Article published online: 2022-05-13

Factors contributing to changes in viscosity and flow rate of a dedicated gel for gel immersion endoscopy

OPEN ACCESS

Authors

Yuji Hiraki[1], Atsushi Ohata[1], Tomonori Yano[2], Yoshimasa Miura[2], Alan Kawarai Lefor[3], Hironori Yamamoto[2]

Institutions

1 Naruto Research Institute, Research and Development Center, Otsuka Pharmaceutical Factory, Inc., Tokushima, Japan

2 Department of Medicine, Division of Gastroenterology, Jichi Medical University, Tochigi, Japan

3 Department of Surgery, Jichi Medical University, Tochigi, Japan

submitted 13.9.2021

accepted after revision 6.12.2021

Bibliography

Endosc Int Open 2022; 10: E703–E706

DOI 10.1055/a-1788-9888

ISSN 2364-3722

© 2022. The Author(s).

This is an open access article published by Thieme under the terms of the Creative Commons Attribution-NonDerivative-NonCommercial License, permitting copying and reproduction so long as the original work is given appropriate credit. Contents may not be used for commercial purposes, or adapted, remixed, transformed or built upon. (https://creativecommons.org/licenses/by-nc-nd/4.0/)

Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

Corresponding author

Tomonori Yano, MD, PhD, Department of Medicine, Division of Gastroenterology, Jichi Medical University, Yakushiji 3311-1, Shimotsuke, Tochigi, 329-0498, Japan

Fax: +81-285-44-8297

tomonori@jichi.ac.jp

ABSTRACT

Background and study aims Gel immersion endoscopy is a novel technique for securing the visual field during endoscopy. Clinical application of a dedicated gel for this technique with an appropriate viscosity to prevent mixing with blood and its efficacy was reported. The aim of this study was to evaluate changes in gel viscosity and flow rate under different conditions.

Methods The viscosity of the gel after injection and flow rate were measured under various conditions changing the injection route and method. Gel viscosity was measured at 25, 10, and 4 °C.

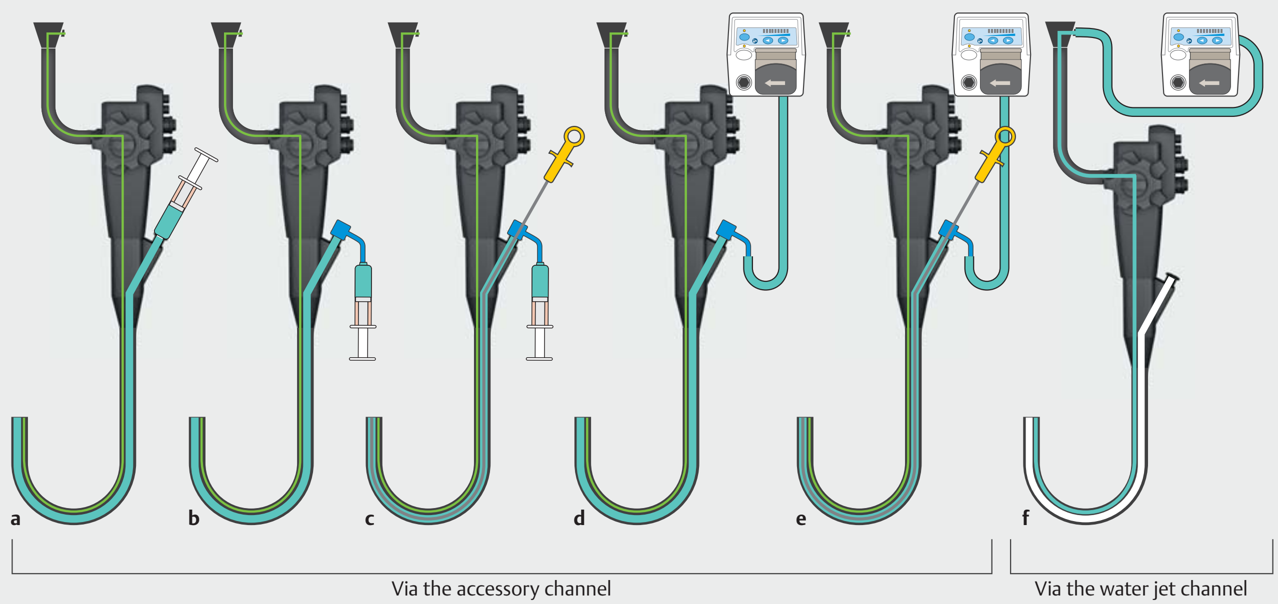
Results A decrease in gel viscosity was found when the gel was injected via the water jet channel compared to the accessory channel. The flow rate and decrease in viscosity of the gel injected via the water jet channel were 220 mL/min and 63.2 %, while when injected via the accessory channel with a clip device inserted were 560 mL/min and 35.8 %. When the gel was kept at a low temperature, the viscosity increased.

