

The Significance of NBI-ME on Chronic Gastritis with Intestinal Metaplasia

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Abstract: In order to prevent the occurrence of gastric cancer, it is very important to find early gastric cancer and precancerous lesions timely. This research discussed diagnostic value of methylene blue staining under white light endoscopy, light blue crest (LBC) and white opaque substance (WOS) under NBI-ME on chronic gastritis with intestinal metaplasia. 227 patients who accepted gastroscopy in our hospital and met the inclusion criteria were selected. Olympus GIF-HQ290 electronic gastroscope was applied to finish examination under the common white light mode, to observe whether there was LBC and WOS under the NBI-ME mode and to observe whether there was baby blue staining area under the methylene blue staining. Biopsy mucosae were conducted on the diseased region. Biopsy histopathology was diagnosed as a "golden standard". Moreover, the relation between special performance and pathology of intestinal metaplasia under three endoscopes was compared. 227 patients were examined, showing that sensitivity, specificity, positive predictive value and negative predictive value of methylene blue were 97.01%, 98.75%, 97.01% and 98.75%, respectively. These of LBC were 80.60%, 97.50%, 93.10% and 92.31%, and these of WOS were 82.09%, 96.88, 91.67% and 92.81%. All of them conducted a chi-square test with pathological results and $P > 0.05$. Three kinds of special performance under the endoscope had higher consistency with pathological results. Three kinds of special performance under the endoscope had higher consistency with pathological results. Methylene blue staining under the gastroscope, LBC under NBI-ME and WOS can be used as a simple and effective method to judge whether there is intestinal metaplasia.

Keywords: Early gastric carcinoma; Intestinal metaplasia; Methylene blue staining; LBC; WOS

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1. Introduction

In 2014, WHO indicated in the research report around the world that newly increased patients with gastric carcinoma and death cases of gastric carcinoma occupied more than 2/5 in the total number in China and ranked in the first place in China. The morbidity and mortality of gastric carcinoma in different areas of China have a difference, but both of them are higher than the internal average level [1].

Through years of studies on gastric carcinoma by domestic and overseas scholars, the normal Correa mode [2] of gastric mucosa-chronic superficial gastritis-chronic atrophic gastritis-intestinal metaplasia-dysplasia-gastric carcinoma has already been widely accepted and recognized by everyone. Timely intervention or interdiction before developing into gastric carcinoma can improve patients' lifetime and life quality to a large extent. With the technical development of ESD under the endoscope in recent years, physicians of endoscope can strip off mucosa at early gastric carcinoma through the endoscope and interdict its further development with the precondition of finding out early gastric carcinoma or precancerous lesions in endoscopy by physicians. However, early gastric carcinoma generally has no specific performance under the white light endoscope and often shows focal mucosa redness or tiny sinking (erosion), so it is often neglected or misdiagnosed. In 2012, Yao [3] indicated that early gastric carcinoma often took place on the basis of some mucosa in diagnostic

analysis of early gastric carcinoma under the endoscope, including helicobacter pylori infection, atrophic gastritis and intestinal metaplasia, etc. Meanwhile, he also proposed an opinion that patients without high-risk background mucosa had a lower risk of early gastric carcinoma. Therefore, in terms of physicians, recognizing whether patients have high-risk background mucosa rapidly and effectively not only can improve checking efficiency, but also can reduce omission diagnostic rate of early carcinoma.

As a part of gastric carcinoma, the close relation [4] between intestinal metaplasia and gastric carcinoma has already been widely concerned in clinic. The pathology is regarded as a golden standard of diagnosing intestinal metaplasia clinically, but intestinal metaplasia is lack of specific performance under the white light observation of common gastroscope. Sampling as Sydney standards in common stomachoscopy still has a higher omission diagnostic rate [5-8]. With the development of staining technique and pigment endoscope under endoscope, clinic work of extensive physicians gradually finds that methylene blue staining [9] under common gastroscope, light but crest (LBC) [10] under NBI-ME and white opaque substance(WOS) have some reminding significance on intestinal metaplasia. NBI-ME has had shorter applied time in clinic, since it was published, thus domestic and overseas reports seldom mention diagnostic significance of LBC on intestinal metaplasia. There is no relevant study on correlation between WOS and intestinal metaplasia.

The main purpose of the study aims to study diagnostic value and feasibility of three kinds of endoscope's specific performance on intestinal metaplasia in stomachoscopy and provide fundamental basis for recognizing high-risk background mucosa of early gastric cancer rapidly and effective in stomachoscopy.

2. Materials and Methods

2.1. Selection of Cases

227 patients who accepted stomachoscopy and biopsy in our hospital from October 2015 to January 2016 were regarded as research objects. Inclusion criterion: patients with 18 years old or above needed stomachoscopy for upper digestive tract symptoms, such as stomachache, abdominal distension, belching and sour regurgitation, etc., and agreed to participate in the experiment. Exclusion criterion: postoperative gastric patients, patients who took antiplatelet drugs and anticoagulant drugs within 1 week, patients who had serious dysfunction in liver, kidney and cardio-pulmonary function, patients with bleeding tendency, and patients who couldn't coordinate in the inspection process.

