OPEN

PRS GLOBAL OPEN

VIEWPOINT

Research

In Vitro Comparative Cytotoxicity Assessment of Sclerosants Used for Venous Malformations

Yuta Moriwaki, MD*; Masakazu Kurita, MD, PhD*; Hiroki Hongo, MD, PhD†; Mutsumi Okazaki, MD, PhD*

Sclerotherapy is an effective treatment for venous malformations. Depending on the clinician's preference and experience, ethanol, polidocanol (POL), sodium tetradecyl sulfate (STS), or ethanolamine oleate (EO) can be employed as sclerosants in various areas such as plastic surgery, oral surgery, and radiology.

Recently in Japan, a multicenter joint clinical trial to assess the efficacy of EO sclerotherapy for venous malformations has started, and some clinicians familiar with sclerotherapy, but without experience with EO, are beginning their first series. Here, we considered that the comparative information between different sclerosants might be helpful for future compatibility of the therapeutics, and as the consistent objective assessment, we comparatively evaluated the cytotoxicities of these four sclerosants in the well-described in vitro cytotoxicity assay.[1]

To measure the cytotoxicity of the four sclerosants, we used the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay that indicates the extent of cell survival.[2] As an in vitro endothelial model for sclerotherapy, we used human umbilical vein endothelial cells.[1] (**See document, Supplemental Digital Content 1**, which describes the method of measuring the cytotoxicity of sclerosants. **http://links.lww.com/PRSGO/B782**.)

The standard concentrations that we used for clinical sclerotherapy were 100% for ethanol, 3% for POL, and 5% for EO. Therefore, we defined these concentrations as the standards in this study. Because STS has never been used in Japan, we defined 3% as the standard with reference to a previous report.[3]

We assessed the cytotoxicities of a series of diluted sclerosants (Fig. 1). For each sclerosant, cytotoxicity had rapidly decreased at specific dilution rates. The 50% cytotoxic concentration was 27% for ethanol, 3.1% for EO, 1.6% for polidocanol, and 0.33% for STS.

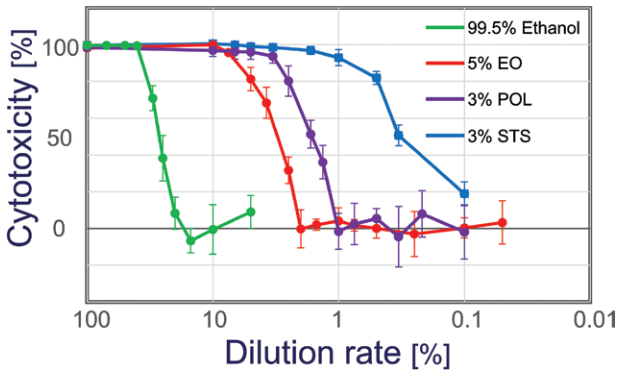

Fig. 1. Relationship between cytotoxicity and the dilution rate. Each measurement was performed in four wells. Error bars indicate SD.

Ethanol kills cells by fixation and causes precipitate formation (ie, embolization) in blood.[1] Its mechanism as a sclerosant is unique; therefore, the difference in resistivity of the dilution series from others was not surprising.

However, the remaining three are biochemically classified as surfactant detergents. EO and STS are anionic surfactants that denature proteins or disrupt membrane protein complexes, whereas POL is a nonionic surfactant that solubilizes membrane proteins without affecting important structural features.[4,5] Interestingly, in our assessment of POL and EO at clinically used concentrations, the degree of decrease in cytotoxicity by dilution was similar in each, whereas STS was more resistant to dilution, and ethanol was prone to lose its cytotoxicity with dilution.

We assessed the in vitro cytotoxicities of four well-known sclerosants. Our comparative data might help clinicians to have a better understanding of sclerotherapy for venous malformations.

*From the *Department of Plastic, Reconstructive and Aesthetic Surgery, The University of Tokyo Hospital, Tokyo, Japan; and †Department of Neurosurgery, The University of Tokyo Hospital, Tokyo, Japan.*

Received for publication June 29, 2021; accepted July 21, 2021.

Plast Reconstr Surg Glob Open 2021;9:e3814; doi: 10.1097/GOX.0000000000003814; Published online 17 September 2021.

Yuta Moriwaki, MD
The University of Tokyo Hospital
7-3-1 Hongo, Bunkyo-ku
Tokyo 1138655
Japan
Email: y.moriwaki147@gmail.com

DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

Related Digital Media are available in the full-text version of the article on www.PRSGlobalOpen.com.

REFERENCES

1. Mol W, Furukawa H, Sasaki S, et al. Evaluation of the sclerotherapeutic efficacy of ethanol, polidocanol, and OK-432 using an in vitro model. *Dermatol Surg.* 2007;33:1452–1459.
2. Berridge MV, Herst PM, Tan AS. Tetrazolium dyes as tools in cell biology: new insights into their cellular reduction. *Biotechnol Annu Rev.* 2005;11:127–152.
3. Jenkinson HA, Wilmas KM, Silapunt S. Sodium tetradecyl sulfate: a review of clinical uses. *Dermatol Surg.* 2017;43:1313–1320.
4. Parsi K. Interaction of detergent sclerosants with cell membranes. *Phlebology.* 2015;30:306–315.
5. Kang JH, Kambayashi J, Sakon M, et al. Mechanism of the haemostatic effect of ethanolamine oleate in the injection sclerotherapy for oesophageal varices. *Br J Surg.* 1987;74:50–53.