

Evaluation of the effectiveness of 4% formalin in the treatment of hemorrhagic actinic proctitis

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ABSTRACT: Radiotherapy is an important discovery as to the treatment of pelvic tumors. Proctitis is frequently observed nowadays, and can be divided into acute and chronic. Treatment with 4% formalin solutions has been used with positive results in literature. **Objective:** To evaluate the effectiveness and morbidity rates related to the use of 4% formalin in hemorrhagic chronic actinic proctitis. **Methods:** We evaluated the sigmoidoscopy records and reports of 11 patients with chronic hemorrhagic actinic proctitis from February to December 2010, coming from the Serbian colorectal University Hospital of the State of Sergipe. **Results:** The study was comprised of 11 patients (36.36% were females and 63.63% were males). Mean age was 67.7 years. Mean time between the end of radiotherapy and the onset of symptoms was 6.6 months. The treatment was completely effective in 27.27% of the cases, and reduced rectal bleeding in 100% of patients. The following main complications were observed: chills (9%), tenesmus (18.18%) and mild stenosis (9%). **Conclusions:** The 4% formalin solution has fewer side effects, and its administration is very inexpensive. The treatment is effective and reduces bleeding in almost 100% of cases.

Keywords: proctitis; formalin; radiotherapy.

INTRODUCTION

Radiotherapy is part of the healing treatment for many malignant pathologies, such as neoplasm of the rectum, uterus, prostate, bladder, anal canal and margin^{1,2}. Despite the benefits of this procedure, the lesions caused by radiation may cause early and late unwanted effects³, ranging from 5 and 20%.

During the radiotherapy treatment of abdominal or pelvic tumors, the intestine is an important organ at-risk⁴. The toxicity of the radiation in the intestine is classified as acute and chronic, according to the onset of symptoms. In less than three months, it is considered as acute, and after this time, it is chronic⁴. The acute

complications are mainly caused by injuries of the radiation in the mucosa. This is due to the action of the radiation on the dividing cells, usually leading to self limited lesions. Chronically, the symptoms are owed to the progressive submucosal fibrosis and endoarterial obliteration, leading to the formation of neovascular telangiectasia, causing fragility and bleeding⁵.

Since the rectum is more fixed and close to the pelvic organs, it is more prone to complications from the radiation³.

Different clinical and surgical therapies may be performed. Derivatives of aminosalicic acid, corticoid, sucralfate, argon plasma, bipolar electrocoagulation, retinol palmitate, rectal misoprostal, vitamin E,

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vitamin C, hyperbaric therapy and different concentrations of formalin are some of the methods used to treat this pathology⁵⁻⁶. The surgical treatment is used in complicated processes, such as obstruction, fistulization or uncontrollable hemorrhage, thus being restricted due to the increased morbimortality rates caused by actinic alterations, which makes the healing more difficult.

Since the 4% formalin has shown positive outcomes, associated with the low cost, simple use and versatility, it can be used as the first treatment in refractory cases⁶.

Despite the decreasing incidence of actinic proctitis with the use of more precise radiotherapy devices, there is still a significant number of patients who need outpatient follow-up.

So, the objective was to assess the efficacy and the morbidity rates of the mentioned method, which is already used in the Service of Proctology of the University Hospital of Sergipe, Brazil.

OBJECTIVES

Main objective:

- To assess the efficacy and morbidity rates related to the use of 4% formalin for hemorrhagic chronic actinic proctitis.

Secondary objectives:

- To assess the demographic profile of actinic proctitis;
- To analyze which pathologies led to the need for radiotherapy, causing actinic proctitis;
- Time between the end of radiotherapy and the onset of symptoms.

MATERIALS AND METHODS

Sample

The medical records of patients coming from the Service of Coloproctology at the University Hospital of Sergipe who presented with hemorrhagic chronic actinic proctitis were analyzed. They were submitted to 4% formalin from February to December 2012. It was not necessary that the patient signed the informed consent form, since the paper consists only on data collection from medical records.

The study was approved by the Research Ethics Committee of *Universidade Federal de Sergipe*.

Statistical analysis

The collected data will be inserted in a database system; afterwards, they will be submitted to statistical analysis. Simple frequency tables will be used to characterize the results, as well as the median, mean and standard deviation.

Methodology

The 4% formol solution was administrated via rectosigmoidoscopy. The highest amount of 4% formalin was 500 mL, administered for 30 s. After the administration, the content was aspirated and irrigated with a 0.9% physiological solution, 1,000 mL, until the complete withdrawal of the solution.

