The Effect of Oral Cola Ingestion for Endoscopic Inspection of Remnant Stomach: Randomized Case Control Study

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Background/Aims: Nasogastric administration of cola for dissolution of phytobezoar was reported but the mechanism is not well understood. We aimed to evaluate the efficacy of cola ingestion for upper gastrointestinal endoscopy in patients who have had distal gastrectomy.

Materials and Methods: Patients were enrolled from July 2007 to October 2007 and all previously received subtotal gastrectomy. We conducted a randomized case-control study which the patients were randomly assigned to two groups. Group A had preparation with cola and group B had no preparation. Cola preparation group ingested about 1,500 mL of cola between 7 PM to 10 PM in the evening before the procedure. Two examiners who were blinded to the type of preparation performed the endoscopy. We assessed the degree of food residue and bile reflux by Japanese classification.

Results: A total of 70 patients were included. The comparison of clinical and laboratory characteristics between the two groups showed no statistically significant difference. During endoscopy, food residue was less found in group A than B, but without statistically significance (group A=12.1%, group B=21.6%, P=0.087). However, bile reflux was significantly less found in group A than B (group A=36.4%, group B=67.6%, P=0.015). Multivariate analysis, cola preparation significantly reduced food residue (OR, 0.032; P=0.001) and bile reflux (OR, 0.102; P=0.001).

Conclusions: Preparation with cola in the evening before endoscopic examination may provide a good quality of preparation in patient with remnant stomach after distal gastrectomy. (Korean J Helicobacter Up Gastrointest Res 2014;14:39-44)

Key Words: Cola; Gastric stump; Gastrectomy; Food residue; Bile reflux

INTRODUCTION

Gastric cancer is the most common cancer and ranks third for cancer mortality in Korea.1,2 Currently, gastrectomy is the only known curative treatment modality for gastric cancer. Due to recent rise in attention to cancer prevention and aggressive surgical treatment, overall survival of gastric cancer patient has been increasing in Korea.3 As cancer recurrence in remnant stomach is increasing due to prolonged survival of gastric cancer patients, its proper surveillance has been an important issue.4 Upper gastrointestinal (UGI) endoscopy is known to be beneficial for detailed observation of the gastric remnant, and has been widely performed as a follow-up examination after distal gastrectomy.5,6

However, endoscopic inspection of a remnant stomach after distal gastrectomy is technically difficult. The narrow luminal space, loss of pyloric function to trap the inflated air, anatomical deformity, food residue, bile reflux and erythema due to gastritis makes the examination a lot more difficult.

Therefore, appropriate preparation to remove food residue material and refluxed bile juice is essential for proper inspection of the remnant stomach. Recently, efficacy of nasogastric administration of cola for the dissolution of gastric phytobezoar was reported.7,8 However, study on its application on remnant stomach after gastric cancer surgery is yet to be published.

In this study, we assumed that oral cola ingestion would influence food digestion and bile reflux in the remnant stomach and aimed to evaluate the efficacy of cola ingestion as the preparation for UGI endoscopy in patients who have had a distal gastrectomy.
MATERIALS AND METHODS

1. Patients

From July 2007 to October 2007, 70 consecutive patients who previously received subtotal gastrectomy in Korea University Guro Hospital (Seoul, Korea) were enrolled for the study. Among them, patients who are planned to receive UGI endoscopy for postoperative surveillance of gastric cancer surgery were eligible for inclusion. Exclusion criteria were history of diabetes, schedule of concomitant total colonoscopy and refusal to enrollment. During the surgery, reconstruction was performed using Billroth I procedure in 52 patients and Billroth II procedure in 18 patients.

2. Study design

We conducted a randomized case-control study which the patients were randomly assigned to two groups. From the total of enrolled 70 patients, 33 patients were assigned to cola preparation group (group A) and 37 patients were assigned to no preparation group (group B). All patients received written instructions on their diet preparation regimen before the endoscopic examination. The preparation included soft meal diet at 6 PM and finishing before 7 PM. All medications which could influence gastric emptying (levosulpride, metoclopramide, domperidone, etc.) were to be stopped from the evening before examination until the end of the endoscopic examination. The cola preparation group ingested about 1,500 mL of cola (The Coca-Cola Company, Atlanta, GA, USA) between 7 PM to 10 PM on the evening before the examination. We had decided to enroll patients who ingested more than 1,200 mL of cola and all of the 70 patients finally were enrolled. No preparation group kept fasting since finishing their evening dinner. At the day of examination, all patients had UGI endoscopy performed by two experienced endoscopists (either experienced more than 50,000 UGI endoscopy cases). Both endoscopists were highly specialized in the diagnosis and treatment of UGI tract cancer. The endoscope used was an Olympus GIF Q260 or H 260 (Olympus, Tokyo, Japan). All examinations took place between 9 AM to 12 PM. Both examiners were blinded to the type of bowel preparation. Before the study, informed consent was obtained from all participated patients and the protocol was approved by Korea University institutional review board.

