

**Background and study aims:** Injection-assisted polypectomy (IAP) is traditionally carried out by using normal saline as the submucosal fluid cushion. However, normal saline, being isotonic, does not maintain the elevation of the mucosa for prolonged periods. It was hypothesized that dextrose 50%, as a hypertonic solution, might be an ideal medium for IAP. This study evaluated the efficacy and safety of dextrose 50% for performing IAP.

**Patients and methods:** All patients undergoing IAP during gastroscopy or colonoscopy were randomly assigned on a prospective basis to receive either normal saline or dextrose 50% as the submucosal fluid cushion. The endoscopist was blinded to the type of solution injected. The volume of solution and number of sites injected to elevate the lesion, the number of times IAP was interrupted to inject more fluid to maintain elevation, the rates of en bloc and complete resections, and the complication rates

were compared in the two groups. The mean follow-up period was 10 months.

**Results:** Fifty-two sessile lesions were removed in 50 patients. In comparison with normal saline, smaller volumes (median 7 ml vs. 5 ml;  $P=0.02$ ) and fewer injections (median 2 vs. 1;  $P=0.003$ ) were required to perform IAP when dextrose 50% was used. The en bloc resection rate was higher with dextrose 50% than with normal saline (82% vs. 44%;  $P=0.01$ ). Elevation of the submucosal area persisted even after completion of IAP in 96% of the patients randomly assigned to dextrose 50%, compared with 20% of those receiving normal saline ( $P<0.001$ ). There were no significant differences in the rates of complete resection or complications between the two groups.

**Conclusions:** Dextrose 50% is superior to normal saline as a submucosal fluid cushion, as it allows better en bloc resection during injection-associated polypectomy.

### Introduction

Injection-assisted polypectomy (IAP) is a technique widely used for removal of sessile lesions or early gastrointestinal neoplasms [1–6]. The injection of various solutions into the submucosa, to create a fluid cushion between a lesion and the deeper layers of the gut wall, is widely used to reduce complications such as bleeding and perforation, as well as to assist en bloc resection of tumors. En bloc resection is considered to provide more accurate histologic assessment and reduces the risk of local recurrence; Walsh et al. reported that 17% of locally recurrent tumors after

piecemeal polypectomy were cancerous, even though the excised specimens had been diagnosed histopathologically as benign adenomas [7].

Normal saline is commonly used for submucosal injections; however, it is difficult to achieve and maintain adequate mucosal elevation, due to the rapid absorption of normal saline by the surrounding tissue. In a recent study, the effectiveness for achieving mucosal elevation of several solutions – such as normal saline, hyaluronate, dextrose 50%, and glycerine – was evaluated in the porcine esophagus [8]. Normal saline had the short-

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est median disappearance time (2.4 min) in comparison with dextrose 50% (4.7 min), glycerine 10% (4.2 min), and hyaluronic acid (22.1 min).

Dextrose 50% is an easily available and inexpensive solution that could be a potential alternative to normal saline for IAP. The value and safety of dextrose 50% for IAP have not been previously evaluated in humans. This study compared the safety and technical results of IAP when using dextrose 50% and normal saline as the injection solutions.

## Patients and methods

### Patients

A prospective study was conducted of consecutive patients with sessile polyps who underwent IAP during gastroscopy or colonoscopy over a 9-month period (October 2004–June 2005). Most of the patients who underwent IAP at gastroscopy had originally been referred for endoscopic ultrasonography (EUS) examinations from outside facilities. Two experienced endoscopists (S. V., R. L. S.,) carried out all of the IAP procedures. The inclusion criteria were as follows: a sessile polyp larger than 2 cm in diameter seen at gastroscopy or colonoscopy, or a sessile polyp larger than 1 cm in diameter but with depressed margins. Patients were included only if the sessile polyp was thought by the endoscopist to be benign in appearance and to be resectable. The exclusion criteria were as follows: lesions that were ulcerated, indurated, or friable; and showed absence of lifting after submucosal injection. Also, patients with inflammatory bowel disease and familial polyposis syndrome were excluded. Patients with lesions that were found on EUS to involve the muscularis layer were excluded. The diameter of the polyp was estimated by placing a polypectomy snare close to the lesion. For lesions that were transected en bloc, the final size was determined by measuring the retrieved specimen on an examination table using a standard measuring scale in millimeters. For lesions that were transected in a piecemeal fashion, the measurement obtained before IAP with aid of a polypectomy snare was regarded as the final size. Forceps biopsy specimens were not routinely obtained before IAP. A data collection sheet was designed to include the relevant information about each tumor, the procedure carried out, complications, and follow-up.

