CLINICAL INVESTIGATION

## Lidocaine is a Novel Antispasmodic Agent during Colonoscopy

Submitted: 30 May 2017; Accepted: 27 June 2017; Published online: 03 July 2017

## Commentary

Hyoscine butylbromide and glucagon are both used as antispasmodic agents to relax muscle tone in the gastrointestinal tract, and may improve mucosal visualization during colonoscopy, thus resulting in a higher polyp/adenoma detection rate [1]. However, hyoscine butylbromide often causes dry mouth, urinary retention, miosis etc., and glucagon also causes hyperglycemia and reactive hypoglycemia. Topical dispersion of peppermint oil [2,3] or warm water [4,5] are alternatives to these antispasmodic agents, but warm water infusion failed to suppress intestinal spasm in clinical trials. In contrast, topical peppermint oil relaxes the intestinal muscle by l-menthol which is the active component of peppermint oil blocking the calcium channels of smooth muscle. [6,7]. In our experience, however, topical peppermint oil has a serious drawback in that the duration of the effect of peppermint oil is rather short. Once the effect disappears, most patients report terrible spasms. Repeated dispersion of peppermint oil does not work in most patients. Therefore, peppermint oil is not widely used, and colonoscopists still seek an ideal antispasmodic agent with long-term duration and no adverse effects.

Lidocaine hydrochloride is an agent familiar to physicians, being used as a local anesthetic or antiarrhythmic agent which acts through blocking Na<sup>+</sup> channels in neuronal tissue, voluntary muscle and involuntary muscles including cardiac muscle [8,9]. In the gastrointestinal tract, lidocaine hydrochloride is speculated to work as an antispasmodic by relaxing smooth muscle tone. In our recent double-blinded clinical trial [10], 60 patients requiring endoscopic resection were randomly allocated to colonoscopy with topical dispersion of lidocaine (n=30)or peppermint oil (n=30). Two endoscopists dispersed the assigned solution and observed for five minutes. The primary endpoint was the duration of spasm inhibition, and the secondary endpoint was the occurrence of rebound spasm. Spasm inhibition was observed in almost all patients in both groups, with a similar median duration. In contrast, rebound spasm occurred less frequently in the lidocaine group. No adverse events occurred in this trial.

In recent colonoscopy practice, nevertheless, we preferably spray 2% or 4% of lidocaine hydrochloride solution through the channel without hesitation when severe intestinal spasm occurs during endoscopic mucosal resection or endoscopic submucosal dissection. Since a 1% lidocaine hydrochloride solution is not effective based on our experience, a 2% or 4% solution of lidocaine hydrochloride solution is best for suppressing these bothersome spasms.

There are three reasons for this preference. First, rebound spasm after dispersion rarely occurs during colonoscopy, which is quite different from peppermint oil. It is well known that lidocaine hydrochloride is an amide local anesthetic with a longer effective Kazutomo Togashi<sup>1</sup>\*, Daiki Nemoto<sup>1</sup>, Daisuke Takayanagi<sup>1</sup>, Taka-aki Koshimizu<sup>2</sup>, Shungo Endo<sup>1</sup>, Alan Kawarai Lefor<sup>3</sup> <sup>1</sup>Department of Coloproctology, Aizu Medical Center Fukushima Medical University, Japan <sup>2</sup>Department of Pharmacology, Jichi Medical University, Japan <sup>3</sup>Department of Surgery, Jichi Medical University, Japan \*Author for correspondence: togashik@fmu.ac.jp period for inhibiting sodium channels, compared with ester-type local anesthetics. The anesthetic effect of lidocaine (2-10%) reportedly lasts for 30-45 minutes in mucous membranes [11]. The long lasting and extensive anesthesia produced by lidocaine is related to the decreased incidence of rebound spasm. Second, lidocaine dispersion works immediately. To get a rapid inhibitory effect, a 4% lidocaine solution should be dispersed using a spraying catheter. This may be useful for resolution of colon spasms seen during intubation/extubation, observation of significant lesions, and advanced therapeutic procedures. Third, no adverse events have been experienced to date. The depth of infiltration and sites of action are different for peppermint oil and lidocaine hydrochloride. l-Menthol infiltrates up to the muscularis propria layer and blocks the voltage-dependent calcium channels

of the smooth muscle, and also the channels of nerves in the submucosal and muscularis propria layers [12]. In contrast, lidocaine blocks sodium channels of the nerves only in the mucosal layer because it cannot infiltrate into the submucosal layer or deeper [11]. Therefore, the amount of lidocaine absorbed into blood is minimal, rarely causing adverse events. The only exception for the topical use of lidocaine hydrochloride is hypersensitivity to components of the formulation.

Recently, we completed patient enrollment in a new multicenter randomized controlled trial comparing lidocaine to saline during colonoscopy. If positive results are obtained, the lidocaine dispersion method could be applied to various endoscopic procedures, such as upper GI endoscopy, biliary endoscopy and enteroscopy. This method may be a useful resolution to the problem of gastrointestinal spasm.

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