Standard needle versus needleless injection modality: animal study on different fluids for submucosal elevation

Alessandro Repici, MD, PhD,[1] Roberta Maselli, MD,[1] Silvia Carrara, MD, PhD,[1] Andrea Anderloni, MD, PhD,[1] Markus Enderle, MD, PhD,[2] Cesare Hassan, MD, PhD[1]

Milan, Italy; Tubingen, Germany

Background and Aims: Submucosal injection is currently used in GI endoscopy to reduce resection risks and to perform submucosal dissection; it is usually performed via an injection needle or a needleless device. The aim of the study was to compare 2 submucosal injection modalities (needle-assisted vs needleless) by using substances with different viscosities.

Methods: Needle and needleless injections were compared by assessing the efficacy of tissue elevation with 5 different substances in an ex vivo porcine model. The height of the submucosal elevation was measured 0(t0), 10(t1), and 30 minutes after injection (t2). Viscosity of the solution was also measured.

Results: For both stomach and rectum, at t0, t1, and t2 no difference in the height of the elevation was found between the needle and needleless technique, irrespective of the substance. Tissue elevation in the stomach was similar between the 2 techniques at t0 (9.9 ± 1.58 vs 9.4 ± 1.3 mm, $P = .3$), t1 (7.2 ± 1.56 vs 6.9 ± 1.4 mm, $P = .26$), and t2 (6 ± 1.6 vs 5.5 ± 1.3 mm, $P = .18$). No difference was found in the rectum at t1 and t2, whereas a slightly higher elevation with the needle-assisted technique was observed at t0 (t0: 12.4 ± 1.3 vs 11.2 ± 1.6 mm, $P = .003$; t1: 8.7 ± 1.3 vs 8.3 ± 1.5 mm; $P = .32$; t2: 7.0 ± 1.4 vs 7.2 ± .76 mm; $P = .75$). When comparing the substances with normal saline solution, more viscous solutions showed a significantly higher elevation at t0, t1, and t2 irrespective of the injection modalities and the location.

Conclusions: No differences were found in the height of submucosal injection or in the persistence of such elevation when comparing needleless with needle-assisted injection, with the only minor exception of the initial elevation in the rectum, which does not appear to be clinically relevant. Viscous solutions resulted in higher and more persistent elevations as compared with normal saline solution. (Gastrointest Endosc 2017;86:553-8.)

Abbreviation: ESD, endoscopic submucosal dissection.

DISCLOSURE: *The following author disclosed financial relationships relevant to this publication: M. Enderle: Employee of Erbe Elektromedizin. All other authors disclosed no financial relationships relevant to this publication.*

0016-5107/$36.00
http://dx.doi.org/10.1016/j.gie.2017.01.029

Received October 10, 2016. Accepted January 7, 2017.

Current affiliations: Digestive Endoscopy Unit, Division of Gastroenterology, Humanitas Research Hospital, Humanitas University, Milan, Italy (1), Research Department, Erbe Elektromedizin GmbH, Tubingen, Germany (2).

Reprint requests: Dr Roberta Maselli, Digestive Endoscopy Unit, Humanitas Research Hospital, Humanitas University, Via Manzoni 56, 20089 Rozzano, Milano, Italy.

If you would like to chat with an author of this article, you may contact Dr Maselli at roberta.maselli@humanitas.it.

Submucosal injection is currently used in GI endoscopy to create a safe fluid cushion during endoscopic GI resection, namely polypectomy, EMR, endoscopic submucosal dissection (ESD),[1-3] and submucosal therapeutic endoscopy (per-oral endoscopic myotomy,[4-7] submucosal tumor endoscopy resection[8-11]). Submucosal injection reduces the risk of perforation and postpolypectomy syndrome and shows the correct layer to cut during ESD and per-oral endoscopic myotomy. The rationale behind submucosal injection is that only the submucosal layer reacts with tissue expansion and creates a cushion when injected, whereas mucosa and muscle layer do not elevate.

Injection is usually performed by an injection needle, which works via puncture of the mucosal layer. The fluid is pushed via standard syringes, and a cushion or bleb forms as soon as the tip of the needle mechanically finds the submucosal layer. Although needle-assisted injection is effective, it also has drawbacks. First, it requires

exchange with EMR/ESD devices, such as snares or ESD knives, and this in turn results in a longer duration of the procedure. Second, it usually requires a second operator, affecting the use of human resources during endoscopic resection. Third, the flow of the liquid is usually modest because of the small caliber of the needle and the relatively low pressure achieved by manual injection. Fourth, the operator may inadvertently push the needle through the full thickness of the bowel wall, causing pain to the patient.