3. Classification of food residue and bile reflux

At UGI endoscopic examination, the endoscopists assessed the degree of food residue and bile reflux as classification system reported by Kubo et al. The degree of food residue was divided into five grades: grade 0, no food residue; grade 1, a small amount of food residue; grade 2, a moderate amount of food residue, but possible to observe the entire surface of the remnant stomach with body rolling; grade 3, a moderate amount of food residue, which hinders observation of the entire surface even with body rolling; and grade 4, a great amount of food residue, for which endoscopic observation is impossible. The bile reflux was divided into three grades: grade 0, absence of bile reflux; grade 1, presence of bile reflux but possible to observe entire surface of the remnant stomach without saline irrigation; grade 2, presence of bile reflux but impossible to observe entire surface of the remnant stomach without saline irrigation.

4. Statistical analysis

The data were analyzed by SPSS version 12.0 for Windows (SPSS Inc., Chicago, IL, USA). The proportion of degree of food residue and bile acid were compared using chi-square analysis. The odds ratio for food residue and bile reflux was obtained on 6 different clinical characteristics by using multiple logistic regression analysis. The level of significance was set at $P<0.05$.

RESULTS

1. Patient characteristics

The comparison of basal clinical characteristics of two patient groups is summarized at Table 1.

The mean age of the cola preparation group (group A) and no preparation group (group B) was 59.9±12.02 and 59.06±12.1 years respectively. Among 33 and 37 patients from group A and B, 17 and 25 patients were male, respectively. In group A, 20 of the primary gastric cancer before surgery was located at the antrum and 13 at
Table 1. The Comparison of Basal Clinical Characteristics of Two Patient Groups

| Characteristic                          | Cola preparation group (group A) | No preparation group (group B) | P value |
|----------------------------------------|----------------------------------|--------------------------------|---------|
| Age (yr)                               | 59.9±12.02                      | 59.06±12.1                     | 0.756   |
| Gender                                 |                                  |                                | 0.171   |
| Male                                   | 17                               | 25                             |         |
| Female                                 | 16                               | 12                             |         |
| Tumor location                         |                                  |                                | 0.099   |
| Antrum                                 | 20                               | 29                             |         |
| Corpus                                 | 13                               | 8                              |         |
| Reconstruction type                    |                                  |                                | 0.376   |
| Billroth I                             | 27                               | 25                             |         |
| Billroth II                            | 6                                | 12                             |         |
| Food residue more than grade 1 in the previous endoscopic examinations | 13 | 8 | 0.099 |
| Endoscopic examination within 6 months from surgery | 6 | 12 | 0.376 |
| Operation to endoscopy interval (mo)   | 48.5±82.1                        | 49.7±66.0                      | 0.942   |

Values are presented as n or mean±SD.

Table 2. Multiple Logistic Regression Analysis of Risk Factors for Food Residue between Cola Preparation Group and No Preparation Group

| Variable                      | Crude OR (95% CI) | Adjusted OR (95% CI) | P value |
|-------------------------------|-------------------|----------------------|---------|
| Age (yr)                      | 1.04 (1.00 ~ 1.10) | 0.957 (0.88 ~ 1.03)  | 0.199   |
| Cola preparation              | 0.251 (0.92 ~ 0.69) | 0.052 (0.01 ~ 0.42)  | 0.001   |
| Operation to endoscopy interval (mo) | 1.00 (0.994 ~ 1.001) | 1.055 (0.99 ~ 1.12) | 0.09    |
| Gender                       | 0.783 (0.30 ~ 2.05) | 3.134 (0.38 ~ 25.54) | 0.61    |
| Location                     | 0.885 (0.30 ~ 2.61) | 0.318 (0.31 ~ 37.14) | 0.32    |
| Operation type               | 0.18 (0.05 ~ 0.62) | 0.00 (0.00 ~ 0.00)    | 0.09    |

In group B, 25 had Billroth I and 12 had Billroth II. Thirteen and eight patients had shown food residue more than grade 1 at least once in the previous endoscopic examinations and in group A and B, respectively. The surgery to endoscopy interval was also compared as group A showed mean interval of 48.5±82.1 months and in group B, 49.7±66.0 months. Additionally, there were 6 patients in group A and 12 patients in group B who underwent endoscopic examination in 6 months after surgery in this study. All six basal clinical characteristics between the two study groups showed no significant statistical difference.

