Original Paper

# Is Submucosal Epinephrine Injection Necessary Before Polypectomy? A Prospective, Comparative Study

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**ABSTRACT**

**Background/Aims:** Polyps of the gastrointestinal tract are usually removed due to their link to bleeding, obstruction and malignancy. However, complications may occur following polypectomy. The aim of this study was to assess whether submucosal epinephrine injection before polypectomy could reduce the incidence of bleeding and perforation.

**Methodology:** Between June 1997 and November 1999, patients with sessile polyps of the gastrointestinal tract found in our endoscopic unit were randomized to receive submucosal epinephrine injection (epinephrine group) or no injection (control group) before polypectomy. In the epinephrine group, epinephrine (1:10,000) was injected surrounding the stalk of the polyp until the mucosa was blanched and bulged. The patients were observed for complications in the following month.

**Results:** A total of 120 patients with 151 sessile polyps were enrolled in this study. In the epinephrine group, 75 polyps (n=68) were randomized to receive epinephrine injection before polypectomy. In the control group, 76 polyps (n=61) underwent polypectomy without epinephrine injection. In both groups, there was no significant difference in clinical features including the sizes of the polyps and their stalks, the location of polyps and the pathological diagnosis. There were a total of nine episodes of post-polypectomy hemorrhage, two in the epinephrine group and seven in the control group (2/75 *vs.* 7/76) ($P$=0.07). One case in the epinephrine group experienced delayed bleeding (4 days later). Immediate hemorrhage occurred less in the epinephrine group than that in the control group (1/75 *vs.* 7/76, $P$=0.03). There was one case of perforation in each group.

**Conclusions:** Epinephrine injection prior to polypectomy is effective in preventing immediate bleeding.

**KEY WORDS:** Complication; Epinephrine; Polypectomy

**ABBREVIATIONS:** Epinephrine (Epi); Control (Ctr); Nonsteroidal Anti-Inflammatory Drug (NSAID); Confidence Interval (CI); Upper Gastrointestinal (UGI)

## INTRODUCTION

Polyps of the gastrointestinal tract are associated with the risks of malignant transformation, bleeding and sometimes obstruction (1-4). Therefore, they are usually removed if no contraindication exists. To avoid the complications of bleeding and perforation with polypectomy (5), several attempts have been made such as submucosal injections of saline (6), hypertonic saline (7), vasoconstricting (8,9) or sclerosing solutions (10) before polypectomy, and use of difference forms of coagulation current (11).

Epinephrine injection has been used widely for treatment of peptic ulcer bleeding (12), but its role in preventing complications of polypectomy is still unclear. The aim of this study was to assess whether prophylactic submucosal epinephrine injection could reduce the incidence of bleeding and perforation after polypectomy in the gastrointestinal tract.

## METHODOLOGY

From June 1997 to November 1999, 122 patients with sessile polyps of the gastrointestinal tract found in our endoscopic unit were randomized to receive prophylactic submucosal epinephrine (Epi) injection (Epi group) or no injection (control, Ctr group). Sealed envelopes containing therapeutic options derived from a randomized table were prepared by a statistician who was not involved in this study. The envelope was opened before polypectomy for every enrolled patient once written informed consent had been obtained.

Patients were excluded from the study if they 1) had bleeding tendency (platelet count <50000/mm$^3$, prothrombin time less than 30%, or taking anticoagulants); 2) were unable or unwilling to give the written informed consent; 3) were pregnant; 4) had inserted a pacemaker or 5) had a history of being allergic to epinephrine.

In the Epi group, epinephrine (1:10,000) 0.5-1mL was injected surrounding the stalk of the polyp until the mucosa was blanched and bulged. A total of 2-10mL epinephrine was injected in this study.

We used an Olympus panendoscope (GIF-PQ20), a

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**TABLE 1 Clinical Features of Patients with Epinephrine Injection (Epi Group) and Patients without Injection (Ctr Group)**

| | Epi (n=68) | Ctr (n=61) |
|---|---|---|
| Median age (95%CI), y | 62.9 (59.8-62.1) | 64.9 (62.1-67.8)[a] |
| Sex, M/F | 40/28 | 40/21[a] |
| NSAID | 4 | 4[a] |
| Smoking | 12 | 11[a] |
| Alcohol | 3 | 3[a] |
| Co-morbid | 28 | 25[a] |

[a]No statistically significant differences were observed between both groups.