The study was approved by the hospital's institutional review board. Informed consent was obtained from all of the patients.

### Methods

All of the patients underwent preparation for colonoscopy by ingesting a polyethylene glycol solution or Fleet Phospho-Soda in a standardized fashion on the day before the procedure. Patients undergoing gastroscopy were asked to not take anything orally on the day of the procedure. Patients were instructed to stop anticoagulant treatment 72 h before the day of the procedure. The procedures were conducted with the patients under conscious sedation (with intravenously administered meperidine and midazolam), with monitoring by pulse oximetry. Once the decision was taken during endoscopy to carry out an IAP, the patients were randomly assigned to receive an injection of either normal saline or dextrose 50% to create the submucosal fluid cushion.

Computer-generated randomization assignments were placed in a sealed envelope and opened by the endoscopy nurse during the procedure if the patients met the criteria for inclusion in the study. The endoscopist was blinded to the nature of the solution being injected. Patients who underwent IAP for colonic lesions were discharged after recovery, with instructions to resume a regular diet. Those who underwent IAP for upper gastrointestinal tract lesions were placed on omeprazole 20 mg/day for 6 weeks and were instructed to remain on a clear liquid diet for 24 h after the procedure. Patients receiving anticoagulants were instructed not to take them for 5 days from the time of the IAP.

**IAP technique.** The sessile polyp was first elevated by injecting either normal saline or dextrose 50% submucosally. The injection was continued until the lesion was adequately elevated. Submucosal injections were made using a standard 23-gauge catheter needle (Acuject, Wilson-Cook GI Endoscopy, Winston-Salem, North Carolina, USA) and a 10-ml syringe. When possible, the initial injections were made at the proximal aspect of the sessile polyp, to allow better visualization of the lesion and to facilitate resection. After the submucosal injection, the open snare (AcuSnare, Wilson-Cook) was placed around the lesion and was gently pressed against the mucosa. Excess air was aspirated from the gastrointestinal lumen in order to reduce distension and facilitate grasping of the targeted polyp. Electrocautery was carried out with an APC generator (Erbe ICC 350; Erbe USA, Inc., Marietta, Georgia, USA). The settings used were automatic cutting at a fixed power of 120 W, as recommended by the manufacturer, along with the "Endo Cut" mode. After snare excision, air was insufflated to visualize the area of resection; any residual tissue was removed in a similar fashion. Every attempt was made to remove the polyp en bloc and during one endoscopy session. The resected specimens were retrieved with grasping forceps. All of the resected material was sent for histopathological assessment.

**Definition.** En bloc resection was defined as one-piece resection of the whole lesion as observed endoscopically. Piecemeal resection was defined as removal of the lesion in pieces, with multiple transections during IAP. Complete resection was defined as removal of the entire lesion, as seen during endoscopy, in one session. In patients with malignant or adenomatous lesions, the completeness of the resection was confirmed by evaluation of the en bloc specimen for tumor-free lateral margins. In patients who had undergone piecemeal IAP, the completeness of the resection was confirmed by a repeat endoscopy with biopsy of the polypectomy site. Incomplete resection was defined as a need for more than one endoscopy session to remove a particular lesion (residual lesion).

**Outcomes of interest.** The volume of solution and the number of sites injected to elevate the lesion, the number of times IAP was interrupted to inject more fluid to maintain elevation of the lesion, the rates of en bloc and complete resections, and the complication rates were compared in the two groups. Persistence of submucosal elevation after IAP was also compared in the two groups.