The study protocol was well tolerated. No patient had any problems with drinking 1,500 mL of cola for preparation of UGI endoscopic exam. Also, no adverse event related to cola ingestion was reported.

2. Food residue

The Fig. 1 shows the percentage of patients in each group that is classified into each food residue grade. Through endoscopic examination, 12.1% of group A and 21.6% of group B showed food residue (group A vs. group B: P=0.087). Although it did not have statistically significant difference, group A expressed a trend of having less food residue than group B. In group A, 29 patients (87.9%) showed no food residue and two patients each was classified as grade 1 and 2 respectively. Meanwhile, group B had six patients classified as grade 1.


Table 3. Multiple Logistic Regression Analysis of Risk Factors for Bile Reflux between Cola Preparation Group and No Preparation Group

| Variable                        | Crude OR (95% CI) | Adjusted OR (95% CI) | P value |
|---------------------------------|-------------------|----------------------|---------|
| Age (yr)                        | 1.04 (1.00 ~ 1.10)| 1.036 (0.98 ~ 1.01) | 0.199   |
| Cola preparation                | 0.251 (0.92 ~ 0.69)| 0.102 (0.03 ~ 0.43) | 0.001   |
| Operation to endoscopy interval (mo) | 1.00 (0.994 ~ 1.001)| 1.005 (0.99 ~ 1.01) | 0.525   |
| Gender (Male vs. female)        | 0.783 (0.50 ~ 2.05)| 0.792 (0.47 ~ 1.35)| 0.609   |
| Location (Antrum vs. corpus)    | 0.885 (0.50 ~ 1.59)| 1.868 (0.57 ~ 6.14)| 0.373   |
| Operation type (Billroth I vs. Billroth II) | 0.18 (0.05 ~ 0.59)| 0.094 (0.02 ~ 0.43)| 0.002   |

3. Bile reflux

The Fig. 2 shows the percentage of patients in each group that is classified into each bile reflux grade. Bile reflux of group A was 36.4% and in group B, 67.6% which showed statistical difference (P=0.015). While 21 patients (65.6%) in group A showed no bile reflux and 10 patients and 2 patients were classified as grade 1 and 2 (30.3%, 6.1% respectively), group B had only 12 patients with no reflux (32.4%) and 24 and 1 patient classified as grade 1 and 2 (64.9%, 2.7%, respectively). Odds ratio of bile reflux by logistic regression analysis in cola preparation was 0.102 (95% CI, 0.03 ~ 0.42; P=0.001) (Table 3).

3. Bile reflux

Fig. 2. Comparison of bile reflux grade between cola preparation group (group A) and no preparation group (group B). Bile reflux grade is defined as grade 0, absence of bile reflux; grade 1, presence of bile reflux but possible to observe entire surface of the remnant stomach without saline irrigation; grade 2, presence of bile reflux but impossible to observe entire surface of the remnant stomach without saline irrigation.

In a recent study, Watanabe et al. reports that 18.7% of the patients who had distal gastrectomy showed food residue at endoscopy. Another study by Jung et al. which included higher proportions of patients who had underwent Billroth I anastomosis reports even higher percentage of food residue of 42%. It is also well known that phytobezoars are common in remnant stomach. These numbers are consistent to our results which show that sufficient fasting time alone is not enough for satisfying preparation before UGI endoscopic examination.

Numerous factors such as the loss of normal gastric motility, pyloric function, low gastric acidity and anatomical deformity are generally known to be associated to food retention and bezoar formation after gastrectomy. Also, several studies report that underlying endocrine or metabolic disorder, postoperative gastric retention and Billroth I reconstruction were independent risk factors.

Meanwhile, bile reflux is main causes of remnant gastritis which refers to endoscopic conditions like redness, edema, and bleeding tendency around anastomosed area. Reflux of bile juice and duodenal contents not only cause remnant gastritis which is reported to be a risk factor for gastric adenocarcinoma, these make endoscopic inspection of the remnant stomach difficult, as the reddish swollen gastric mucosa caused by reflux is difficult to distinguish pathologic lesion from benign mucosa.

