

# Formalin Application for the Treatment of Radiation-Induced Hemorrhagic Proctitis

Sun-Il Lee,<sup>1</sup> Yoon-Ah Park,<sup>2</sup> and Seung-Kook Sohn<sup>2</sup>

<sup>1</sup>Department of Surgery, Korea University College of Medicine, Seoul, Korea;

<sup>2</sup>Department of Surgery, Yonsei University College of Medicine, Seoul, Korea.

Radiation-induced hemorrhagic proctitis (RIHP) is a serious complication of pelvic irradiation, and a 4% formalin solution has been used for 20 years in treating this sequelae. The first case involving formalin application for treatment of RIHP in Korea was reported in 1996, but there are no additional studies beyond this date. Our study reviews the use of formalin instillation and selective application. The purpose of this study was to retrospectively evaluate the outcome of such treatments, beginning with the first case at our hospital. From 1996 to 2005, five RIHP patients had received formalin treatment for RIHP symptoms intractable to other medical treatments. All treatments were performed by a single surgeon in the operating room, under spinal anesthesia or intravenous sedation. The mean duration of symptoms before treatment was 15.6 months (which was longer than in other studies), and the transfusion before treatment varied from once per month to twice per week. Using sigmoidoscopy, 100 ml of a 4% formalin solution was instilled directly (or by using a formalin-soaked gauze) and irrigated for five minutes. Formalin-soaked cotton was then applied selectively to focal remnant lesions. Four patients improved after the first treatment, but one patient received the treatment twice because of recurrent symptoms. Complications after treatment included perianal pain (one case), and aggravated incontinence (one case), which improved three months after conservative management. In conclusion, the formalin combination application method in our study is comparable to other formalin treatments for intractable RIHP.

**Key Words:** Radiation-induced hemorrhagic proctitis, formalin

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Reprint address: requests to Dr. Seung-Kook Sohn, Department of Surgery, Yongdong Severance Hospital, Yonsei University College of Medicine, 146-92 Dogok-dong, Kangnam-gu, Seoul 135-720, Korea. Tel: 82-2-2019-3370, Fax: 82-2-3462-5994, E-mail: sksohn@yumc.yonsei.ac.kr

## INTRODUCTION

Radiation therapy is an effective treatment for pelvic malignancies.<sup>1</sup> However, 2% to 5% of patients who receive radiation therapy for such a malignancy suffer from severe proctitis.<sup>2,4</sup> The most troublesome symptom of the proctitis is chronic hemorrhage, and in many cases, repeated transfusions are required. Several materials have been used for the treatment of proctitis,<sup>5-8</sup> and a 4% formalin solution has been used effectively worldwide for 20 years. However, there is still controversy surrounding the indications and methods involved in formalin therapy.<sup>8-10</sup> The first formalin treatment for radiation-induced hemorrhagic proctitis (RIHP) in Korea was reported about 10 years ago, and involved a combined method of both formalin instillation and selective formalin application.<sup>11</sup> Since then, however, reports regarding the use of formalin treatment of RIHP are rare in Korea. The aim of this study was to evaluate the therapy and outcome of the combined formalin application therapy since the first reported case in Korea.

## MATERIALS AND METHODS

From January 1996 to August 2005, the records of five patients who had received formalin application for intractable RIHP at Yongdong Severance Hospital were reviewed. Gender, age, type of malignancy, method of treatment, complication, and recurrence of symptoms during the follow-up period were evaluated. The candidates for formalin treatment were those experiencing

hemorrhagic proctitis intractable to other medical treatments, with or without additional symptoms. The patients were evaluated with a rigid or flexible sigmoidoscope for diagnosis and measurement of the involved area before treatment. The patients were placed in the lithotomy position, and either spinal anesthesia or intravenous sedation was used during the procedure. A Foley catheter was positioned at the proximal portion of the lesion, and a formalin solution or soaked gauze was used in each case.