2.2. Materials and Reagents

Olympus GIF-HQ290 electronic gastroscope with NBI-ME function, Olympus CLV290SL electronic processor, OEV-262H display, 0.5% of methylene blue injection (Taizhou Changpu Chemical Reagent Co., Ltd), lidocaine hydrochloride (Jiangsu Jichuan Pharmacy Production Company), Simethicone (Percy, Berlin Chemical Joint-Stock Company (Menarini Group), protease (Deyou, Beijing Ted Pharmacy Co., Ltd), sodium bicarbonate (Beijing Ted Pharmacy Co., Ltd) and biopsy forceps, etc., were applied.

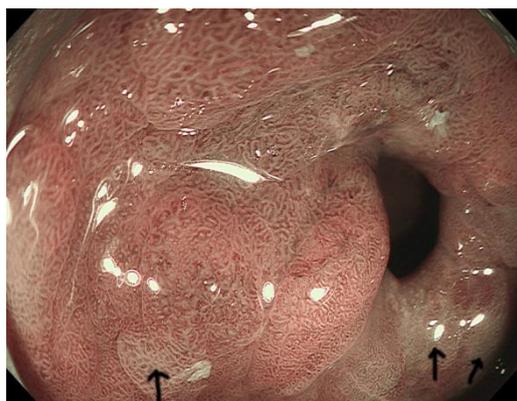


Figure 1. WOS.

2.3. Methods and Steps

Preoperative conversations: Explained conditions and contraindications to patients, consulted with patients whether they agreed and accepted to apply magnifying stomachoscopy and to use methylene blue staining, as well as signed informed consent.

Preoperative preparation: Before 30 min of

inspection, pronase 2000u, 10g of sodium bicarbonate, and 5ml of Percy were melted in 100ml of warm water for taking orally, so as to eliminate intragastric mucus and bubbles for convenient observation; before inspection, take lidocaine mucilage to do pharyngeal anesthesia.

Stomachoscopy: Conventional stomachoscopy was conducted firstly; Switched to NBI-ME mode and observed whether there were WOS (Figure 1) and LBC (Figure 2). 30ml of 0.5 % Methylene blue solution was sprayed to sinuses ventriculi and the surface of gastric body mucosa evenly. After 1 min, saline was used to wash and observed whether there was baby blue staining area (Figure 3);



Figure 2. LBC.

Took biopsy and sent to pathology department for pathological examination. Pathological sampling gave priority to judge the position of intestinal metaplasia under the above-mentioned endoscope. If there was no intestinal metaplasia under the endoscope, greater curvature side of sinuses ventriculi *1, lesser curvature side of sinuses ventriculi *1, angle of stomach *1, greater curvature side of gastric body *1, lesser curvature side of gastric body *1 were conducted pathological diagnosis. The pathological diagnosis referred to diagnostic criteria about intestinal metaplasia in new Sydney standards. The dependency of pathological results and specific performance under three kinds of endoscope was conducted statistical analysis. Conduct chi-square test. $P < 0.05$ had a statistical difference.

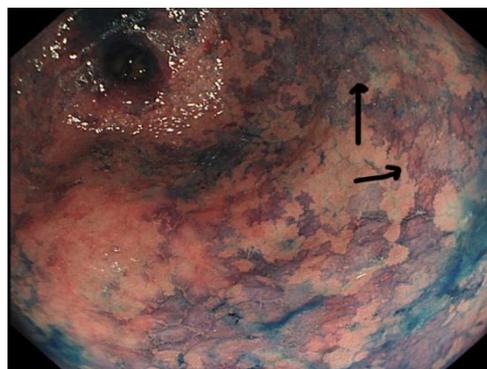


Figure 3. Mythylene Blue Staining Area.

2.4. Statistical methods

SPSS 20.0 software was used to calculate sensibility, specificity, positive predicative value, negative predictive value and conduct chi-square test. $P < 0.05$ had a statistical difference.

3. Results

In the experiment, we collected 227 patients (including 108 male patients and 119 female patients). Through the stomachoscopy, there were a total of 58 patients with LBC (28 males and 30 females), a total of 60 patients with WOS (29 males and 31 females), a total of 67 patients (33 males and 34 females) with baby blue staining area after methylene blue staining, and a total of 67 patients (33 males and 34 females) who were diagnosed as intestinal metaplasia after pathological examination. Intestinal metaplasia and three kinds of performance of intestinal metaplasia had no statistical significance in males and females ($P > 0.05$).

Under three kinds of endoscope, sensitivity, specificity, positive predictive value and negative predictive value of diagnosing intestinal metaplasia were shown in Table 1. Three of them and pathological results were conducted the chi-square test. P was greater than 0.05.