Treatments for food retention and remnant gastritis due to bile reflux are not well established. In majority of pa-

DISCUSSION

In many cases of follow up endoscopic inspection of remnant stomach after gastrectomy, delayed gastric emptying and bile reflux are big obstacles. Our study revealed that 21.6% of patients who did not undergo preparation had shown food material at endoscopic inspection. It also demonstrated that 67.6% of no preparation group had bile reflux which hindered endoscopic examination.
tients, food retention in remnant stomach does not cause any symptoms and nutritional problems. \(^{10}\) Phytobezoars are commonly conservatively treated by liquid diet or drugs with prokinetic effect, like cisapride, domperidone, etc. \(^{15,16}\)

Recently, many studies on treatment of gastric phytobezoars by cola in non-operated patients have been reported. Since Ladas et al. \(^{8}\) first reported that cola lavage can be an effective and safe treatment option for gastric phytobezoars in 2002, successful treatment of gastric bezoars by other methods like drinking and endoscopic injection of cola were reported. \(^{17-21}\) These studies have demonstrated that cola ingestion was cost effective, easy to perform, and safe for treatment of gastric bezoar.

The reason of cola’s effectiveness on dissolution of gastric bezoars is not well understood, but few possible mechanisms are suggested. \(^{7,8,19}\) The mucolytic effect of NaHCO\(_3\) and digestion of concreted fiber by CO\(_2\) bubbles contained in cola are the main theories. Also, cola contains carbonic and phosphoric acids which makes cola’s pH similar to that of gastric acid and exert positive effect on gastric motility. \(^{9}\)

How much cola should be used for efficient preparation is not yet established. Although a study which cola is used for UGI preparation is not yet reported, there are some reports that cola ingestion without endoscopic intervention is used for gastric phytobezoar dissolution. From a study by Ladas et al., \(^{8}\) they lavaged 3,000 mL of cola through a double-lumen nasogastric tube over 12 hours and reported that the gastric phytobezoar was completely dissolved. Lee et al. \(^{22}\) reported 2 cases that were successfully treated by drinking 700∼800 mL of cola daily for 2 months. Considering patients’ compliance, easy to purchase and check volume of ingestion, we decided the cola ingestion volume of protocol as 1,500 mL.

It is uncertain whether the good preparation was due to cola or effect of liquid intake. There was a report that ingestion of 1 L of water on the day before endoscopy can significantly reduce food residue. \(^{23}\) Although it is difficult to compare the results of two studies directly because of the difference of ingestion volume, the percentage of grade 0 food residue was higher after cola ingestion than water intake. We presume that good preparation after cola ingestion is due to phytobezoar lytic effect in addition to liquid intake effect. Further additional studies comparing cola with the same volume of water ingestion will be needed.

There was no significant adverse effect of cola preparation except mild nausea and epigastric fullness, but careful observation is needed because vomiting and aspiration might be possible especially in the elderly. And there was a report of intestinal obstruction due to the migration of a phytobezoar during cola-lysis in a patient who had undergone partial gastrectomy, so we need caution about this problem. \(^{28}\)

As far as we know, this is the first study that reports cola ingestion was effective in food and bile clearance of remnant stomach. Our results are very promising as it proved that the preparation of UGI examination for follow up inspection of remnant stomach after gastrectomy can be achieved in a very easy, fast, safe and cost effective way.

The limitations of our study are that the study material was not compared with other possible preparation method like other kinds of soda drinks or prokinetic drugs. As cola was already established as safe and cost effective treatment option of gastric bezoars, we wanted to see if it could be applied to preparation of UGI endoscopy in patients who had problems with gastric emptying. Also, our study was not blinded to the patients and could have caused placebo effect or statistical bias. We also did not assess the patient’s pre-examination clinical symptom which could have helped to predict risk factors for food residue or bile reflux.

As we have shown in this study that cola is effective in emptying of remnant stomach, study on how to select the patients and establishing the indications of cola administration before the endoscopic examination is needed. In the near future, a further report on predicting the need of cola preparation by patient’s clinical symptoms assessed by a validated, structured, self administered questionnaire is warranted.

To conclude, the preparation with a 1,500 mL of cola in the evening before procedure was helpful for effective UGI endoscopy and provides a good quality of bowel preparation in patient with remnant stomach after distal
gastrectomy. Cola preparation was shown to lessen the risk of bile reflux and food residue independently. Further studies on correlations with clinical symptoms involving larger cases are required to assess the effectiveness and to identify the efficient indication in which cola may have an overall benefit for bowel preparation.

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