Conclusions Gel injection via the accessory channel should be the first choice for efficient use considering the viscosity and flow rate.

Introduction

During endoscopy for acute gastrointestinal bleeding and intraprocedural bleeding, it is often difficult to secure the visual field due to the presence of fresh blood and blood clots. Because injected water mixes immediately with blood, the visual field becomes cloudy. To solve this problem, the gel immersion method was developed [1, 2]. After injecting clear gel into the gastrointestinal lumen via the accessory channel instead of water, the visual field can be secured within the space occupied by the clear gel. The gel for this method needs to be of an appropriate viscoelasticity to ensure injectability via the accessory channel and the ability to secure the visual field. An electrolyte-free gel dedicated to this method “VISCOCLEAR” was launched in Japan in October 2020 [3] and its efficacy was reported in clinical practice [4–9]. “VISCOCLEAR” is a gel with a three-dimensional network structure due to the molecular interaction of xanthan gum and locust bean gum. This gel demonstrates thixotropy which causes the viscosity to decrease when strong external mechanical force is applied [10].

The gel is usually injected via the accessory channel using a manual syringe or a water pump and injected via the accessory channel with the irrigation valve “BioShield irrigator” when a therapeutic device is inserted into the channel. However, the gel is sometimes injected via the water jet channel using a water pump due to the lack of availability of the irrigation valve



▶ **Fig. 1** Schematic diagram of gel injection. **a** The gel was injected via the accessory channel using a syringe, **b** syringe and BioShield irrigator **c** with the clip device, and **d** the OFP-2 pump and BioShield irrigator **e** with the clip device. f Gel was injected via the water jet channel using the OFP-2 pump.

and staff resources needed in an emergency setting. The cross-sectional area of the accessory channel with a diameter of 3.2mm is 10 times larger than the water jet channel with a diameter of 1 mm. Even after inserting a therapeutic device, it is 2.7 times larger [11]. In addition, the water jet channel is almost twice as long as the accessory channel due to the different inlet locations. Thus, more force is required to push the gel through the water jet channel, and its viscosity may decrease. In this study, we evaluated the effect of different injection settings and temperatures on gel viscosity.

Methods

The EG-580RD endoscope (working length; 1,100 mm, accessory channel diameter; 3.2 mm, water jet channel diameter; not provided by the manufacturer but measured at 1.0 mm, Fujifilm, Tokyo, Japan), BioShield irrigator (U.S. Endoscopy, Mentor, Ohio), HX-110QR clip device (Olympus, Tokyo, Japan), 50 mL syringe, OFP-2 water pump (combination with MAJ-1607 auxiliary water tube, Olympus Medical Systems, Tokyo, Japan), and VISCOCLEAR (Otsuka Pharmaceutical Factory, Tokushima, Japan) were used in this experiment. The inner diameter of the BioShield irrigator and the discharge orifice of the syringe are not provided by the manufacturer but were measured at 3 mm and 2 mm respectively. The inner diameter of the water tube MAJ-1607 is also not provided by the manufacturer but was measured at 6 mm in the main-tube part and 3 mm in the connecter part.