All patients underwent at least two rectosigmoidoscopies. At first, before the use of formalin, the endoscopic classification was level I (less than 10 telangiectasias), II (more than 10 telangiectasias, with coalescence of 2 telangiectasias at most), III (multiple coalescent telangiectasias), or IV (ulcers) (Figure 1) at the first use of formalin. After one month, the second rectosigmoidoscopy was performed for endoscopic grading, and if the patient had no more complaints, the treatment would be suspended. If the complaints persist, new formalin solutions were used every month until the total remission of the hemorrhage.

RESULTS

The study consisted of 11 patients with hemorrhagic chronic actinic proctitis, and 36.36% of them were males and 63.63% were females. For males, the basal disease that led to radiotherapy was prostate cancer in 100% of the cases; for females, the radiotherapy was a result of uterine cervical neoplasm.

Mean age was 67.7 years (ranging from 56 and 66 years), with median of 66.5 years. For males, the mean was 67.75 years, and for females, it was 67.71 years.

Mean time between the end of radiotherapy and the onset of symptoms was 6.6 months, ranging from 1 month to 11 months. The dose and the type (teletherapy and/or brachytherapy) were not accounted for, since most patients did not have the radiotherapy report.

Out of the common endoscopic findings observed among patients, there are: telangiectasis, fri-

ability and small ulcers. Rectal bleeding and sphincter irritability were observed in 100% of the patients; tenesmus, in 80%; diarrhea and mucus in 60% of the cases, and essential hemorrhage in 9% of them. Mild stenosis and a small ulcer in the posterior anal canal were observed in one patient; after the biopsy, the anatomopathological was compatible with actinic proctitis.

Response to treatment was classified as to the endoscopic classification of the rectosigmoid mucosa in: level I (less than 10 telangiectasias), II (more than 10 telangiectasias, with coalescence of 2 telangiectasias at most), III (multiple coalescent telangiectasias), or IV (ulcers).

In the beginning of the treatment, the findings were 18.18% of level I; 27.27% of level II; 36.36% of level III and 18.18% of level IV. Complications such as perforations and fever were not observed. However, the chills were observed in 9% of the patients, tenesmus, in 18.18% of them, and mild stenosis, in 9%. Only one patient (9%) had to terminate the treatment, since he had aplastic anemia as a complication of radiotherapy.

The treatment was completely effective in 27.27% of the cases. For all other patients, rectal bleeding was significantly reduced. After the beginning of the treatment, hemotransfusion was necessary for only three patients (27.27%). No ostomy was necessary for transit deviation due to uncontrolled bleeding.

Table 1 shows data regarding the patients treated with 4% formalin.

DISCUSSION

Radiotherapy was a major discovery to treat several diseases, leading to cure without the need for surgery. However, it is not a complication-free procedure. The hemorrhagic chronic actinic proctitis is one of these complications; this pathology leads to great morbidity rates, limiting activities and even mortality.

There is a great range of substances that have been studied for the clinical treatment of this disease (derivatives of aminosalicic acid, sucralfate, argon plasma, bipolar electrocoagulation, short-chain acids, hyperbaric oxygen and different concentrations of formalin)⁷.

Due to the great possibility of technical complications, since local fibrosis is caused by the radiation and the adherence of pelvic organs, the surgical treatment is restrict to local complications (fistulae), persistence of symptoms and uncontrollable bleeding⁶. For patients without surgical roof, it is possible to use the derivation of intestinal transit⁸⁻⁹.

The formalin has been used since the past century. At first, it was used for cases of hemorrhagic cystitis, by Brown, in 1968. It was first introduced by Rubinstein et al. to treat hemorrhagic chronic proctitis at a 3.6% concentration, showing good results. Thus, some papers have been showing the success and safety in using 4% formalin¹⁰⁻¹⁵.

Mean age of the patients in our paper was 67.7 years (56 to 77 years), which is in accordance with literature. There is no difference between women and men as to mean ages (67.71 and 67.75 years, respectively).

Table 1. Patients treated with 4% formalin.

Initials	Gender	Age	Neoplasm	Period of Time (months)
JCS	F	68	UCN*	7
AAO	F	75	UCN*	3
MR	F	56	UCN*	6
MMS	M	65	PN**	8
RFL	F	67	UCN*	11
MJM	M	72	PN**	10
JAS	M	67	PN**	1
JBS	M	67	PN**	3
MFS	F	77	UCN*	4
MCJ	F	64	UCN*	11
EBA	F	67	UCN*	9

*Uterine Cervical Neoplasm.

**Prostate Neoplasm.

Table 2. Pathologies that lead to radiotherapy treatment.

Authors	N. of Patients	Mean Age (Years)	Prostate Neoplasm	Uterine Cervical Neoplasm	Endometrial Neoplasm	Anal Canal Neoplasm	Rectal Neoplasm
Mathai and Sheow-Choen ¹¹ *	29	67 (38–94)	03	25	00	00	01
Biswal et al. ¹³	16	50 (40–60)	00	14	02	00	00
Saclarides et al. ¹⁴	16	73.1 (50–83)	10	03	00	03	00
HUWC Group	33	65.39 (36–77)	19	09	03	02	00
HUSE Group	11	67.7 (56–77)	04	07	00	00	00

* Including the initial sample by Seow-Choen et al. (1993).

