Clinical Trial: Precise Administration of Sucralfate Powder in Prevention of Delayed Postpolypectomy Bleeding. A Randomized Controlled Trial

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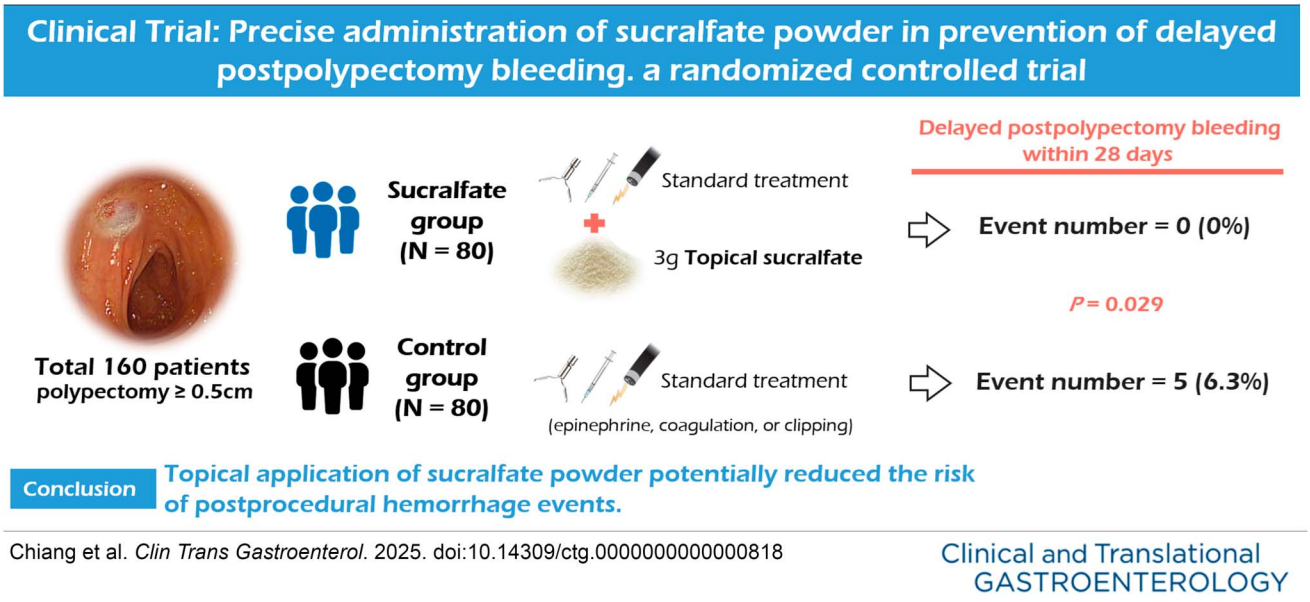
INTRODUCTION: **Delayed postpolypectomy bleeding occurs in approximately 1%–2% of all patients undergoing colonoscopic polypectomy, and this rate increases to 6% in patients with large (>2 cm) colon polyps. Sucralfate can protect the mucosa and promote its healing. This study was conducted to investigate whether colonoscopic spraying of sucralfate powder on polypectomy wounds can prevent delayed postoperative bleeding.**

METHODS: **This randomized controlled trial included patients with polyps (size ≥0.5 cm) who had undergone colonoscopic polypectomy at our hospital between May 2023 and January 2024. After polypectomy, the patients received standard treatment for immediate bleeding. Then, they were randomly allocated to either a sucralfate group (prophylactic spraying of sucralfate powder [3 g] on polypectomy wounds) or a control group. All patients were monitored for delayed bleeding within 28 days after colonoscopy.**



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RESULTS: **A total of 160 patients were divided into the sucralfate and control groups (80 per group). The baseline characteristics were balanced between the groups. The rate of delayed postpolypectomy bleeding (0% vs 6.3%, respectively; $P = 0.029$) and postpolypectomy overt bloody stool (2.4% vs 18.8%, respectively; $P = 0.001$) were lower in the sucralfate group than in the control group. The duration of freedom from delayed bleeding was longer in the sucralfate group than in the control group ($P = 0.024$). Multivariate Cox regression analysis confirmed the additional sucralfate spray as an independent factor against postpolypectomy overt bloody stool (relative risk, 0.03; 95% confidence interval, 0.003–0.43; $P = 0.009$).**

DISCUSSION: **Colonoscopic spraying of sucralfate powder is a safe approach with potential to reduce the risk of delayed postpolypectomy bleeding. Trial registration: NCT05817656.**

KEYWORDS: colon polyp; delayed postpolypectomy bleeding; sucralfate; endoscopic powder spray

SUPPLEMENTARY MATERIAL accompanies this paper at http://links.lww.com/CTG/B275

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INTRODUCTION

Colonoscopic polypectomy is a key procedure for prevention of colorectal cancer and reduction of associated mortality risk. However, this procedure carries a risk of postpolypectomy bleeding (1,2). Postoperative bleeding can occur immediately (intraoperatively, manageable during colonoscopy) or after a while (for example, a month after colonoscopy) (3,4). The causes of delayed postpolypectomy bleeding include detachment of eschar because of stool passage and extension of submucosal necrosis because of hot snare polypectomy (5,6). The incidence rate of delayed postpolypectomy bleeding ranges from 1% to 2%; this rate increases to 6% in patients with large (>2 cm) colon polyps (5–7). Risk factors of this complication include hot snare polypectomy, chronic kidney disease, liver cirrhosis, antiplatelet agent or anticoagulant use, and pedunculated colon polyps (6).

