A randomized controlled trial of prophylactic antibiotics in the prevention of electrocoagulation syndrome after colorectal endoscopic submucosal dissection

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Background and Aims: Endoscopic submucosal dissection (ESD) is currently commonly performed, but colorectal ESD has a substantial risk of adverse events, including post-ESD electrocoagulation syndrome (PEECS). We investigated whether the use of prophylactic antibiotics can reduce the occurrence of PEECS.

Methods: Patients who underwent colorectal ESD were randomly assigned to 1 of 2 treatment regimens. Ampicillin and/or sulbactam mixed with normal saline solution was administered 1 hour before ESD in group 1 then additionally injected every 8 hours twice more. In group 2, normal saline solution without antibiotics was administered following the same schedule. We investigated the characteristics of the patients and tumors, the incidence of PEECS, laboratory findings, and the visual analog scale (VAS) score for abdominal pain measured on the morning after ESD.

Results: A total of 100 cases (50 per group) were finally analyzed, and 97 tumors were successfully resected en bloc. The number of patients having C-reactive protein (CRP) levels $\geq$1 mg/dL and the number of patients having VAS scores for abdominal pain $\geq$1 were greater in group 2 than in group 1 ($P = .008$ and .023, respectively). The incidence of PEECS in group 2 also was higher than that in group 1 (1 and 8 in groups 1 and 2, respectively; $P = .031$).

Conclusions: The prophylactic use of ampicillin and/or sulbactam in colorectal ESD is associated with reduced risk of PEECS, decreased CRP levels, and decreased abdominal pain. The use of prophylactic antibiotics in colorectal ESD may be an effective tool for reducing the risk of PEECS. (Clinical trial registration number: KCT0001102.) (Gastrointest Endosc 2017;86:349-57.)

Endoscopic submucosal dissection (ESD) is accepted as an effective treatment method for early gastric cancer and gastric adenoma.[1] This technique also has been applied successfully to tumors in the colorectal area.[2-4] However, colorectal ESD is technically difficult, because of the thin wall and tortuous folds of the organ, and it has a substantial risk of adverse events.[5-8] In particular, post-ESD electrocoagulation syndrome (PEECS) is one of the most common adverse events.[9-11]

PEECS is characterized by peritoneal inflammation in the absence of frank perforation that occurs after ESD.[9,12] Patients typically present with abdominal pain, fever, leukocytosis, and major signs of peritoneal inflammation. The reasons for PEECS are unknown; however, it seems to be related to excessive coagulation in the muscularis propria, catheter-related infection, and mucosal defect that is exposed after ESD.[12-15] Using an electrocautery device can cause transmural burning because of the electric current and can cause symptoms mimicking colon perforation. In some cases, it may eventually result in delayed perforation.[16]

A previous study revealed that PEECS occurred in only 7.1% of patients who underwent gastric ESD.[17] However, in colorectal ESD, the incidence was substantially higher, but varied from 40.2% to 12.1%; a previous study showed

Abbreviations: CRP, C-reactive protein; ESD, endoscopic submucosal dissection; LST, laterally spreading tumor; LST-G, granular LST; LST-GH, homogenous LST; LST-GM, nodular mixed LST; LST-NG, nongranular LST; LST-NGF, flat elevated LST; LST-NGPD, pseudo-depressed LST; PEECS, post-endoscopic submucosal dissection electrocoagulation syndrome; VAS, visual analog scale.