**Complications.** Bleeding was classified into two types: immediate and delayed. Immediate bleeding was defined as active bleeding during the procedure that required endotherapy (e.g., Hemoclip placement or injection of epinephrine with cautery

Table 1 Demographic data and indications for endoscopy in patients undergoing injection-assisted polypectomy

Characteristic	Dextrose 50% (n = 27)	Normal saline (n = 23)	P	Total (n = 50)
<b>Age</b>				
Mean $\pm$ SD	66.8 $\pm$ 13.1	61.7 $\pm$ 9.8	0.08 <sup>1</sup>	64.4 $\pm$ 11.9
Median (range)	67 (40–87)	61 (46–90)		63.5 (40–90)
<b>Sex</b>				
Men	12 (44.4%)	14 (60.9%)	0.27 <sup>2</sup>	26 (52.0%)
Women	15 (55.6%)	9 (39.1%)		24 (48.0%)
<b>Procedure</b>				
EGD	13 (48.1%)	9 (39.1%)	0.58 <sup>2</sup>	22 (44.0%)
Colonoscopy	14 (51.9%)	14 (60.9%)		28 (56.0%)
<b>Indications (n)</b>				
Screening	5	7		12
Heme-positive stool	6	5		11
Abnormal imaging <sup>3</sup>	5	2		7
Dyspepsia	2	4		6
Gastrointestinal bleeding	3	2		5
Abdominal pain	2	1		3
Dysphagia	2	–		2
GERD	–	1		1
Anemia	1	–		1
Heartburn	–	1		1
Nausea	1	–		1

SD, standard deviation; EGD, esophagogastroduodenoscopy; GERD, gastroesophageal reflux disease.

<sup>1</sup> Unpaired *t* test.

<sup>2</sup> Fisher's exact test.

<sup>3</sup> Abnormality detected by barium study or computed tomography.

application). Delayed bleeding was defined as melena or bloody stool. Perforation was diagnosed endoscopically during the resection and/or by the presence of free air on a plain abdominal film or computed tomography. Patients were contacted by telephone on days 3 and 10 after IAP to obtain information about any procedure-related adverse events.

**Repeat endoscopy.** Patients in whom IAP was incomplete underwent repeat endoscopy within 6 weeks for excision of the residual polyp. Patients with malignant lesions, tubulovillous polyps, and those in whom IAP had been carried out in a piecemeal fashion underwent repeat endoscopy within 3 months to evaluate the site for any residual lesion. In patients with serrated adenomas or adenomatous polyps > 2 cm in size, a follow-up endoscopy was carried out within 3–5 months. Patients found to have residual lesions at the repeat endoscopy underwent further sessions at 3-month intervals to eradicate any local tumor growth. In accordance with the American Gastroenterological Association recommendations, follow-up endoscopy was not performed when pathology revealed nonadenomatous lesions and in patients with small polyps that were completely resected at the initial colonoscopy [9].

**Statistical analysis.** The effects of dextrose 50% and normal saline were assessed with regard to various characteristics in the patients undergoing IAP. Continuous variables were reported as means plus or minus standard deviation and medians (with ranges). The means in the two groups were compared using Student's unpaired *t* test when the data were normal. When the data were not normal, the medians in the two groups were compared using the Mann–Whitney–Wilcoxon test (a nonparametric test). Categorical variables were reported as frequencies with percentages, and the two groups were compared using Fisher's exact

test. En bloc resection, as a marker for the efficacy of IAP treatment, was used to calculate the required sample size. To detect a statistically significant difference between the two groups with a power of 80% and an alpha (type I error) of 0.05, the required sample size was 18 for each group. To calculate the sample size, P1 was equal to 0.25, where P1 was the proportion of patients with en bloc resection in the normal saline group. P2 was equal to 0.75, where P2 was the proportion of patients with en bloc resection in the dextrose 50% group. As there have been no studies, to our knowledge, comparing dextrose 50% with normal saline, the study by Lishi et al., in which 25% of the patients in the normal saline group had en bloc resection of sessile colon polyps using normal saline as the submucosal fluid cushion, was used as a basis [5]. It was hypothesized that the rate of en bloc resection with dextrose 50% would be higher than that of normal saline, and the P2 was therefore estimated to be 75%. Statistical significance was set at 0.05 (two-tailed). Data were analyzed using the SAS statistical program, version 9.0 (SAS Institute, Inc., Cary, North Carolina, USA).