**TABLE 2 Size and Location of the Polyps with Epinephrine Injection (Epi Group) and Polyps without Injection (Ctr Group)**

| Epi (n=75) | Ctr (n=76) | |
|---|---|---|
| Size of polyps (cm, median, 95%CI) | 0.8, 0.8-1.3 | 0.8, 0.8-1.1[a] |
| <1.0cm | 41 | 45[a] |
| ≥1, <2.0cm | 29 | 23[a] |
| ≥2.0cm | 5 | 8[a] |
| Size of stalks (cm, median, 95%CI) | 0.4, 0.4-0.5 | 0.4, 0.4-0.6[a] |
| **Location** | | |
| **Colon** | | |
| Ascending | 2 | 8[a] |
| Transverse | 0 | 4[a] |
| Descending | 1 | 6[a] |
| Sigmoid | 26 | 24[a] |
| Rectum | 10 | 6[a] |
| **Stomach** | | |
| Antrum | 10 | 5[a] |
| Body | 19 | 18[a] |
| Cardia | 2 | 3[a] |
| Fundus | 1 | 0[a] |
| Duodenum | 1 | 2[a] |
| Esophagus | 3 | 0[a] |

[a]No statistically significant differences were observed between both groups.

colonoscope (CF-230L), a sigmoidoscope (CF-230S), an injection needle (Olympus NM-4U-1) and an electrocautery snare (Olympus SD-9L-1 in UGI tract and SD-5U-1 in colon) to perform polypectomy. The size of the polyps and their stalks was measured by an endoscopic meter (Olympus M2-4K). Polypectomy was executed according to the conventional method (7,8). In short, the snare was tightly placed around the base of the polyp. It was then pulled towards the cavity of the gastrointestinal tract. Coagulating current was applied with the setting of either 2.5 or 3.0. At the same time, the snare was tightened gradually until the polyp was resected. To minimize the difference of endoscopic techniques, all resections in this study were performed by one senior, experienced endoscopist (H. J. Lin).

The patients were followed one week and one month later at our out-patient department. They were questioned about the presence of melena, hematemesis, abdominal pain or other discomfort.

Post-polypectomy hemorrhage was defined as continuous bleeding (oozing or pulsatile hemorrhage) persisting for 3 minutes. We classified bleeding into minor bleeding (without hemodynamic alternations) and major bleeding (with hemodynamic changes demanding blood transfusion). Immediate bleeding was defined as bleeding occurring during the procedure or within 24 hours of polypectomy. Delayed bleeding was defined as bleeding occurring between the 2nd and the 30th day after polypectomy.

A positive history of nonsteroidal anti-inflammatory drug (NSAID) ingestion was defined as >1 tablet/day NSAID ingestion within seven days of polypectomy. Positive cigarette smoking was defined as ≥10 cigarettes per day for at least one year. Positive alcohol drinking was defined as ≥40g/day alcohol consumption for at least six months.

Statistical analysis was carried out using Fisher's exact test and Student's $t$ test if appropriate. Data were expressed as median and 95% confidence interval (CI). A $P$ value less than 0.05 was considered significant.

## RESULTS

During the period of this study, 122 patients with sessile polyps were included initially. Two of them were excluded because of bleeding tendency (n=1) and pacemaker insertion (n=1). Finally, a total of 120 patients with 151 sessile polyps were enrolled. In the Epi group, 75 polyps (n=68) were randomized to receive Epi injection before polypectomy. In the Ctr group, 76 polyps (n=61) underwent polypectomy without Epi injection. Twenty-six patients had more than one polyp (2 polyps, n=22; 3 polyps, n=3; 4 polyps, n=1). The median volume of Epi solution injected in the Epi group was 3mL (95% CI: 2.45-4.31mL). There was no significant difference in clinical features between both groups **(Table 1)**.

**TABLE 3 The Pathological Diagnosis of the Polyps with Epinephrine Injection (Epi Group) and Polyps without Injection (Ctr Group)**

| | Epi (n=75) | Ctr (n=76) |
|---|---|---|
| **Colon** | | |
| Non-neoplastic | 7 | 5[a] |
| Tubular | 25 | 34[a] |
| Tubulovillus | 6 | 7[a] |
| Villus | 1 | 1[a] |
| Carcinoid | 0 | 2[a] |
| **UGI tract** | | |
| Hyperplastic | 17 | 13[a] |
| Inflammatory | 10 | 8[a] |
| Adenomatous | 7 | 6[a] |
| Others [b] | 2 | 1[a] |

[a]No statistically significant differences were observed between both groups.

[b]Others included a hemangioma and a granulation tissue in esophagus (Epi group) and an ectopic pancreas in duodenum (Ctr group).

**TABLE 4 Details of Patients who Experienced Post-polypectomy Hemorrhage**

| Group | Age (y) | Sex | Volume (mL | Location | Size of polyp (cm) | Size of stalk (cm) | Pathology | Management |
|---|---|---|---|---|---|---|---|---|
| Epi | 19 | M | 4 | Esophagus | 0.6 | 0.4 | Granulation tissue | Bleeding 4 days later, BT 750mL |
| Epi | 71 | F | 4 | Stomach, body | 1.5 | 0.6 | Hyperplastic polyp | HPT |
| Ctr | 55 | M | 0 | Stomach, body | 5 | 1 | Hyperplastic polyp | HPT and BT 1000mL |
| Ctr | 71 | M | 0 | Stomach, cardia | 1.2 | 0.6 | Hyperplastic polyp | HPT |
| Ctr | 70 | M | 0 | Ascending colon | 0.3 | 0.2 | Tubular adenoma | HPT |
| Ctr | 74 | M | 0 | Descending colon | 0.6 | 0.4 | Tubular adenoma | Epinephrine injection |
| Ctr | 39 | F | 0 | Stomach, body | 1.5 | 1.2 | Inflammatory polyp | HPT |
| Ctr | 44 | F | 0 | Stomach, cardia | 1 | 0.3 | Hyperplastic polyp | HPT |
| Ctr | 80 | F | 0 | Stomach, cardia | 0.4 | 0.3 | Inflammatory polyp | HPT |

Volume: volume of epinephrine injected; HPT: heater probe thermocoagulation; BT: blood transfusion.