We injected gel under the following test conditions (▶ **Fig. 1**), and the water pump was set to low (3/9 on the display), middle (6/9), or maximum (9/9) and the flow rates measured.

The syringe was inserted into the biopsy valve and gel injected via the accessory channel (▶ **Fig. 1a**) with manual force applied adjusted to inject the gel at 50 mL per 30 seconds. Then, the syringe was attached to the BioShield irrigator and gel was injected via the accessory channel (▶ **Fig. 1b**) with the same manual force. A syringe was attached to the BioShield irrigator and gel was injected via the accessory channel with the clip device inserted (▶ **Fig. 1c**) with the same manual force as in the first method. A water tube was connected to the OFP-2 pump to the BioShield irrigator and gel was injected via the accessory channel (▶ **Fig. 1d**). A water tube was connected to the OFP-2 pump to the BioShield irrigator and gel was injected via the accessory channel with the clip device inserted (Fig.1e). The edge of the water tube attached to the OFP-2 pump was inserted into the VISCOCLEAR bag and gel was injected via the water jet channel (▶ **Fig. 1f**).

Gel discharged from the tip of endoscope was collected and the gel flow rate was measured using a graduated cylinder, and then viscosity immediately measured using a rheometer (HAAKE RheoStress 6000, Thermo Fisher Scientific, Tokyo, Japan, measurement temperature: 25 °C, measurement geometry: P35/Ti, preheating time: 1 min, measurement time: 15 min, frequency: 0.5 Hz, shear stress: 200 mPa, gap: 0.500 mm). The gel was placed in a refrigerator, and the viscosity measured temperatures of 25 °C, 10 °C and 4 °C.

All data are presented as the mean ± standard deviation (SD). Tests for statistical significance were performed with the Dunnett test using EXSUS Ver.10 software (EP Croit CO, Tokyo, Japan). The significance level was set at $P < 0.05$.

▶ **Table 1** Flow rate and gel viscosity using different injection methods.

Injection method Flow rate (mL/min)/Viscosity (mPa·s)			
Syringe (50 ml)			
AC		100/788 ± 54.0	
AC + BSI		100/706 ± 100	
AC + BSI + CD		80/690 ± 16.0	
Water pump (OFP-2)	**Low (3/9)**	**Mid (6/9)**	**Maximum (9/9)**
AC + BSI	180/716 ± 88.8	340/653 ± 47.9[1]	740/584 ± 11.5[1]
AC + BSI + CD	–	–	560/562 ± 75.6[1]
WJC	100/482 ± 180[1]	140/452 ± 65.4[1]	220/321 ± 143[1]

AC, accessory channel; BSI, BioShield irrigator; CD, clip device; WJC, water jet channel.
Data were collected from three independent injections and presented as the mean ± standard deviation. Statistical analysis was performed with the Dunnett test.
[1] $P < 0.05$ versus the viscosity of prior to injection (875 ± 18.0 mPa·s).