## Results

Sixty patients met the criteria for enrollment. Ten were excluded. Five patients with gastric lesions were excluded because the mass was involving the muscularis layer. Five other patients with duodenal lesions were excluded, as the lesions were multifocal in three, while the other two had familial polyposis syndrome. Fifty patients were randomly assigned to undergo IAP using dextrose 50% or normal saline, and a total of 52 sessile lesions were removed. There were no differences in the patients' demographic data or in the characteristics of the lesions among the patients randomly assigned to the two groups (Table 1). Six-

**Table 2** Technical outcomes of injection-assisted polypectomy. A total of 52 lesions were resected in 50 patients

Characteristic	Dextrose 50% (n = 27)	Normal saline (n = 25)	P	Total (n = 52)
Volume injected (ml)				
Mean $\pm$ SD	5.6 $\pm$ 2.1	7.4 $\pm$ 3.1		–
Median (range)	5 (3–10)	7 (3–15)	0.02* <sup>1</sup>	–
No. of sites injected				
1	22	10		32
2	2	7		9
3	3	6		9
4	–	2		2
Mean $\pm$ SD	1.3 $\pm$ 0.7	2.0 $\pm$ 1.0		1.6 $\pm$ 0.9
Median (range)	1 (1–3)	2 (1–4)	0.003* <sup>1</sup>	1 (1–4)
Intermittent injections (n, %)				
Yes	1 (3.7%)	6 (24.0%)	0.05 <sup>2</sup>	7 (13.5%)
No	26 (96.3%)	19 (76.0%)		45 (86.5%)
Resection method (n, %)				
Piecemeal	5 (18.5%)	14 (56.0%)	0.01* <sup>2</sup>	19 (36.5%)
En bloc	22 (81.5%)	11 (44.0%)		33 (63.5%)
Resection (completeness; n, %)				
Complete	26 (96.3%)	20 (80.0%)	0.09 <sup>2</sup>	46 (88.5%)
Partial	1 (3.7%)	5 (20.0%)		6 (11.5%)
Persistent elevation				
Yes	26 (96.3%)	5 (20.0%)	<0.001* <sup>2</sup>	31 (59.6%)
No	1 (3.7%)	20 (80.0%)		21 (40.4%)
Complications				
Yes	–	3 (12.0%)		3 (5.7%)
No	27 (100%)	22 (88.0%)	0.10 b	49 (94.2%)
Repeat IAP	20 (74.0%)	17 (68.0%)	0.40 b	37 (71.1%)
Residual lesion	1	6		7

IAP, injection-assisted polypectomy; SD, standard deviation. \* Statistically significant. <sup>1</sup> Mann–Whitney–Wilcoxon test. <sup>2</sup> Fisher's exact test.

teen patients with various upper gastrointestinal lesions underwent EUS before IAP and were deemed to have disease confined to the mucosal layers (T1). The mean follow-up period was 126 days (range 45–262 days).

### Technical outcomes

The volume of solution injected (median 5 ml vs. 7 ml;  $P=0.02$ ) and the number of sites that were injected around a lesion to maintain an adequate submucosal fluid cushion (median 1 vs. 2;  $P=0.003$ ) were significantly lower in the patients randomly assigned to dextrose 50% than in those receiving normal saline (Table 2). IAP had to be interrupted more often to inject additional fluid to maintain a submucosal fluid cushion among the patients receiving normal saline than in those assigned to dextrose 50% (24% vs. 4%;  $P=0.05$ ). After completion of the IAP procedure, submucosal elevation of the polypectomy site persisted in 96% of the patients randomly assigned to dextrose 50%, in comparison with 20% of those in the normal saline group ( $P<0.001$ ).

More IAPs were performed en bloc among patients receiving dextrose 50% than in those with normal saline (81.5% vs. 44.0%;  $P=0.01$ ). IAP was complete in 96% of patients receiving dextrose 50% (26 of 27), in comparison with 80% of those with normal saline (20 of 25;  $P=0.09$ ). Twenty patients who were assigned to dextrose 50% underwent repeat endoscopy; no residual tumor was seen in 19 of them. One patient with a carcinoid tumor in the stomach was found to have a positive resection margin at histopathology. This patient underwent repeat IAP with en bloc removal of the lesion. One patient with gastric carcinoma in situ

(T1 on EUS), who was randomly assigned to dextrose 50%, had clear resection margins. Seventeen patients who were assigned to normal saline underwent repeat endoscopy; no residual disease was noted in 11 of them, while six others who had previously had an incomplete IAP underwent repeat IAP with successful removal of the residual lesion. One patient with adenocarcinoma in situ in a resected sigmoid polyp was found to have no residual lesion at the repeat endoscopy. The histopathological analysis of the resected specimens (Table 3) in both groups of patients did not reveal undue tissue damage secondary to injection of the submucosal solution, except for cautery artifacts (Figure 1). There were no significant differences in the duration of the IAP procedure or in the procedure time between the two groups of patients (data not shown).