Delayed postpolypectomy bleeding is a major complication that requires prompt management. Patients with delayed bleeding usually present with hematochezia, anemia, hemodynamic instability, or end-organ damage (8). Hemostasis often requires repeated colonoscopic procedures and hospitalization, which

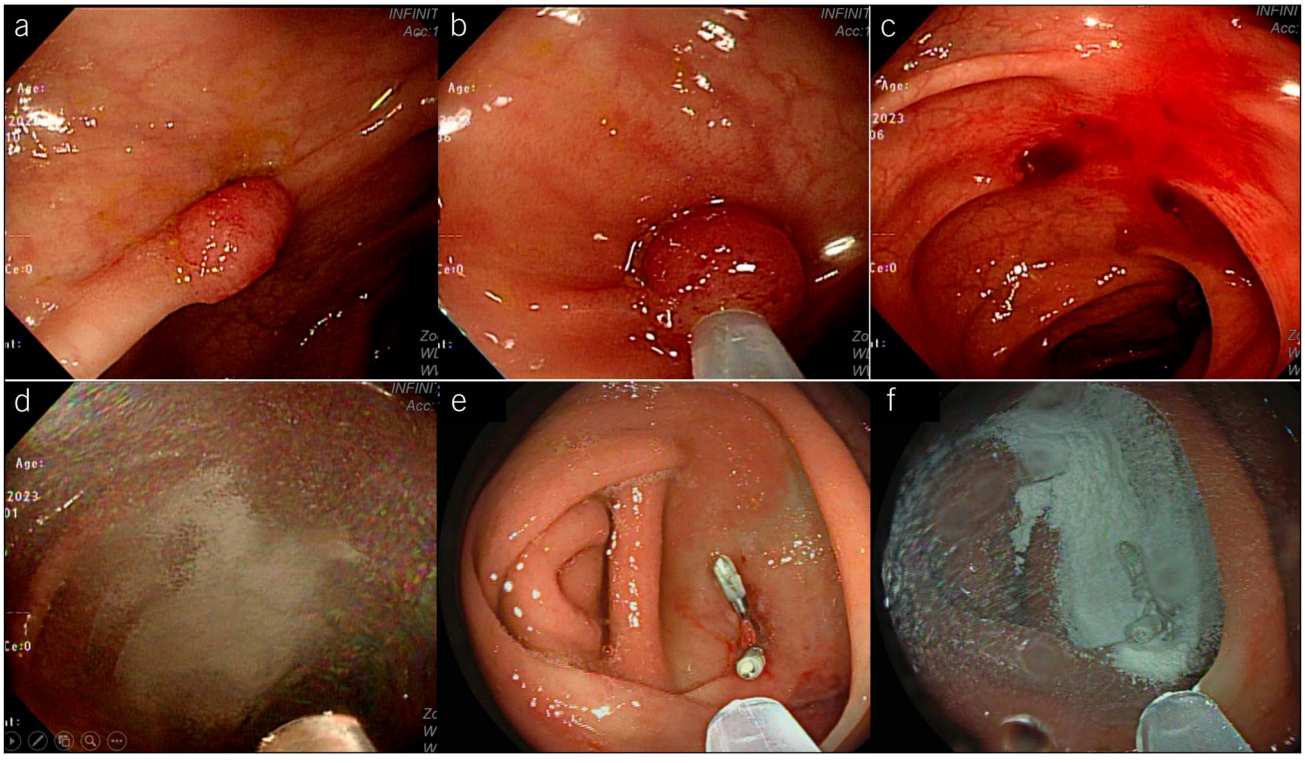

Figure 1. Polyp management in a patient. (**a**) A 0.9 cm colon polyp was observed at the transverse colon. (**b**) This polyp was resected through cold snare polypectomy. (**c**) Blood oozing stops after 30 seconds of observation. (**d**) Sucralfate powder (3 g) was sprayed on the polypectomy wound. (**e**) Another colon polyp resected with prophylactic clips. (**f**) Sucralfate powder (3 g) was delivered on the wound for the full coverage.