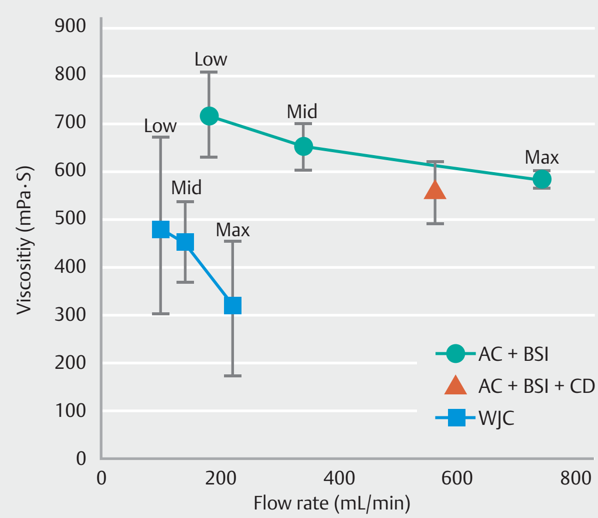
Results

The gel was injectable under all test conditions. There was a decrease in gel viscosity in all groups compared to the viscosity prior to injection but the decrease in viscosity was minimal when the gel was injected via the accessory channel using a syringe (▶ **Table 1**). The viscosity decreased as the pump flow rate increased in the OFP-2 pump groups and the rate of decrease was especially notable with the gel injected via the water jet channel compared to the accessory channel (▶ **Fig. 2**). The maximum decrease in viscosity and the maximum flow rate using the water pump were 63.2 % and 220 mL/min when the gel was injected via the water jet channel, and 35.8 % and 560 mL/min when the gel was injected via the accessory channel with the clip device inserted. The gel viscosity increased when kept at a low temperature (▶ **Table 2**).

Discussion

To perform the gel immersion method using VISCOCLEAR effectively, the characteristics of the gel should be understood. The results of this study show that the viscosity of the gel decreased significantly with rapid injection using a water pump or injection through the water jet channel, due to its thixotropy. The gel viscosity increased when the gel was kept at a low temperature.

VISCOCLEAR is a gel product with optimized viscoelasticity for ensuring both injectability via the accessory channel and the ability of securing the visual field by pushing away blood and blood clots to create a transparent space that does not mix with blood immediately. Based on a previous study, an ex vivo experiment showed that viscoelastic properties including a viscosity of 230 to 1900 mPa·s, tanδ ≤ 0.6 and hardness of 240 to 540 N/cm^2 were needed to secure the visual field [3]. The current study shows that the gel was injectable via the water jet channel using a water pump, but its viscosity decreased significantly because of the high pressure applied to the gel during injection. When the gel was injected via the water jet channel using a water pump at a high rate, its viscosity decreased by 63.2 %. The decrease in viscosity leads to a loss of physical strength of the gel, which represents the elastic com-



▶ **Fig. 2** Flow rate and gel viscosity using a water pump with different settings. AC, accessory channel; BSI, BioShield irrigator; CD, clip device; WJC, water jet channel.

▶ **Table 2** Change in viscosity of VISCOCLEAR with temperature.

Temperature (± 0.5 °C)	Viscosity (mPa·s)
25 °C	768 ± 42.0
10 °C	973 ± 10.0[1]
4 °C	998 ± 77.2[1]

Data were collected from three independent injections and are presented as the mean ± standard deviation. Statistical analysis was performed with the Dunnett test.
[1] $P < 0.05$ versus the viscosity of 25 °C.

ponent, and is thought to reduce its beneficial effects during endoscopy. Compared to the results of our previous study [3], this reduction in viscosity was close to the lower limit of the viscosity range required for securing the visual field. In addition, the flow rate when injecting via the water jet channel was significantly lower than the flow rate when injecting via the accessory channel with the clip device inserted. Poiseuille's equation explains the mathematical relationship between cross-sectional area, length of the water-jet channel and flow rate.

While the required viscosity and flow rate of the gel depends on the size of the lumen, the presence of distal attachments, and the direction and speed of bleeding, a gel with both the highest possible viscosity and flow rate is desirable. Although there is a trade-off between viscosity and flow rate for each injection method, injection through the accessory channel can be done with both higher viscosity gel and higher flow rate than injection via the water jet channel.

Even if the viscosity of the gel extremely decreases, at least the gel does not mix with blood as immediately as water. Therefore, even when the gel is injected via the water jet channel using a water pump, it may be possible to secure the visual field without spreading blood under gel immersion in areas that are easily filled with the gel or where bleeding is mild. In fact, Miyamoto used this method to inject and immerse the gel into the duodenal lumen via the water jet channel using a water pump and reported that it was useful for identification of bleeding points until hemostasis was achieved [4].

Based on these results, gel injection via the accessory channel should be the first choice for its efficient use considering both viscosity and flow rate. However, the irrigation valve is necessary for this approach, since an additional gel injection after inserting the therapeutic device is often required during the procedure. In contrast, gel injection via the water jet channel enables additional gel injection after inserting the therapeutic device without the irrigation valve. When the irrigation valve is unavailable, gel injection via the water jet channel is an alternative.

