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Advances in Endoscopic Mucosal Resection Using Elevation

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Figure 1. Elevation for submucosal injection.

Introduction

Colorectal cancer (CRC) is the third most common cancer and the second leading cause of cancer death in the United States, with over 50,000 deaths each year.¹ Screening has played a significant role in reducing incidence and mortality rates.² Among the screening methods, colonoscopy is particularly effective because it allows direct mucosal visualization and removal of precancerous polyps.^{3,4} Recent analyses, however, reveal that incomplete polyp resection contributes to the occurrence of cancer after colonoscopy.³

Standard polypectomy techniques have been associated with substantial rates of incomplete resection.⁵ In the CARE (Complete Adenoma Resection) study of 346 neoplastic polyps removed by 11 gastroenterologists, results showed a 10.1% incomplete resection rate (IRR) with large neoplastic polyps being 2 times more likely to be incompletely resected than small polyps.⁵ In addition to increasing polyp size, IRRs are higher with serrated lesions compared with conventional adenomas when standard polypectomy methods are used.^{5,6}

Endoscopic mucosal resection (EMR) usually refers to the technique of injection of submucosal fluid under lesions followed by either en bloc or piecemeal snare resection.⁷ Submucosal fluid lifts mucosal lesions, improving the safety of resection by separating them from the muscularis propria and altering the presentation to more polypoid shapes, which often makes snaring easier.⁷ EMR is more effective when the injected submucosal fluid includes

a contrast agent, such as methylene blue or indigo carmine.⁷ The contrast agent serves multiple purposes: First, it delineates the edges of the lesion so that the lesion perimeter is easily tracked during resection. Second, the contrast agent stains the submucosa, allowing easy recognition of any muscle injury during EMR. Colon muscularis propria is white, and the cut edges of muscle are easily recognized against a background of submucosa stained blue by the contrast agent—known as the “target sign.” Recognition of a muscle injury is followed by clip closure of the defect, effectively preventing delayed perforation. Thus, EMR overcomes many of the deficiencies of standard polypectomy techniques.

The use of EMR in colonoscopy appears to be expanding rapidly. EMR is becoming standard practice for improving the efficacy and safety of resection of flat and sessile lesions that are at least 20 mm in size.⁵ Several studies have shown that EMR is essential to the effective resection of large sessile serrated polyps, including 10- to 20-mm lesions.^{5,8-10}

Elevation has been FDA 510(k) cleared as a medical device for submucosal injection in endoscopic procedures in the upper and lower gastrointestinal tract following extensive testing in animal and, more recently, human trials.¹¹ Elevation is a submucosal injectate useful for EMR and potentially for procedures such as endoscopic submucosal dissection and peroral endoscopic myotomy.

Eleviev for Submucosal Injection in EMR

Eleviev is a premixed blue, sterile, clear emulsion that assists in visualizing the margins of the target lesion and elevating the mucosal layer and tissue to be excised, while reducing the risk for damage to the external muscular layer as well as perforation (Figure 1). The component ingredients of Eleviev include water for injection, medium-chain triglycerides, poloxamer 188 as the cushioning agent, polyoxyl 15 hydroxystearate as the surfactant, and sodium chloride as the osmotic agent.¹¹ Eleviev contains methylene blue as a contrast agent to delineate the edges of

the lesion, helping to ensure a complete resection.¹¹ Inclusion of methylene blue eliminates the recent problems associated with its poor availability and cost as a separate agent.¹²

Eleviev is ready to use and available in units of five 10-mL ampules.¹¹ Each ampule has an easy twist-off top. Eleviev is drawn from the ampule into a 10-mL luer lock syringe and injected with either a 23- or 25-gauge injection needle.¹¹ When injected into the submucosa beneath the lesion, Eleviev forms links to glycan moieties, creating a submucosal cushion of optimal height and duration that remains focused with limited lateral diffusion,