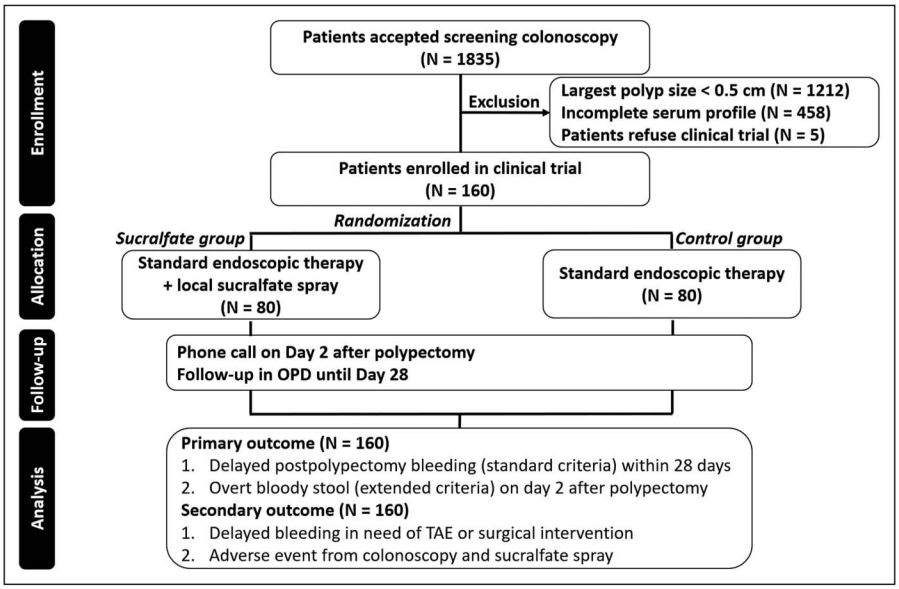

Figure 2. Flowchart depicting patient selection. OPD, out-patient department; TAE, transcatheter arterial embolization.

increases patient discomfort and treatment costs (8,9). In complex cases, emergent surgical intervention or transarterial embolization may become necessary (8). Therefore, the prevention of delayed postpolypectomy bleeding is crucial for both patients and clinicians.

Sucralfate, a basic aluminum salt of sucrose octa sulfate, has been used in the treatment of gastrointestinal ulcers; this powder accelerates healing and prevents bleeding (10–13). The mechanisms underlying its effects involve binding to exposed proteins on damaged cells and creating a protective layer that shields the mucosa from further injury (14). Sucralfate can also bind to growth factors and thus promote angiogenesis and mucosal healing (15). Pharmacodynamic insights have suggested that local application of sucralfate is more effective in promoting wound healing than systemic administration, likely because of its ability to locally adhere to damaged mucosa, forming a sticky

Table 1. Baseline characteristics of patients in the sucralfate and control groups

N = 160	Sucralfate group (N = 80)	Control group (N = 80)	*P* value
Age (year old, mean ± SD)	64.1 ± 13.2	63.9 ± 8.8	0.933
Gender (M: F)	47: 33	58: 22	0.096
Hemoglobin (g/dL, mean ± SD)	13.1 ± 1.8	12.9 ± 2.4	0.589
Platelet ($10^3/\mu L$, mean ± SD)	224.0 ± 64.0	227.0 ± 77.0	0.839
PT-INR (mean ± SD)	1.1 ± 0.1	1.1 ± 0.1	0.399
Serum creatinine (mg/dL)	1.3 ± 1.8	1.4 ± 1.5	0.576
Use of antiplatelet (%)	6 (7.5)	11 (13.8)	0.305
Use of anticoagulant (%)	6 (7.5)	5 (6.3)	0.999
Hypertension (%)	33 (41.2)	32 (40.0)	0.999
Coronary artery disease (%)	7 (8.8)	11 (13.8)	0.454
Cirrhosis (%)	2 (2.5)	2 (2.5)	0.999
Cerebrovascular accident (%)	7 (8.8)	4 (5.0)	0.534
ESRD (%)	3 (3.8)	2 (2.5)	0.999
Endoscopic polyp size (largest, mm, mean ± SD)	8.8 ± 3.5	9.6 ± 5.1	0.248
Pathologic polyp size (largest, mm, mean ± SD)	8.7 ± 3.8	9.7 ± 5.5	0.156
Prophylactic clipping (%)	47 (58.8)	53 (66.3)	0.414
Endoscopic procedure time (minute, mean ± SD)	37.3 ± 21.3	39.2 ± 25.6	0.623
Polyp numbers (mean ± SD)	2.1 ± 1.5	2.2 ± 1.8	0.606

ESRD, end-stage renal disease; PT-INR, prothrombin time international normalized ratio.

Table 2. Characteristics of colon polyps in the sucralfate and control group

Polyp number (n) = 341	Sucralfate group (n = 165)	Control group (n = 176)	*P* value
Polyp pathology			
Tubular adenoma (%)	113 (68.5)	102 (57.9)	0.562
Tubulovillous adenoma (%)	16 (9.7)	27 (15.3)	0.147
Villous adenoma (%)	4 (2.4)	1 (0.6)	0.176
Sessile serrated lesion (%)	8 (4.8)	8 (4.5)	0.999
Non-neoplastic (%)	22 (13.3)	35 (19.9)	0.289
Polyp size			
5 mm–9 mm (%)	130 (78.8)	135 (76.7)	0.789
10 mm–19 mm (%)	32 (19.4)	37 (21.0)	0.595
≥ 20 mm (%)	3 (1.8)	4 (2.3)	0.701
Polyp morphology			0.950
Pedunculated (%)	38 (23.0)	39 (22.2)	
Polyp size (mm, mean ± SD)	12.8 ± 4.4	14.1 ± 5.3	0.244
Nonpedunculated (%)	127 (77.0)	137 (77.8)	
Polyp size (mm, mean ± SD)	7.5 ± 2.0	7.4 ± 3.1	0.763
Paris 0-Is (%)	74 (44.8)	65 (36.9)	
Paris 0-IIa (%)	46 (27.8)	67 (38.0)	
Lateral spreading tumor (%)	7 (4.2)	5 (2.8)	
Polyp position			0.308
Proximal (cecum to hepatic flexure, %)	54 (32.7)	48 (27.3)	
Distal (transverse colon to rectum, %)	110 (67.3)	128 (72.7)	
Polypectomy method			0.407
Cold snare polypectomy (%)	126 (76.4)	119 (67.6)	
Hot snare polypectomy[a] (%)	41 (24.6)	49 (33.4)	
Prophylactic clipping			
Wounds with clipping (%)	58 (35.1)	64 (36.4)	0.904
Size			
5 mm–9 mm (%)	23 (39.6)	23 (35.9)	0.921
≥ 10 mm (%)	35 (60.4)	41 (64.1)	0.999
Morphology			
Pedunculated (%)	38 (65.6)	38 (59.4)	0.999
Nonpedunculated (%)	20 (34.4)	26 (40.6)	0.597
Method			
Cold snare polypectomy (%)	17 (29.3)	15 (23.4)	0.836
Hot snare polypectomy[a] (%)	41 (70.7)	49 (76.6)	0.999