Because gel at a low temperature has a higher viscosity, a more beneficial effect to secure the visual field can be expected. In addition, since previous studies [12, 13] reported that cold water reduced the strength of peristaltic waves in the esophagus, cold gel may reduce peristalsis and spasms. However, the effect of cold gel on peristalsis of the gastrointestinal tract is not clarified.

This study has limitations. We did not test the durability of devices associated with the injection of gel using a water pump or injection via the water jet channel. In addition, we did not confirm the safety of low temperature gel injected into the human gastrointestinal tract.

Conclusions

This study shows that the rate of viscosity reduction of VISCOCLEAR is different with injection using a water pump or injection via the water jet channel, but the rate of reduction may also depend on the device specifications. Although the gel immersion method using VISCOCLEAR is expected to be a third method of securing the visual field instead of gas and water, it is important to fully understand the characteristics of the gel and its use as clarified in this study for successful securing of the visual field.

Competing interests

This study was funded by Otsuka Pharmaceutical Factory, Inc. Drs. Yano and Ohata hold patents for and are the inventors of the dedicated gel for the gel immersion method. Drs. Hiraki and Ohata are employed by the Otsuka Pharmaceutical Factory, Inc.

References

[1] Yano T, Nemoto D, Ono K et al. Gel immersion endoscopy: a novel method to secure the visual field during endoscopy in bleeding patients (with videos). Gastrointest Endosc 2016; 83: 809–811

[2] Yano T, Takezawa T, Hashimoto K et al. Gel immersion endoscopy: Innovation in securing the visual field – Clinical experience with 265 consecutive procedures. Endosc Int Open 2021; 09: E1123–E1127

[3] Yano T, Ohata A, Hiraki Y et al. Development of a gel dedicated to gel immersion endoscopy. Endosc Int Open 2021; 09: E918–E924

[4] Miyamoto S, Suzuki K, Kinoshita K. Efficiency of a novel gel product for duodenal ulcer bleeding. Dig Endosc 2021; 33: e63–e64

[5] Toyonaga H, Takahashi K, Kin T et al. Gel immersion technique for the examination and treatment of an ampullary tumor. Endoscopy 2021: doi:10.1055/a-1408-0458

[6] Yamamoto K, Kanomata N, Ikeya T. Utility of under-gel endoscopic mucosal resection with partial submucosal injection for a laterally spreading tumor. Endoscopy 2021: doi:10.1055/a-1381-6915

[7] Tashima T, Miyaguchi K, Terada R et al. Gel immersion endoscopic submucosal dissection using a novel gel product for a duodenal epithelial tumor. Endoscopy 2021: doi:10.1055/a-1443-4796

[8] Tashima T, Nakano Y, Jinushi R et al. Gel immersion endoscopic submucosal dissection for an anorectal tumor with hemorrhoids close to the dentate line. Endoscopy 2021: doi:10.1055/a-1519-6939

[9] Maruyama T, Murakami T, Akazawa Y et al. A case of improved visibility with gel immersion in the presence of ongoing bleeding during colorectal endoscopic submucosal dissection. VideoGIE 2021: doi:10.1016/j.vgie.2021.06.009

[10] Dolz M, Hernández MJ, Delegido J et al. Influence of xanthan gum and locust bean gum upon flow and thixotropic behaviour of food emulsions containing modified starch. J Food Engineer 2007; 81: 179–186

[11] Yano T, Ohata A, Hiraki Y. Gel injected via the accessory channel more efficiently secures the visual field than gel delivered via the water jet channel. Dig Endosc 2021; 33: 991

[12] Elvevi A, Bravi I, Mauro A et al. Effect of cold water on esophageal motility in patients with achalasia and non-obstructive dysphagia: a high-resolution manometry study. J Neurogastroenterol Motil 2014; 20: 79–86

[13] Choi YJ, Park MI, Park SJ et al. The effect of water bolus temperature on esophageal motor function as measured by high-resolution manometry. Neurogastroenterol Motil 2014; 26: 1628–1634