HUWC: Hospital Universitário Walter Cantídio – Universidade Federal do Ceará.

HUSE: Hospital Universitário de Sergipe – Universidade Federal de Sergipe.

Table 3. Complications.

Authors	N. of patients	Stenosis	Diarrhea	Fissure/ Ulcer	Incontinence	Anal pain	Fever/ Chills	Tenesmus/ Proctalgia	Total
Mathai and Sheow-Choen ¹¹	29	01	00	00	00	00	00	00	01 3.44%
Biswal et al. ¹³	16	00	00	00	00	00	00	00	00
Saclarides et al. ¹⁴	16	00	00	04	00	01	00	00	05 31.25%
HUWC Group	33	01	03	00	00	04	01	03	12 36.36%
HUSE Group	11	01	00	00	00	00	01	02	04 36.36%

HUWC: Hospital Universitário Walter Cantídio – Universidade Federal do Ceará.

HUSE: Hospital Universitário de Sergipe – Universidade Federal de Sergipe.

In literature, the pathology that is mainly responsible for pelvic radiation was uterine cervical neoplasm, which confirms our study, since it presented 63.63% of the patients with such neoplasm.

Most patients with complications presented colorectal alterations, which appear from 12 to 18 months after radiotherapy. Mean time between the onset of hemorrhagic symptoms and the end of radiotherapy was 6.6 months, ranging from 1 to 11 months.

Rectal bleeding, tenesmus, diarrhea, mucus stool, abdominal pain, and sphincter irritability are the more

common symptoms of hemorrhagic chronic actinic proctitis. The lower gastrointestinal bleeding caused by telangiectasias may cause severe anemia, leading to the need for multiple hemotransfusions. In our study, three patients (27.27%) needed a hemotransfusion after the administration of 4% formalin.

The concentration of 4% formalin was obtained after observations; some studies showed that such dilution is efficient and presents no adverse effects¹⁶. The technique of intrarectal administration is safe when the time of contact with rectal mucosa is

about 30 to 60 seconds, and the volume is 400 to 500 mL¹³.

The complications described in literature range from 0 to 36.36%. In our study, one patient presented with chills, another one had mild stenosis, and two others had tenesmus, accounting for 36.36% of complications. Only one patient had to interrupt the participation in the study due to aplastic anemia as a complication from the radiotherapy.

As to the general effectiveness of the treatment (improvement of symptoms, capacity to control hematocrit and hemoglobin levels, avoiding the need for hemotransfusion), it ranged from 93.1 to 100%; the results in our studies were compatible with literature (100%).

CONCLUSION

After the literature review and the results of the use of 4% formalin, it is possible to observe that:

- The treatment of hemorrhagic chronic actinic proctitis is a challenge to the doctors; prevention is the most important step;
- The 4% formalin solution has a few side effects, besides being low-cost.
- The treatment is effective, and reduces the bleeding in almost 100% of the cases.

With these results, we suggest the administration of 4% formalin as an effective treatment for hemorrhagic chronic actinic proctitis.

RESUMO: A radioterapia foi uma importante descoberta, no que tange o tratamento das neoplasias de pelve. A proctite é uma das complicações bastante observadas atualmente, podendo ser dividida em aguda e crônica. O tratamento com solução de formalina a 4% vem sendo utilizado com resultados positivos na literatura. **Objetivo:** Avaliar a eficácia e morbidade do uso da formalina a 4% na retite actínica crônica hemorrágica. **Métodos:** Foram avaliados os prontuários e laudos das retossigmoidoscopias de 11 pacientes portadores de retite actínica crônica hemorrágica entre o período de fevereiro a dezembro de 2010, oriundos do Serviço de Coloproctologia do Hospital Universitário do Estado de Sergipe. **Resultados:** O estudo foi composto de 11 pacientes (36,36% feminino e 63,63% masculino). A média das idades foi de 67,7 anos. O tempo médio entre o término da radioterapia e o início dos sintomas foi de 6,6 meses. O tratamento foi completamente efetivo em 27,27%, sendo reduzido sangramento retal em 100% dos pacientes. Como principais complicações foram observadas: calafrio (9%), tenesmo (18,18%) e estenose leve (9%). **Conclusão:** A solução de formalina a 4% apresenta poucos efeitos colaterais, sendo muito barata a sua administração. O tratamento é efetivo, reduzindo, em praticamente 100% dos casos, o sangramento.

Palavras-chave: retite; formalina; radioterapia.

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