**Table 2** shows the size and location of the polyps in both groups. More than half of the polyps were less than 1cm (55% and 59% in Epi and Ctr groups, respectively). The sizes of the polyps and their stalks were comparable between both groups. The locations of polyps were similar in both groups **(Table 2)**.

The pathological findings of the polyps were listed in **Table 3**. Tubular adenoma was the most common polyps in both groups (33% *vs.* 45%), followed by hyperplastic polyps. The pathological diagnosis was similar between both groups.

There were totally nine episodes of post-polypectomy hemorrhage, two in the Epi group and seven in the Ctr group ($P$=0.07) **(Table 4)**. Delayed bleeding occurred (4 days later) in one case of the Epi group. Immediate hemorrhage occurred less in the Epi group than in the Ctr group (1/75 *vs.* 7/76, $P$=0.03) **(Table 5)**. Each group had one case of perforation. They received operation thereafter. No bleeding or perforation occurred in patients with polyps larger than 2cm. No cardiovascular complication was observed in the Epi group.

## DISCUSSION

Several factors have been reported to increase the risk of bleeding after polypectomy, e.g., larger polyps size (13), sessile polyps or larger stalk (13,14), coagulopathy, ingestion of NSAIDs (15,16), older patient age (17), and polyps of ascending colon (18). Factors influencing perforation include sessile polyps (14), larger polyp size, and concurrent mucosal inflammation (19).

**TABLE 5 Numbers of complications which Occurred in Polyps with Epinephrine Injection (Epi Group) and Polyps without Injection (Ctr Group)**

| | Epi (n=75) | Ctr (n=76) | *P* value |
|---|---|---|---|
| Bleeding | 2 (2.6%) | 7 (9.2%) | NS |
| Immediate | 1 | 7 | 0.03 |
| Delayed | 1 | 0 | NS |
| Perforation | 1 (1.3%) | 1 (1.3%) | NS |
| Mortality | 0 (0%) | 0 (0%) | NS |
| Total | 3 (3.9%) | 8 (10.5%) | NS |

NS: not significant.

In this study, we found no statistical difference of the above risk factors in both groups.

In our study, the overall bleeding rate of the polyps in the Ctr group was 9.2 % (7/76), which was higher than previous reports (20-22). This may be due to the fact that we included minor bleeding episodes (7/9) in this study. In addition, only patients with sessile polyp were included in our study, which have been linked to high bleeding risk. In contrast, bleeding following polypectomy occurred less in the Epi group (2/75, 2.6%) ($P$=0.07). Although the difference between both groups was not statistically significant, Epi injection tended to prevent hemorrhage following polypectomy.

The risk of bleeding after polypectomy in the colon is reported to be 0.3 to 6.1% (20), while bleeding rate after gastric polypectomy is believed to be higher (1-7%) (21,22). In this study, we have a similar finding: bleeding rate was higher in the upper gastrointestinal (UGI) tract than that in the colon (7/63 *vs.* 2/88, $P$<0.05)

There was a case of delayed major bleeding (4 days later) in the Epi group. Its cause may be premature shedding of the coagulated eschar produced by polypectomy (11). However, in our experience, this phenomenon is not frequently encountered. Local submucosal Epi injection may reduce the bleeding rate through the following mechanisms: vasoconstriction (23), mechanical compression of blood vessels (24) and platelet aggregation (25). All these effects persist for only a few hours. Unlike ethanol, it does not cause vessel thrombosis and thus has no long-term hemostatic effect (23). Therefore, Epi injection would have less effect on delayed hemorrhage. In our study, immediate bleeding was more in the Ctr group than that in the Epi group ($P$=0.03).

Iishi *et al.* have reported that submucosal saline injection made endoscopic resection of sessile polyps safer (6). The ulcers created after polypectomy with saline injection were confined to submucosal layer and shallower than those of the controls. Shirai *et al.* also confirms that hypertonic saline-epinephrine solution injection prior to polypectomy had a similar effect (7). According to these findings, Epi injection may theoretically prevent perforation after polypectomy. Unfortunately, we had one case of perforation in each group. To avoid type II error, we have to increase case

number in the future.

The cardiovascular side effects of submucosal Epi injection may be important to the elderly. Epi has a significant first pass extraction by the liver (26). Theoretically it will not cause adverse effect. However, according to Sung *et al.* a significant amount of submucosally injected Epi may enter the systemic circulation (27). Fortunately the high serum concentration was transient. Neither our study nor other reports have found any serious adverse event with Epi injections.

In conclusion, endoscopic polypectomy with prophylactic epinephrine injection is safe and effective in preventing immediate bleeding. Further studies are needed to determine its influence on delayed hemorrhage and perforation.

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