### Complications

Three patients who received normal saline experienced immediate bleeding after en bloc IAP. One was a patient with a duodenal lipoma (41 mm, causing luminal obstruction), the second was a patient with large hyperplastic gastric polyp (35 mm), and the last was a patient with a malignant polyp in the sigmoid colon (48 mm). Bleeding was managed in all three of these patients by local injection of epinephrine and application of Hemoclips.

### Discussion

En bloc resection of sessile lesions is difficult, and various efforts have been made to overcome this. This study demonstrated that

**Table 3** Characteristics of lesions resected using injection-assisted polypectomy. A total of 52 lesions were resected in 50 patients

Characteristic	Dextrose 50% (n = 27)	Normal saline (n = 25)	P *	Total (n = 52)
<b>Size</b>				
Mean ± SD	2.5 ± 1.2	2.2 ± 0.9		2.3 ± 1.0
Median (range)	2.5 (1–5)	2.0 (1–4)	0.48	2.0 (1–5)
<b>Location</b>				
Antrum	3	7	–	10
Duodenum	6	3		9
Cecum	4	4		8
Right colon	2	6		8
Transverse colon	3	2		5
Sigmoid colon	3	1		4
Greater curvature	3	–		3
Rectum	2	1		3
Esophagus	1	–		1
Lesser curvature	–	1		1
<b>Histology</b>				
Tubular adenoma	13	7	–	20
Tubulovillous adenoma	9	4		13
Hyperplasia	2	8		10
Serrated polyp	–	3		3
Lipoma	–	2		2
Gastric cancer (T1)	1	–		1
Carcinoid	1	–		1
Granular cell tumor	1	–		1
Sigmoid mass (Tis)	–	1		1

SD, standard deviation. \* Mann–Whitney–Wilcoxon test.

submucosal injection of dextrose 50% is safe and can provide better technical results than injecting normal saline at IAP.

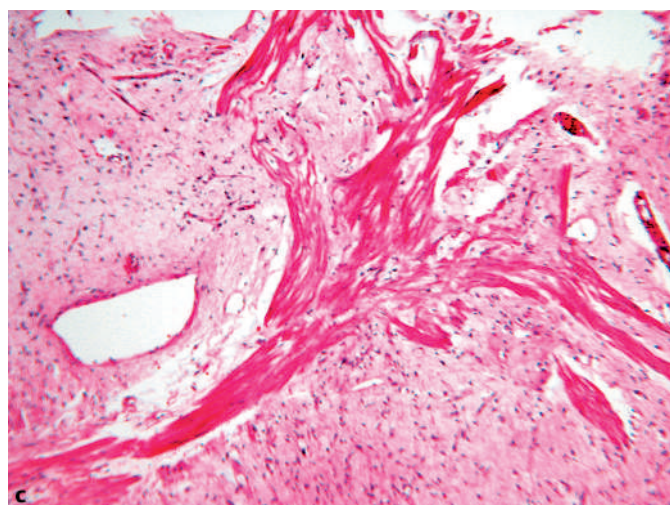
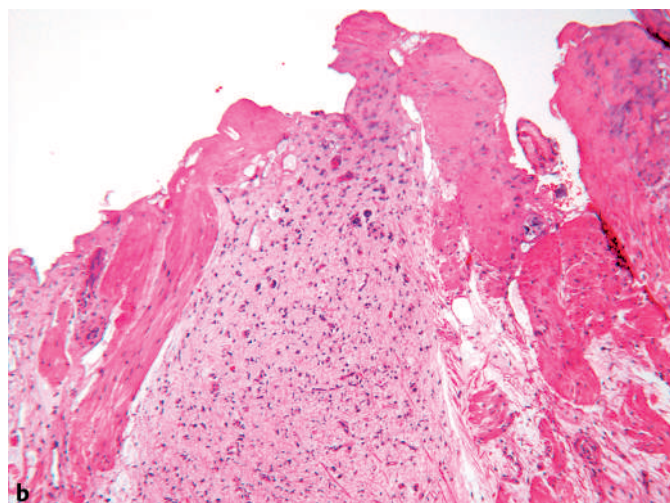
The better en bloc resection rates with dextrose 50% should have resulted in superior complete resection rates. A positive trend was observed for dextrose 50%, but there was no statistically significant difference due to the small size of the sample (type II error). In more than 95% of the patients who were randomly assigned to receive dextrose 50%, the elevation of the submucosal fluid cushion persisted even after completion of the IAP. This was not observed when IAP was carried out using normal saline. The prolonged submucosal elevation provides a technical advantage, in that it is less often necessary to interrupt the procedure to inject more submucosal fluid and maintain the elevation. Also, smaller volumes of dextrose 50% achieved better submucosal elevation than normal saline. The volume of solution required to carry out IAP in this study was small, as the lesions removed were predominantly nonmalignant in nature. We would recommend that dextrose 50% should be transferred to a 10-ml syringe before submucosal injection, as excessive pressure is required to inject the hypertonic fluid directly from the ampule.