Features under three kinds of endoscope were conducted chi-square test. All of them have no statistical difference ($P > 0.05$).

In the experimental process, parts of patients were observed under NBI-ME after methylene staining of LBC and WOB in step It could be found that after methylene, it wouldn't impact observation of LBC and microstructure, but it would cause some influences on observation of WOS and capillaries.

After the operation, 227 patients were conducted follow-up visit. Except that 32 patients had blue pee, nausea and abdominal discomfort after finishing inspection, all participators had no other relevant adverse drug reaction, such as heart rate increase and blood pressure reduction, etc.

Table 1 The relation between performance and pathology under three kinds of endoscope.

	Pathological Results		Sensitivity	Specificity	Positive predictive value	Negative predictive value	p
	Intestinal metaplasia +	Intestinal metaplasia-					
LBC	54	4	80.60	97.50	93.10	92.31	>0.05
	13	156					
WOS	55	5	82.09	96.88	91.67	92.81	>0.05
	12	155					
Methylene blue	65	2	97.01	98.75	97.01	98.75	>0.05
	2	158					

4. Discussion

With the constant updating of gastroscope and equipment in recent years, new theories and new inspection methods have been widely applied in clinic. Lesion before gastric carcinoma has already become a key point of lots of physicians. Early detection and early interdiction can delay or interdict development of gastric carcinoma effectively and improve life quality and lifetime of patients. For intestinal metaplasia, our cognition should not be limited to precancerous lesion and we also should notice its guiding value on early carcinoma in stomachoscopy. In the process of endoscopy, as the background mucosa of early carcinoma, once there is evidence reminding there is intestinal metaplasia, we should notice the occurrence of early gastric carcinoma and carry out ME-NBI

observation in a corresponding area. Even if there is not allowable condition, it also need white light to inspect again, for fear of omission. The study showed that performance of intestinal metaplasia under three kinds of endoscope had higher specificity, sensitivity, positive predictive value and negative predictive value. However, the statistical inspection showed that all of them had higher consistency with pathology. All of them had some guiding value on diagnosing intestinal metaplasia. LBC and WOS is a sign of new intestinal metaplasia under the endoscope. The sensitivity in both of them was relatively lower (80.60% and 82.09%, respectively). This might be related to miss diagnosis.

Though three kinds of endoscope showed that pathological results have higher consistency, their principles are different. Mythylene blue staining means that 0.2-0.5% of methylene blue solution is sprayed in

a suspicious area. Methylene is used to be absorbed by goblet cells by intestinal metaplasia mucosa, but it won't be absorbed by others. The intestinal metaplasia area presented baby blue for staining, but non-intestinal metaplasia area, such as normal mucosa, anabrosis scar and polyp, etc., doesn't color [8]. Because everyone had no sufficient cognition on the ration between background mucosa and gastric carcinoma at early times, it was seldom applied in clinic, even if lots of evidences proved that methylene blue staining had a diagnostic value on intestinal metaplasia. In 2005, Uedo et al found and reported LBC. Its definition is: slender and azury lineage structure [9] that is located in the surface of epithelial cells or brain return sample's structural ridge. They also indicated that it might be the characteristic performance of intestinal metaplasia. Afterwards, studies show that LBC only occurs in mucosa without canceration. In the area of canceration, there is no LBC. In other words, LBC only occurs in the area with intestinal metaplasia. It is necessary to observe the area disappearing LBC in the area of intestinal metaplasia to notice the occurrence of early carcinoma. In 2007, Yao K found WOS [10, 12, 13] and conducted relevant studies. He proposed a new idea that WOS might be a new sign of intestinal metaplasia, but current extensive scholars only concentrate on studying diagnostic value on early carcinoma. Moreover, WOS not only remind diagnosis of early gastric carcinoma, but also remind colon early carcinoma. However, the generation mechanism of WOS is not clear.

Methylene blue staining is equipped with some features, such as easy observation, clear display and easy understanding of beginners. Though there was no case with serious adverse reaction in the experiment, it may not exclude the possibility of occurring adverse reaction completely. Beginners or centers with poor basic equipment should apply methylene blue staining to improve diagnostic accuracy under the situation of acquiring patients' informed consent [14]. LBC and WOS need to observe under the NBI-ME mode. Because generation mechanism of them is optical mechanism, this may avoid from a series of adverse responses caused by chemical stains. However, it has some disadvantages, such as long operation time, large difficulty, omission in some areas, influences of light conditions on imaging, higher requirements for physicians and equipment, so it is necessary to operate carefully and avoid from omission.

To sum up, physicians should notice whether patients have high-risk background mucosa in endoscope operation. It suggests that the above-mentioned methods can be applied to improve judgment on background mucosa and reduce omission diagnostic rate of early gastric carcinoma.

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