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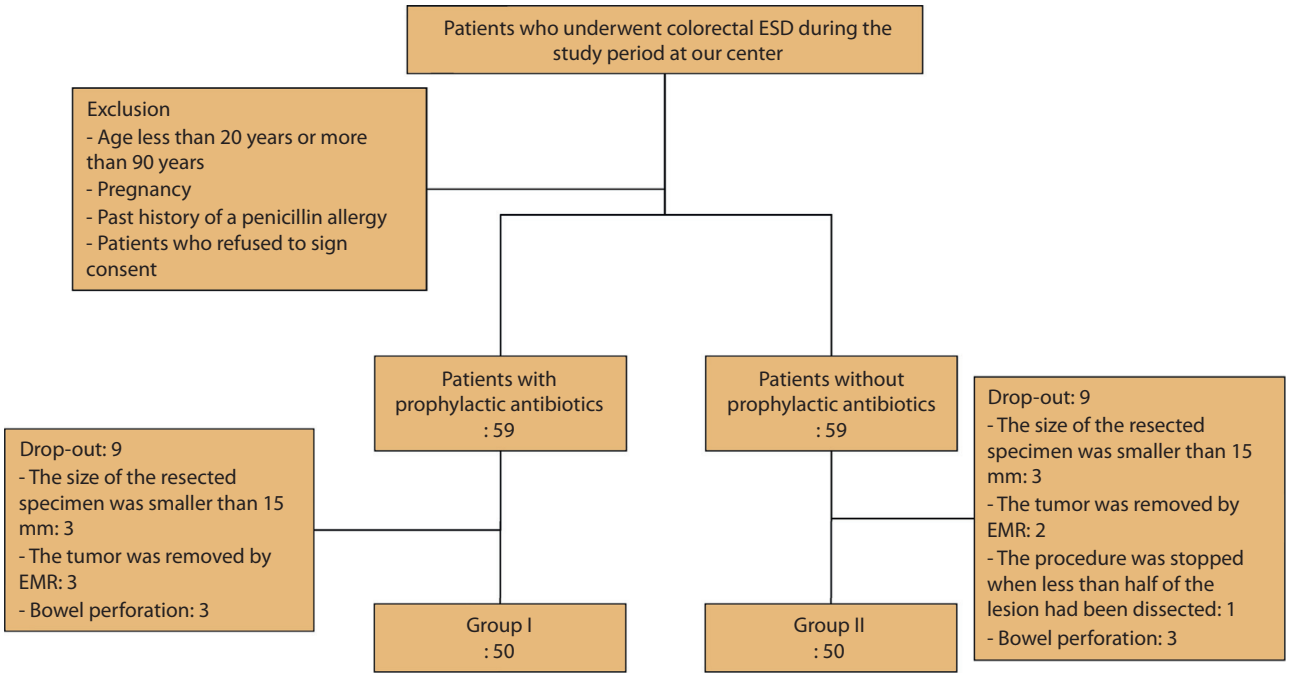

Figure 1. Flowchart of the study. The patients who underwent colorectal endoscopic submucosal dissection (ESD) were randomly assigned to 1 of 2 groups. Eighteen patients dropped out of our study for the following reasons: small-sized specimen (<15 mm), tumor removed by EMR, bowel perforation, or when the procedure was stopped when less than half of the lesion had been dissected. Finally, a total of 100 ESD cases (50 per group) were enrolled.

that PEECS occurred in 33 of 82 patients who underwent colorectal ESD, but another recent study showed that PEECS arose in 21 of 173 cases.[9,11]

In practice, if PEECS is suspected after colorectal ESD, antibiotics are frequently used, because we cannot rule out the possibility of microscopic perforation or delayed perforation. PEECS also may lengthen the hospitalization period and may require additional tests, including CT. Therefore, it is important to prevent PEECS to reduce additional pain and medical costs.

We assumed that the use of prophylactic antibiotics before and after colorectal ESD may decrease the risk of PEECS. However, little is known about the effect of prophylactic antibiotics. Thus, we investigated whether the use of prophylactic antibiotics can reduce the occurrence of PEECS and improve patients' clinical course, by comparing patients treated with or without prophylactic antibiotics.

METHODS

Patients

From April 2014 to October 2016, patients who underwent ESD because of colorectal tumors in Konkuk University Hospital were included in this prospective, randomized, double-blind study. The indications for colorectal ESD were based on the Criteria of Indications for Colorectal ESD, proposed by the Colon ESD Standardization Implementation Working Group.[18]

The exclusion criteria were age <20 years or >90 years, pregnancy, history of a penicillin allergy, or refusal to sign consent (Fig. 1). Recruited patients were randomly divided into 2 equal-sized groups by using the patient identification number generated in Microsoft Excel 2010 (Microsoft, Redmond, Wash, USA). The random table was preordered by a researcher who was not involved in the study. The endoscopic methods included in this study were ESD and simplified ESD. Simplified ESD was defined as an ESD procedure that involved snaring after the circumferential incision and sufficient submucosal dissection.[19] If the procedure was stopped before the completion of the ESD because of severe fibrosis, it was termed *ESD failure*.[11] Among the ESD failure cases, if less than half of the whole dissection procedure was performed, the case was dropped out of the study. In addition, the following cases also were dropped out of the study: those in which the size of the final resected specimen was <15 mm in diameter; those in which the tumor was removed through EMR instead of ESD; or those in which bowel perforation occurred during or after the procedure.

This study was approved by the Institutional Review Board (IRB) of Konkuk University School of Medicine, which confirmed that the study was in accordance with the ethical guidelines of the Helsinki Declaration (KUH1010556). After IRB approval, this study was registered as Clinical Research Information Service (CRIS) ID: KCT0001102. Informed consent for the procedure was obtained from the patients before their examinations, and all