" reported that Coca-Cola exhibited the highest phytolytic activity, with an  $18.5\% \pm 5.8\%$  decrease in weight, while Coke Zero also demonstrated substantial phytolytic action ( $16.1\% \pm 0.4\%$ ). In patients who consumed carbonated beverages, bezoars were easily broken when grasped with forceps, which was not observed in patients who consumed water, cellulose or papain. These findings provide scientific evidence supporting the efficacy of Coca-Cola in bezoar lysis<sup>[14]</sup>. Although the exact mechanism of the dissolution of bezoars by Coca-Cola has not been fully explained, it may be attributed to the low acidity. The pH of Coca-Cola is 1.9, which is more acidic than that of 0.010 mol/L hydrochloric acid (pH 2.0). Furthermore, the pH of Coca-Cola remains relatively stable (2.0) even after 3 h of exposure to room air <sup>[12]</sup>. The dissolution effect of Coca-Cola on bezoars may be attributed to carbonic and phosphoric acids, which are believed to be important for fiber digestion <sup>[7, 12, 13, 15]</sup>. Acetic acid ( $\text{CH}_3\text{COOH}$ ) reacts with calcium phosphate to form calcium acetate [ $\text{Ca}(\text{CH}_3\text{COO})_2$ ] and phosphoric acid, both of which are water-soluble<sup>[16]</sup>(16). Additionally, the mucolytic effect of  $\text{NaHCO}_3$  and the presence of  $\text{CO}_2$  bubbles may contribute to the mechanism of dissolution <sup>[12]</sup>. The consumption of a large volume of Coca-Cola can enhance gastrointestinal motility, leading to the rapid decomposition and elimination of phytobezoars. "Cola lysis" serves as a clinically appropriate term to describe the mechanism of phytobezoar dissolution, signifying the dissolution and lysis of the accumulated mass<sup>[7]</sup>.

In terms of adverse effects, short-term Coca-Cola therapy may cause temporary bloating, reflux, and gastritis. However, the long-term use of Coca-Cola can lead to tooth decay and osteoporosis. These issues should be taken into account when utilizing Coca-Cola as a therapeutic intervention for GPBs. The participants in our study had no obvious side effects because of the short regimen.



Intestinal obstructions caused by phytobezoars are a rare occurrence in adults with normally functioning intestinal tracts<sup>[17]</sup>. However, in cases where ileus is present or when patients have refractory bezoars, surgical removal becomes necessary<sup>[18]</sup>. Avoiding severe complications associated with phytobezoars poses a challenge for medical professionals. Partially dissolved bezoars have the potential to pass through the pylorus and obstruct the small bowel, particularly in the presence of ankylosis, enterostasis, or poor gastric motility <sup>[13, 19-25]</sup>. Therefore, it is crucial for patients receiving Coca-Cola therapy to be vigilant about their stool and monitor symptoms of ileus. Once a patient is confident that the bezoar has been discharged in the stool, they can discontinue the Coca-Cola diet to prevent small bowel obstruction. The duration of Coca-Cola consumption can be prolonged as necessary without any set limitations. Additionally, a low-fiber diet during Coca-Cola therapy is recommended to support the treatment process.

GPBs as foreign bodies located in the stomach, can cause mechanical friction and/or compression, leading to erosion, ulceration, or bleeding of the gastric mucosa <sup>[2]</sup>. The incidence of gastric ulcers associated with phytobezoars is approximately 80% <sup>[26]</sup>. The presence of a gastric bezoar can result in gastric mucosal injury, but as the bezoar dissolves, the gastric mucosa becomes less affected. In our study, the gastric ulcer occurrence <sup>1</sup>rate in the intervention group (70.00%) was lower than that in the control group (86.25%). This lower rate of gastric ulcers in the intervention group may be attributed to the consumption of Coca-Cola. Coca-Cola softens bezoars <sup>[27]</sup>, and the gastric mucosa becomes less irritated once bezoars are softened. Gastric ulcers can manifest as single or multiple lesions located in various regions of the stomach, including the angulus, body, or antrum. The overall occurrence of gastric ulcers in our study was 78.13%, which aligns with previous findings. The timely administration of Coca-Cola appears to yield better outcomes, as the occurrence rate of gastric ulcers decreases with the dissolution of bezoars.

## CONCLUSION

Treating GPBs with Coca-Cola consumption offers a practical, cost-effective, and effective approach. Patients with GPBs should consume Coca-Cola at the earliest opportunity to minimize the occurrence of gastric ulcers, making it a routine practice in clinical settings. However, the optimal dosage and duration of Coca-Cola ingestion for treating GPBs have not been definitively established through large-scale experimental studies. Therefore, further extensive research is warranted to investigate and establish guidelines regarding the appropriate dose and duration of Coca-Cola consumption in the treatment of GPBs.

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