[a]Hot snare polypectomy was performed after submucosal epinephrine injection.

coating that accelerates healing (10,16,17). Liquid sucralfate has demonstrated healing efficacy in endoscopic mucosal resection-induced gastric ulcers (18). Rectosigmoid ulcer lesions can also be treated with topical sucralfate by enema (19). In radiation proctitis and idiopathic ulcerative proctitis, sucralfate enemas produced clinical and endoscopic improvement (19). Compared with the drug powder, we think the liquid formulation would soon drain away from the wound. Therefore, we hypothesized that the local application of sucralfate powder to polypectomy wounds would effectively prevent delayed postpolypectomy bleeding.

METHODS

Study design and ethics

This single-center, randomized controlled trial was approved by our hospital's Institutional Review Board (approval number: A-BR-111-085) and was registered at ClinicalTrials.gov (registration ID: NCT05817656). Our study included patients aged

Table 3. Outcomes of colonoscopic polypectomy in both groups

N = 160	Sucralfate group (N = 80)	Control group (N = 80)	*P* value
Immediate bleeding (%)	17 (21.3)	13 (16.3)	0.544
Postprocedural hemorrhage events (%)			
Delayed postpolypectomy bleeding	0 (0)	5 (6.3)	0.029
Overt bloody stool (Day 2)	1 (2.4)	13 (18.8)	0.001
Bleeding cessation without intervention	1	8	0.016
In need of transcatheter arterial embolization (TAE)/surgery	0	0	0.999
Severe adverse event			
Bowel perforation	0	0	0.999
All-cause mortality	0	0	0.999

20 years or older who underwent colonoscopy. The findings of this study are reported in accordance with the Consolidated Standards of Reporting Trials statement. Informed consent was obtained from all patients: all individuals agreed to the use of their data. All authors had access to the study data and reviewed and approved the final manuscript.

Patient selection

This study included patients with polyps (size ≥0.5 cm) who had undergone colonoscopic polypectomy at our hospital between May 2023 and January 2024. We excluded patients who lacked complete data (serum creatinine, platelet count, and prothrombin time) pertaining to the previous 6 months; those who did not discontinue antiplatelet agents or anticoagulants; and those who had a known allergy to sucralfate. Routine colonoscopic examinations were conducted for the included patients. All operators are experienced endoscopists who performed more than 1,000 cases of colorectal polypectomy.

After identifying a resectable colon polyp (size ≥0.5 cm), the operator performed a polypectomy. The method of polypectomy, such as cold snare, hot snare, or endoscopic mucosal resection, was selected based on suitability. After polypectomy, the wound was observed for 30 seconds to detect potential immediate bleeding. Standard endoscopic interventions such as diluted epinephrine injection, heat coagulation, or clipping were promptly administered if immediate bleeding occurred. Prophylactic clipping was performed for relatively high-risk patients, including those with pedunculated polyps, polyps measuring ≥1 cm, individuals with end-stage renal disease, and those who underwent hot snare polypectomy. Subsequently, the patients were randomly assigned to either the sucralfate or control groups.

After polypectomy and appropriate management (Figure 1a–c), approximately 3 g of sucralfate powder was colonoscopically sprayed on the polypectomy wounds of patients in the sucralfate group (Figure 1d, Video 1). The powder spray aimed for the full coverage of the polypectomy wound even if prophylactic clips were placed (,). Six sucralfate tablets (500 mg per Weizip tablet; Yung Shin Pharmaceutical Industries, Taichung, Taiwan) were ground to collect 3 g of sucralfate powder. This powder was then delivered through a functional powder delivery system (7F polyethylene