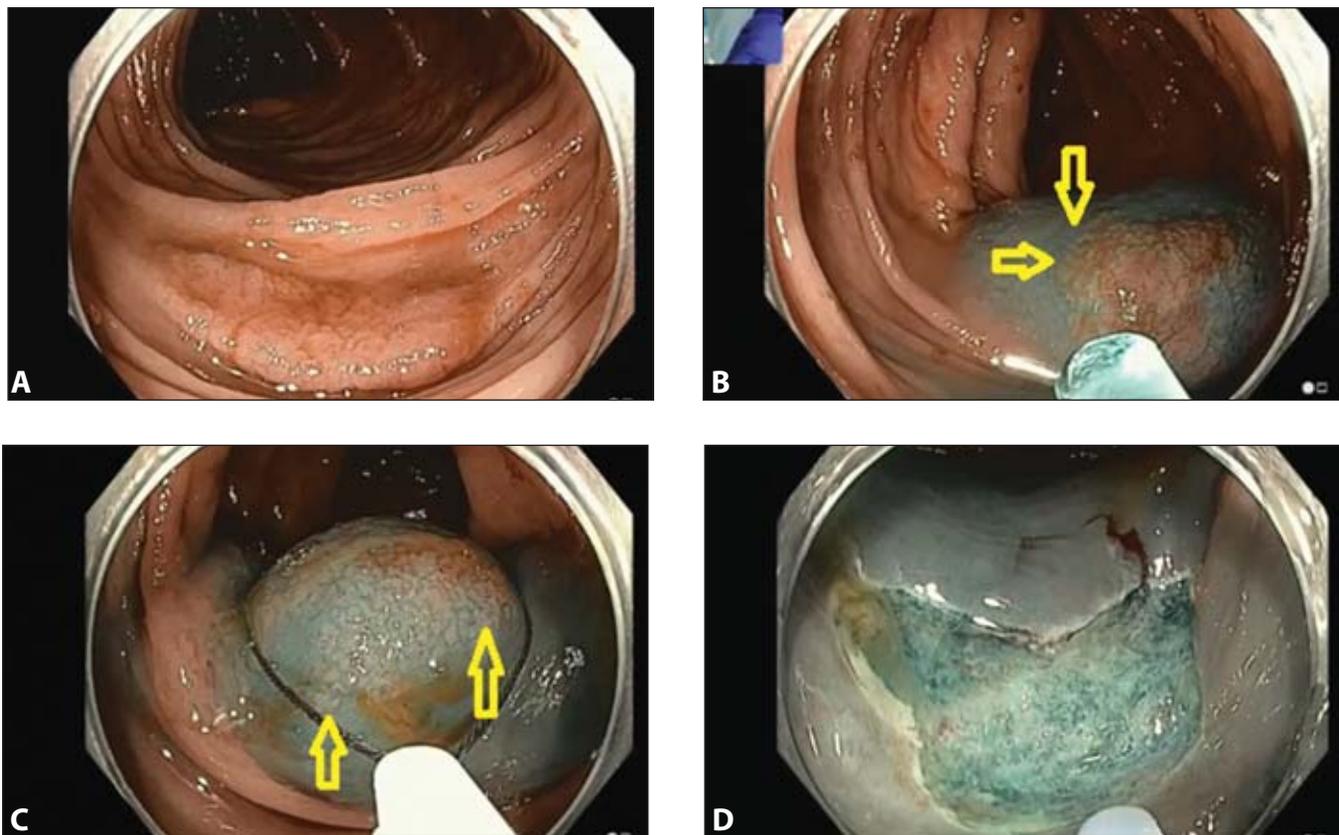


Figure 2. Endoscopic removal of a sessile serrated lesion in the transverse colon using Eleviev.

(A) A 20-mm serrated lesion before and (B) after submucosal injection using Eleviev. (C) Eleviev provides clear delineation of the lesion border for endoscopic snare resection. (D) The lesion site immediately after piecemeal EMR.