## RESULTS

The five patients were followed up for 13.6 months (range, 5-25 months) after completing the formalin instillation treatment. The mean patient age was 69.4 years, the interval from the conclusion of radiation therapy to the onset of symptom was 7.2 months, and the mean duration of hematochezia before formalin application was 15.6 months (Table 1). In all cases, previous treatments before formalin application included sucralfate enemas and corticosteroid enemas. Frequent blood transfusions, ranging from once per month (case 1) to twice a week (case 4), were required before treatment. Rectum and distal sigmoid colon were involved in case 1, but only rectum was involved in the other cases. Anal incontinence for gas and liquid were noted in case 3 before treatment. In three cases (1, 2, and 3), 100 ml of formalin solution was instilled and irrigated with normal saline for five minutes. In the other cases

(4 and 5), formalin-soaked gauze was used instead of the solution. Remnant bleeding lesions were treated precisely by direct contact of formalin-soaked cotton for about three minutes, and it was repeated until all bleeding lesions disappeared. Treatment time was 78 minutes (range, 65-95 minutes), and no complications were noted during the treatment. Patients experiencing mild anal and perianal discomfort after the treatment showed improvement within a week. In case 5, the patient suffered from perianal pain during the first two months of follow-up, but symptoms improved after that. Incontinence was aggravated in case 3, but improved three months after treatment. In case 2, the patient received an additional formalin treatment for symptom recurrence, but the other patients' symptoms resolved after the initial treatment.

## DISCUSSION

This retrospective study showed that formalin instillation is an effective treatment for intractable radiation-induced hemorrhagic proctitis. The duration from the beginning of hemorrhagic symptoms to formalin treatment in this study was longer than that of others.<sup>9,12,13</sup> However, as formalin treatment becomes more common, this delayed referral time is expected to decrease. Eighty percent of the patients improved after the initial treatment, and 20% improved after the second treatment. Complete cessation of bleeding after the first treatment ranged from 34% to 100%,

**Table 1.** Clinical Features and Results of Formalin Treatment (n=5)

Case	Sex/ Age	Diagnosis	Interval* (months)	Duration <sup>†</sup> (months)	Formalin instillation		Result after first treatment
					Initial application (%)	Selective application (%)	
1	F/69	Cervical cancer	6	20	Solution (4)	/ Cotton (10)	Complete resolution
2	M/72	Prostate cancer	6	7	Solution (10)	/ --	Relapse <sup>‡</sup>
3	F/70	Cervical cancer	7	25	Solution (4)	/ Cotton (10)	Complete resolution
4	M/69	Prostate cancer	10	16	Gauze (4)	/ Cotton (10)	Complete resolution
5	F/68	Anal cancer	7	10	Gauze (4)	/ Cotton (4)	Complete resolution

\*Interval from the cessation of radiation therapy to the onset of hemorrhagic proctitis.

<sup>†</sup>Duration from the beginning of hemorrhagic proctitis to formalin treatment.

<sup>‡</sup>Completely resolved after second repeated instillation treatments.

and the methods of application varied.<sup>4,9,12</sup> Two methods have frequently been used for the application of formalin, although many more methods may exist. Three hundred milliliters to 400 ml of a 4% formalin solution were divided into 30 ml to 50 ml fractions, and were applied on the rectum repeatedly. Alternately, a 4% formalin solution soaked cotton gauze was selectively placed on the lesion for several minutes.<sup>10,12,13</sup> Diffuse rectal wall, rather than a solitary lesion, is involved in radiation-induced hemorrhagic proctitis; therefore, the fluid-instilling method may be more effective. However, the aforementioned fractionated volumes do not always cover the entire area of involvement, and the selective application of a soaked cotton gauze under guidance of rigid sigmoidoscope is not always effective for a such a large area. We combined the two methods, instilling a formalin solution or soaked gauze for a few minutes, and then precisely localizing contact of the formalin-soaked cotton for remnant lesions. A canine model showed that the systemic toxicity of formalin is less severe in the sequential instillation of fractionated solution than in a bolus instillation of the total amount, and that a lower concentration with lesser contact time is important to decrease systemic toxicity.<sup>14</sup> Some studies<sup>4,8</sup> show that a solution of less than 4% formalin can successfully be used without major toxicity. The half-life of systemically absorbed formalin is known to be 90 minutes, and the initial histological change after treatment is limited to the mucosal layer.<sup>12,14</sup> Nevertheless, more studies regarding formalin safety and the ideal method for formalin application are needed. Complications after treatment are known to include acute proctitis, worsening of a radiation stricture, worsening of incontinence, and severe pain.<sup>10</sup> In this study, some patients experienced worsening of incontinence and severe pain. However, these symptoms improved over time. Patients with pre-existing symptoms, or those arising from radiation injury, should carefully be evaluated before treatment. Argon plasma coagulation or hyperbaric oxygen has been used for treatment, and these could also be applicable treatments for patients who fail formalin therapy.<sup>2,15-17</sup>

In conclusion, the combined method of formalin instillation and the precise application of formalin

in the present study was found to be a simple and effective treatment modality for radiation-induced hemorrhagic proctitis intractable to other treatments. More studies are needed to improve the efficacy and to minimize complications.

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