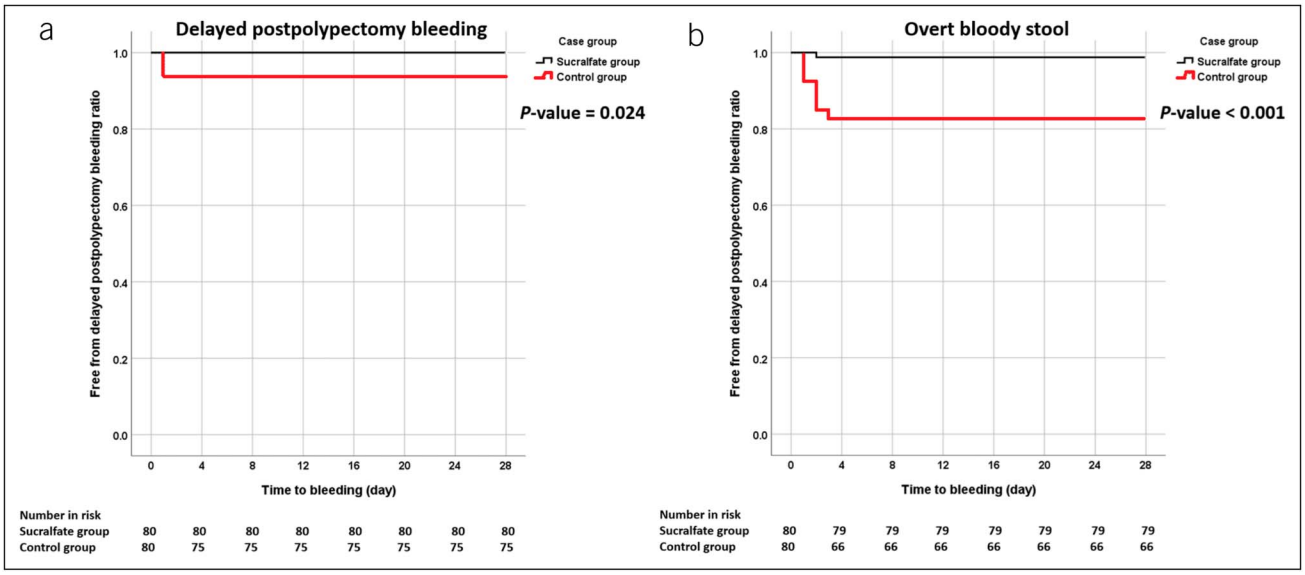

Figure 3. Kaplan-Meier curves for freedom from postprocedural hemorrhage events in the sucralfate and control groups within 28 days after colonoscopy. Curves for postprocedural hemorrhage events including (**a**) delayed postpolypectomy bleeding and (**b**) overt bloody stool.

Table 4. Risk factors interfering with postprocedural hemorrhage events

	Univariate Cox regression analysis		Multivariate Cox regression analysis	
N = 160	RR (95% CI)	*P*	RR (95% CI)	*P*
Characteristics				
Age	1.01 (0.96–1.05)	0.821		
Gender (male)	0.46 (0.13–1.65)	0.239		
Platelet count	0.99 (0.99–1.00)	0.851		
PT-INR > 1.2	5.95 (1.89–18.74)	0.002	12.38 (0.92–165.61)	0.057
Hot snare polypectomy	7.68 (2.16–27.23)	0.002	4.54 (0.28–73.75)	0.287
Maximal polyp size[a]	6.23 (3.25–11.95)	<0.001		
With colon polyp ≥ 2 cm[a]	8.81 (1.76–44.03)	0.008	3.87 (0.42–35.62)	0.232
With pedunculated polyp	9.75 (2.75–34.59)	<0.001	7.91 (0.71–87.90)	0.092
With proximal colon polyp	1.76 (0.60–5.13)	0.297		
Comorbidity				
Use of antiplatelet	2.16 (0.61–7.66)	0.232		
Use of anticoagulant	0.95 (0.12–7.22)	0.961		
ESRD	2.21 (0.29–16.82)	0.443		
Immediate bleeding	1.72 (0.59–5.05)	0.319	5.12 (0.75–34.98)	0.095
Treatment				
Prophylactic clipping	0.24 (0.05–1.09)	0.065	0.22 (0.13–3.98)	0.309
Sucralfate spray (+)	0.06 (0.01–0.51)	0.009	0.03 (0.003–0.43)	0.009

CI, confidence interval; ESRD, end-stage renal disease; PT-INR, prothrombin time international normalized ratio; RR, relative risk.
[a]Maximal polyp size and colon polyp ≥ 2 cm were highly correlated covariates. We selected the covariate with a larger weight in multivariate analysis.

catheter in connection by an oxygen cannula to the air source; propelling power: 1 L/min airflow from the hospital's air source, oxygen or CO2) (20). If the patient had more than 1 polyp, the maximum dose of sucralfate was 9 g, aiming to cover all polypectomy wounds.

After colonoscopy, the patients were advised to avoid strenuous exercise for 2 weeks. A follow-up phone call was arranged to obtain information on the color of the stool 2 days after the colonoscopy. In the case of severe hematochezia, the patients were instructed to visit the hospital for follow-up endoscopy. Patients using antiplatelet agents or anticoagulants resumed their medications 2 days after colonoscopy.

Group allocation

Group allocation (1:1) was performed using opaque sealed envelopes containing random numbers representing either the sucralfate group or the control group (21). For this, an allocation sequence was generated through a computer program for random sorting. Sealed envelopes containing various numbers were prepared by an assistant other than the clinician members in this study (22). After enrollment, each patient received a sealed envelope indicating their group allocation.