EMR, endoscopic mucosal resection

enabling an easy and safe resection (Figure 2). Additionally, Eleview provides more immediate, longer-lasting submucosal cushions that separate the mucosal layers up to 45 minutes.¹³

Table 1. Primary and Secondary End Points in a Randomized Controlled Trial Comparing Eleview With Saline for Submucosal Injection in EMR

Primary End Points
Total injected volume needed to complete the EMR procedure
Total injected volume per lesion size
Time to resect the lesion completely
Secondary End Points
Sydney Resection Quotient
Number of tissue pieces
Procedural complications
Proportion of patients with en bloc resection
Ease of use

EMR, endoscopic mucosal resection

Data Analysis

Results of a multicenter, international, double-blind, randomized controlled clinical trial comparing Eleview with saline for effective and safe EMR of large, flat and sessile colorectal lesions (≥ 20 mm) were presented at the 2017 Digestive Disease Week.¹⁴ Sponsored by Cosmo Pharmaceuticals NV, the trial was performed at 3 sites in the United States, one in the United Kingdom, and one in Italy. Co-investigators were Douglas K. Rex, MD, Mike Wallace, MD, Prateek Sharma, MD, Pradeep Bhandari, MD, and Alessandro Repici, MD. A total of 211 patients with lesions were randomly assigned to Eleview (n=102) and saline (n=109). Saline for injection had methylene blue added in identical concentration to Eleview to maintain investigator blinding.

The primary and secondary end points for the study are shown in Table 1. All lesions were measured and photographed using a stiff 20-mm-diameter snare to ensure that the lesions met the specified size. The initial volume injected to obtain an adequate lift was lower with Eleview compared with saline (mean 10.4 vs 15.3 mL, respectively; $P < 0.001$) (Table 2). Similarly, the total volume injected (16.1 vs 31.6 mL; $P < 0.001$) and the total volume injected after adjustment for lesion size (0.53 vs 0.92 mL/mm; $P < 0.001$) were lower with Eleview. There was no difference in time to perform the resection between procedures in the Eleview and saline groups (19.2 vs 29.7 minutes, respectively; $P = 0.326$), reflecting large standard deviations in procedure times in both arms of the study.¹⁴

Table 2. Key Results of a Randomized Controlled Trial Comparing Eleview With Saline For Submucosal Injection in EMR

End Point	Eleview	Control	Relative Improvement With Eleview, %	P Value
Total injected volume per lesion size, mean mL/mm	0.53	0.92	42.4	<0.001
Total injected volume, mean mL	16.1	31.6	49.2	<0.001
Injected volume for initial lift, mean mL	10.4	15.3	31.9	<0.001
Time to resect lesion, mean min	19.2	29.7	35.5	0.326
Sydney Resection Quotient, mean	10.3	8.0	28.9	0.044
Number of tissue pieces, mean	5.7	6.5	11.9	0.052
Proportion of patients with en bloc resections, %	18.6	11	58.3	0.125

EMR, endoscopic mucosal resection

To measure the efficiency of resection, the Sydney Resection Quotient (SRQ) was calculated by dividing the size of the lesion by the number of tissue pieces removed during the resection. The SRQ was better for Eleview compared with saline (Table 2). Clear trends favored Eleview in the mean number of tissue pieces resected (5.7 vs 6.5; $P=0.052$) and the proportion of patients with en bloc resections (18.6 vs 11; $P=0.125$). "Ease of use" of Eleview, reflecting factors such as ease of injection, was rated comparably between Eleview and saline. There were no significant differences in adverse events between Eleview and saline. There were 6 patients with post-polypectomy syndrome and no perforations in the Eleview arm compared with 3 patients with post-polypectomy syndrome and 1 perforation in the saline arm.¹⁴

Visit www.eleviewus.com/resources for procedural demonstration videos using Eleview. For more information about Eleview™, including Instructions for Use, visit EleviewUS.com.

Conclusion

The introduction of Eleview is a major event in the history of submucosal injection fluids for EMR; it is the first FDA-cleared and commercialized ready-to-use product that features a contrast agent. Studies have shown Eleview to offer significant advantages over saline as a submucosal injection fluid for EMR. With the contrast agent already included, Eleview reduces the time needed to prepare the submucosal fluid for injection, thus providing the opportunity to improve procedure efficiency.

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Important Safety Information about Eleview

The endoscopist injecting Eleview™ must be experienced in the administration technique.

The safety of Eleview™ has not been established in pregnant or lactating women.

Contraindications

Patients with known sensitivity to any of the components contained in Eleview™.

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