A needleless device has been introduced into the market. This device, the HybridKnife (Erbe Elektromedizin GmbH, Tubingen, Germany), uses an external pump force to directly inject a solution into the submucosal space via tissue-selective discrimination between fibrin-rich muscle and water-soluble mucosa (high-pressure tissue elevation).[12] The HybridKnife also combines the function of dissection and coagulation to speed up and simplify procedures (no need to change device to inject, cut, and coagulate).[13-16]

When comparing the needle with the needleless technique of injection, a relevant variable is represented by the solution, because different viscosity may affect the level of lifting and the desirable prolonged duration of the submucosal cushion. The most common fluid used to form a cushion in the submucosal layer is .9% sodium chloride solution, but different solutions have been reported as safe and effective for submucosal elevation.[13-16] Presently, the only solution used with the HybridKnife in clinical studies is normal saline solution.[16] The aim of the study was to compare 2 submucosal injection modalities (needle assisted vs needleless) by using substances with different viscosities, which are either used in clinical practice or proposed as alternative solution for advanced endoscopic resection.

METHODS

Needle and needleless injections were compared in an ex vivo animal model by assessing the technical efficacy of tissue elevation with different substances. In detail, tissue elevation (height in millimeters over the muscle layer) was evaluated at both injection time, namely t0, and over time, that is, after 10 minutes, t1, and after 30 minutes, t2.

Solutions used and measurement of viscosity

The following substances were used with each of the 2 techniques: .9% sodium chloride (normal saline solution; B. Braun Melsungen AG), glycerol (Chugai Pharmaceutical Co. Ldt), 4% Gelafundin solution (B. Braun Melsungen AG), 10% Voluven solution (Fresenius Kabi Deutschland GmbH), and Eleview (Cosmo Pharmaceuticals). Eleview is the only solution approved by the U.S. Food and Drug Administration for GI-endoscopic injection. To better understand the differences among solutions, viscosity measurements were performed on each with a standard rheometer with the temperature between 20°C and 37°C by the IMeter (MSB Breitwieser, Augsburg, Germany).

Animal model

All experiments were performed in an ex vivo porcine model. The stomach and rectum of 6 domestic pigs were obtained from the slaughterhouse. Tissue was frozen and stored until usage, when it was then thawed in a water bath at 25°C for 2 hours to prevent rigidity and to allow a homogeneous defrost of all parts of the organ. Thereafter, the ex vivo model was left at room temperature (25°C) for the entire duration of the study.

Tissue elevation

For the needle-assisted modality a 23G catheter injection needle (NM-201L-0423; Olympus, Tokyo, Japan) in conjunction with a 1-mL standard syringe (B. Braun Melsungen AG) was used for submucosal injection. Injection was manually performed with a maximal pressure of less than 3.8 bar (55 psi) and an approximate speed rate of 2 to 3 mL/s.

High-pressure tissue elevation (needleless) was performed with the water-jet system ErbeJet2 (Erbe Elektromedizin GmbH) using effect 40 for the stomach and effect 20 for the rectum, in conjunction with the needleless water-jet applicator HybridKnife T-Type (Erbe Elektromedizin GmbH). The application angle was 30 degrees in both modalities.

Elevation was performed with 5 mL of fluid for both injection systems and all types of tissue. All fluids were used at room temperature. The needle and needleless techniques were used in the same tissue model. Elevations were separated by a distance between injection cushions of at least 2 cm. The height of the submucosal elevation was measured (expressed in millimeters over the mucosal layer) using a marking gauge 0 minutes (t0), 10 minutes (t1), and 30 minutes after injection (t2). The same observer, blinded to the solution injected, was responsible of submucosal elevation measurements.

Statistical analysis

All analyses were performed by using PRISM version 6.0 (Graphpad Software Inc, La Jolla, Calif). Data were collected and analyzed by means of descriptive statistics (mean and standard deviation) and hypothesis testing. Normality of distributions was verified using the Kolmogorov-Smirnov test. Differences between normally distributed, independent quantitative data were analyzed using the Student t test and 1-way analysis of variance following Dunnett's multiple comparisons test. For non-normally distributed data the Kruskal-Wallis test was used. $P < .05$ were considered statistically significant. No