Outcome measures

All patients were monitored for 28 days after polypectomy by outpatient department follow-up and telephone on day 2 and day 28. If the patient reported an overt bloody stool on day 2, we provided health education to return emergency department if the amount of blood in the stool increased in the following days. The primary outcome was postprocedural hemorrhage events, including delayed postpolypectomy bleeding (standard criteria) and postpolypectomy overt bloody stool (extended criteria) within 28 days after colonoscopy. Delayed postpolypectomy bleeding was defined as the need for reintervention or hospitalization, indicating a clinically significant bleeding event (3). To exclude the effect of immediate bleeding-related residual blood clots, the postpolypectomy overt bloody stool was defined as the presence of overt bloody stool 2 days after polypectomy with or without spontaneous cessation of bleeding. Overt bloody stool with spontaneous bleeding cessation was regarded as minor bleeding. The secondary outcomes were bleeding from polypectomy wounds necessitating transarterial embolization or emergency surgery and severe adverse events, such as bowel perforation and all-cause mortality.

Statistical analysis

On the basis of the literature, we set the rate of delayed postpolypectomy bleeding at 5% and the corresponding odds ratio to 0.1 for the use of sucralfate powder. Sample size calculation by survival analysis was applied for the 28-day observation period. At least 76 patients per group were required to reject the null hypothesis of equal effects between the 2 groups, with a power probability of 0.8 and a type I error of 0.05. Anticipating a 5% dropout rate, we enrolled 160 patients (80 per group) to achieve the statistical power.

Baseline and outcome data were analyzed using the Student *t*, Mann-Whitney *U*, χ^2, or Fisher exact test. Univariate and multivariate Cox regression analyses were performed to identify the

risk factors of delayed postpolypectomy bleeding. A log-rank test was performed for between-group comparison of the Kaplan-Meier curves for freedom from delayed postpolypectomy bleeding. A P value of < 0.05 indicated statistical significance. Statistical analyses were performed using SPSS (version 25.0; IBM Corporation, Armonk, NY) or SAS (version 9.4; SAS Institute, Cary, NC).

Ethics statement

This study was approved by the Institutional Review Board of the National Cheng Kung University Hospital (A-BR-111-085).

RESULTS

From May 2023 to January 2024, 1,835 patients underwent colonoscopy at our hospital. From them, 623 with colon polyps measuring ≥0.5 cm were screened for potential enrollment. We excluded patients who lacked data on recent renal function or bleeding profile (n = 458) and those who declined to participate in this trial (n = 5). Finally, 160 patients were included in this study; each group comprised 80 patients. Figure 2 presents a flowchart depicting patient selection.

As presented in Table 1, the baseline characteristics, blood test results, comorbidities, and antiplatelet agent or anticoagulant use were balanced between the sucralfate and control groups. The groups were also similar regarding the size of the largest polyp, number of polyps, duration of procedure time, and use of prophylactic clipping (Table 1). In the study cohort, a total of 341 colon polyps measuring ≥0.5 cm were resected, with consistent pathology, size, morphology, and polypectomy method observed across both groups (Table 2). Among 265 colon polyps, sized between 0.5 and 0.9 cm, 241 polyps (90.9%) were resected by cold snare polypectomy (pedunculated: n = 25, nonpedunculated: n = 216), and 24 polyps (9.1%) were resected by hot snare polypectomy (pedunculated: n = 21, nonpedunculated: n = 3). For the remaining 76 colon polyps with size ≥ 1 cm, 10 polyps (13.2%) underwent cold snare polypectomy (pedunculated: n = 0, nonpedunculated: n = 10), and 66 polyps (86.8%) underwent hot snare polypectomy (pedunculated: n = 31, nonpedunculated: n = 35). Among the sucralfate group, 2 patients received 9 g sucralfate, 11 patients received 6 g sucralfate, and 67 patients received 3 g sucralfate. The average sucralfate dose was 3.5 ± 1.3 g.

A total of 14 patients (8.8%) reported overt bloody stool on postoperative day 2; of these patients, 5 (3.1%) did not have spontaneous cessation of bleeding and thus received colonoscopic hemostasis. Notably, the rate of postprocedural hemorrhage events was lower in the sucralfate group than in the control group; this was true for delayed postpolypectomy bleeding (0% vs 6.3%, respectively; $P = 0.029$; Table 3) and postpolypectomy overt bloody stool (1.3% vs 16.3%, respectively; $P = 0.001$; Table 3). The Kaplan-Meier curves revealed that the duration of freedom from postprocedural hemorrhage events was longer in the sucralfate group than in the control group; this was true for delayed postpolypectomy bleeding ($P = 0.024$; Figure 3a) and postpolypectomy overt bloody stool ($P < 0.001$; Figure 3b).

Subgroup analyses were performed for high-risk patients. The duration of freedom from postprocedural hemorrhage events was longer in the sucralfate group than in the control group for both patients with large polyps (≥1 cm; n = 56 [35%]; Supplementary Figure 1a,b, http://links.lww.com/CTG/B275) and those with pedunculated polyps (n = 49 [31%]; Supplementary Figure 1c,d, http://links.lww.com/CTG/B275). Focusing on the high-risk polypectomy method (hot snare polypectomy), subgroup analyses also compared the effect of sucralfate spray. Among 90 polyps resected by hot snare polypectomy (41 in the sucralfate group, 49 in the control group, Table 2), the delayed bleeding rate was lower in the sucralfate group than in the control group (0% vs 10.2%, $P = 0.043$). For those high-risk patients with prophylactic clips, the rate of postprocedural hemorrhage events was lower in the sucralfate group than in the control group (Supplementary Table 1, http://links.lww.com/CTG/B275); this was true for delayed postpolypectomy bleeding (0% vs 9.4%, respectively; $P = 0.038$) and postpolypectomy overt bloody stool (0% vs 24.5%, respectively; $P < 0.001$).