As with any new technique, there is always concern about safety and complications, but dextrose 50% has previously been used intravenously in the treatment of hypoglycemia [10,11] and as a sclerosing agent to obliterate esophageal varices [12]. In a recent study by Fujishiro et al. in an animal model, injection of submucosal dextrose water  $\geq 20\%$  was associated with mucosal and muscle damage on the day of injection, with ulceration extending to the submucosal layer within a week after injection [13]. Histopathology did not reveal any tissue damage in the resected specimens in the present study, and no immediate or late com-

plications were encountered in any of the patients who underwent IAP with dextrose 50%. We believe that if dextrose 50% is injected carefully into the submucosal area, given its hypertonicity, it remains confined to that compartment without penetrating deeper layers. Also, IAP is usually performed within minutes of submucosal injection, and hence it is unlikely that tissue damage will be encountered in the resected specimen. Most of the lesions resected in this study were nonmalignant in nature, and the volumes of dextrose 50% used were therefore relatively small (median 5 ml). It is not clear whether the larger volumes that might be required when carrying out IAP for malignant lesions would cause tissue damage. One advantage of using a hypertonic solution is that it may obliterate the local vasculature, potentially minimizing the risk for local bleeding after IAP. Other solutions, such as hyaluronic acid, hydroxypropyl methylcellulose, and glycerol have been tried and were found to demonstrate better and longer-lasting lifting of the mucosa [14–17]. However, these solutions, unlike dextrose 50%, are not readily available at most endoscopy units in the West.

One limitation of this study is the small number of patients enrolled. Larger numbers would allow better assessment of the complication risks and the influence of dextrose 50% on the histopathological analysis. In addition, most of the lesions treated were nonmalignant in nature, with the exception of two patients. However, the study does reflect the real-life situation encountered in routine endoscopy practice.

In summary, IAP of sessile lesions is a challenge. The injection of normal saline does not maintain submucosal elevation for sufficiently long periods, leading to suboptimal results. The role of dextrose 50% as an injection agent in IAP has not previously



**Figure 1** **a** A 3-cm sessile gastric polyp removed using injection-assisted polypectomy after a submucosal injection of dextrose 50%. **b** At histopathology, the lesion was found to be a fibrous gastric polyp. Apart from the cautery effect, the resection margins do not show any evidence of tissue damage due to injection of dextrose 50%. **c** No tissue damage is seen within the polyp as a result of the use of dextrose 50%, at 1 cm from the resection margin.

been evaluated. This study has shown that dextrose 50% is safe and is superior to normal saline for creating a submucosal fluid cushion, as it yields better rates of en bloc resection during injection-assisted polypectomy.

### In brief

The ideal solution for use in injection-assisted polypectomy and endoscopic mucosal resection would ideally be long-lasting and inert; this is one of the very few clinical studies that has compared one of the substances available, dextrose 50%, with the saline solution normally used. It was found that elevation of lesion persisted much more often (96% vs. 20%), leading to a higher en bloc resection rate (82% vs. 44%).

**Competing interests:** None

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