Cox regression analysis was performed to evaluate the effects of risk factors interfering with postprocedural hemorrhage events listed in Table 4. The univariate analysis indicated that the sucralfate spray was associated with a lower rate of postprocedural hemorrhage events (relative risk [RR], 0.06; 95% confidence interval [CI], 0.01–0.51; $P = 0.009$) and that higher prothrombin time international normalized ratio (PT-INR) > 1.2 (RR, 5.95; 95% CI, 1.89–18.74; $P = 0.002$), hot snare polypectomy (RR, 7.68; 95% CI, 2.16–27.23; $P = 0.002$), larger polyp size (RR, 6.23; 95% CI, 3.25–11.95; $P < 0.001$), pedunculated polyp (RR, 9.75; 95% CI, 2.75–34.59; $P < 0.001$), and polyp size ≥2 cm (RR, 8.81; 95% CI, 1.76–44.03; $P = 0.008$) were associated with a higher rate of postprocedural hemorrhage events. The multivariate analysis indicated that the additional sucralfate spray was still an independent factor that prevented postprocedural hemorrhage events (RR, 0.03; 95% CI, 0.003–0.43; $P = 0.009$).

The characteristics of the 5 patients with delayed postpolypectomy bleeding are listed in Supplementary Table 2 (http://links.lww.com/CTG/B275). All 5 patients had no cardiovascular disease or cirrhosis. They received hot snare polypectomy with prophylactic clipping, and the median blood loss was 2.7 g/dL (IQR: 2.6–3.4 g/dL). Endoscopic hemostasis was successful for all 5 patients experiencing delayed postpolypectomy bleeding. No patient required surgical intervention or transarterial embolization. Furthermore, no case of colon perforation was recorded (Table 3).

DISCUSSION

To the best of our knowledge, this study is the first to evaluate the efficacy of sucralfate powder in preventing postprocedural hemorrhage events after polypectomy. Topical application of sucralfate considerably reduced the rate of delayed postpolypectomy bleeding and overt bloody stool. This effect was also observed in both patients with large polyps and those with pedunculated polyps, which highlights the efficacy of sucralfate. High-risk patients with prophylactic clips can also benefit from additional topical sucralfate. Moreover, this approach was found to be safe, with no instances of severe adverse events being noted.

After the spray application, sucralfate rapidly mixes with the fluid on the colon mucosa and forms a mucosal barrier, subsequently accelerating wound healing by binding to epidermal growth factors and stimulating epithelial proliferation (13). Thus, sucralfate's topical application outperforms its systemic administration in promoting wound healing (13,23). Studies have demonstrated the benefits of topical sucralfate against gastrointestinal ulcers (24,25). Our study extends the paradigm to include polypectomy wounds. We found the additional sucralfate powder reduced the rate of overt bloody stool 2 days after polypectomy. Multivariate Cox regression analysis also proved additional

sucralfate spray as an independent factor in preventing postprocedural hemorrhage events. This finding may indicate faster healing of polypectomy wounds in the sucralfate group.

Hemostatic powders have been used to manage active bleeding after polypectomy (26,27). However, thus far, few prospective studies have evaluated the efficacy of these powders in preventing postpolypectomy bleeding (28). Unlike other hemostatic powders, sucralfate avoids eschar detachment and facilitates wound healing, thus exhibiting relatively superior activity in preventing wound bleeding (13). We demonstrated that topical application of sucralfate powder, with or without clipping, can effectively reduce the risk of delayed postpolypectomy bleeding. Notably, the additional step of sucralfate powder spraying did not significantly increase the overall duration of procedure time (Table 1). Furthermore, it resulted in no severe adverse events (Table 3). During outpatient follow-up, no patient in the sucralfate group reported constipation or diarrhea.

Preventing delayed postpolypectomy bleeding is a challenge, and current evidence for effective treatment remains inconclusive (6–8). Despite the widespread use of prophylactic clipping, its efficacy in closing polypectomy wounds remains debatable (29). Not all patients benefit from prophylactic clipping (30,31), potentially due to incomplete wound closure and clip detachment (32). As a result, current clinical guidelines do not recommend routine use of prophylactic clipping (3). While prophylactic clipping for polyps larger than 20 mm in the proximal colon may reduce bleeding rates (33), its efficacy for lesions between 10 and 20 mm or in the distal colon remains controversial. Consequently, endoscopists in our hospital could not reach a consensus, making it challenging to persuade some investigators to avoid prophylactic clipping for 10–20 mm lesions. In this study, to ensure consistency and minimize variation among investigators, all pedunculated, >10 mm, and hot snare polypectomy lesions received prophylactic clipping. This may have reduced the bleeding rate and masked the effect of sucralfate spray. Nevertheless, our study demonstrated that sucralfate still provided benefits in reducing delayed postpolypectomy bleeding, as presented in Supplementary Table 1 (http://links.lww.com/CTG/B275), where no delayed bleeding occurred in the sucralfate plus clipping group compared with 5 cases in the standard clipping group.

This study included not only high-risk patients but also some low-risk patients, which may have diluted the observed effect. Despite this, our findings indicate that sucralfate is beneficial. Consistent with existing literature, our data showed that smaller or nonpedunculated polyps rarely resulted in delayed bleeding. By contrast, larger and pedunculated polyps were associated with higher bleeding risks, where additional coverage with sucralfate powder demonstrated preventive effects against delayed bleeding (Supplement Figure 1, http://links.lww.com/CTG/B275). Further studies focusing on applying sucralfate powder to larger polyps with higher bleeding risk are needed to demonstrate a greater magnitude of benefit, potentially making it more cost-effective in clinical practice.

Our study demonstrates the efficacy of sucralfate. However, it was used as an adjunct to prophylactic clipping. A more relevant question for future research is whether sucralfate spray could replace clipping. A comparative analysis against standard prophylactic clipping or other hemostatic methods would enhance the clinical relevance of sucralfate spray. Therefore, future research could focus on directly comparing the efficacy of sucralfate spray with clipping for bleeding prevention, to determine its potential as a primary preventative treatment.

Our study has several limitations. First, we recruited only 160 patients from a single medical center in Taiwan, and the enrolled cases had heterogeneous backgrounds. Second, delayed postpolypectomy bleeding occurred in only 5 patients (3.1%), and the low incidence limited our ability to conduct subgroup and multivariate analyses. To address this, we recorded postprocedural hemorrhage events (14/160, 8.7%) and performed a multivariate analysis to account for potential confounding factors, as presented in Table 4, which identified sucralfate as the most significant factor in reducing bleeding. Although the randomized design may have minimized this limitation, our findings need further validation in larger-scale studies. Third, our study was not a double-blinded trial. Nonetheless, all events of immediate bleeding were successfully managed, and the rates of prophylactic clipping were balanced between the 2 groups. Therefore, the risk of bias was low, according to the Cochrane risk-of-bias tool. Fourth, only 7 of our patients (4.3%) had polyps measuring ≥2 cm. Thus, whether our findings are applicable to patients with polyps measuring ≥2 cm remains to be validated. Finally, patients without discontinuation of antiplatelet agents or anticoagulants were excluded from the study. Whether sucralfate has a protective effect on patients ongoing antiplatelet agents or anticoagulants needs further validation.

In conclusion, we demonstrated that topical application of sucralfate powder potentially reduced the risk of postprocedural hemorrhage events, including both delayed postpolypectomy bleeding and overt bloody stool. Colonoscopically, spraying 3–9 g of sucralfate powder seems to be a safe hemostatic approach, with no major adverse events. A head-to-head comparison between sucralfate powder and clipping is needed to identify the preventative potency. Future large-scale, multicenter studies are warranted to validate and extend our findings.

CONFLICTS OF INTEREST

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Specific author contributions: H-C.C.: Conceptualization: Equal; Project administration: Equal; Data curation: Lead; Formal analysis: Lead; Methodology: Lead; Visualization: Lead; Writing—original draft: Lead; Writing—review & editing: Equal. P-J.C.: Conceptualization: Equal; Project administration: Equal; Data curation: Equal; Formal analysis: Equal; Methodology: Equal; Visualization: Equal; Writing—original draft: Equal; Writing—review & editing: Equal. E-H.Y.: Data curation: Equal; Project administration: Equal; Investigation: Equal; Supervision: Equal. T-L.K.: Project administration: Equal; Resources: Equal. M-T.H. and J-W.K.: Project administration: Equal; Investigation: Equal; Supervision: Equal. H-C.C.: Data curation: Equal; Supervision: Equal. W-L.C.: Investigation: Supporting; Supervision: Equal. W-Y.C.: Conceptualization: Equal; Project administration: Equal; Investigation: Equal. H-C.C., M-Y.L., T-C.H., C-M.C., W-C.C., K-K.H., M-H.W., M-H.L.: Project administration: Supporting; Investigation: Supporting. C-Y.C.: Conceptualization: Equal; Project administration: Equal; Investigation: Equal. X-Z.L.: Conceptualization: Lead; Funding acquisition: Lead; Resources: Lead; Writing—review & editing: Equal. C-H.C.: Conceptualization: Lead; Project administration: Equal; Resources: Lead; Writing—review & editing.
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Patient consent statement: Informed consent was obtained from all participants included in the study.
Clinical trial registration: This study was registered on clinicaltrials.gov (NCT05817656). https://register.clinicaltrials.gov/prs/app/action/SelectProtocol?sid=S000D4ZR&selectaction=Edit&uid=U00064HR&ts=2&cx=-xd7e5o

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Study Highlights

WHAT IS KNOWN

- ✓ Delayed postpolypectomy bleeding occurs in approximately 1%–2% of all patients undergoing colonoscopic polypectomy.
- ✓ The efficacy of prophylactic clipping after polypectomy remains debatable.

WHAT IS NEW HERE

- ✓ Colonoscopic spraying of sucralfate powder on polypectomy wounds can reduce the risk of delayed postpolypectomy bleeding.

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