ORIGINAL RESEARCH PAPER

Gastroenterology

ENDOSCOPIC VS COMBINED MEDICAL AND SURGICAL MODALITIES OF TREATMENT OF RADIATION INDUCED PROCTOCOLITIS – OUR INSTITUTE EXPERIENCE

KEY WORDS: radiation, GI injury, strictures, proctocolitis, endoscopy

Kani Shaikh Mohamed* Associate Professor, Department of Medical Gastroenterology, Kilpauk Medical College, Chennai. *Corresponding Author

Boojala Avinash Reddy Resident, Department of Medical Gastroenterology, Kilpauk Medical College, Chennai.

ABSTRACT

Background: GIGastrointestinal injury may occur following irradiation of thoracic, abdominal, and pelvic malignancies limiting radiation doses that can be delivered as well as causing significant morbidity requiring intervention. Radiation proctocolitis, both acute and chronic, is one such complication requiring multidisciplinary management for good outcomes. We analyzed the injury with respect to spectrum of injury, severity, morbidity and compared endoscopic vs combined medical and surgical modalities of treatment.

Methods: Patients with acute and chronic radiation proctocolitis defined as illness presenting before and after 3 months respectively, of radiation treatment were included in the study. The study period was five years.

Results: Total number of patients studied were 75. Acute disease was seen in 5 patients, presenting predominantly with diarrhea, abdominal pain and acute intestinal pseudo-obstruction. Chronic radiation proctocolitis was seen in 70 patients. Bleeding per rectum was the most common symptom. Anemia was the commonest sign. Grade 2 injury was most commonly seen. Pharmacotherapy was equally effective in grade 1 injury whereas Endoscopic treatment was superior to pharmacotherapy in Grade 2,3. Surgery offered lesser rates of rehospitalization in grade 3 but was associated with higher complications. There were no deaths in endoscopic arm while there were 2 deaths in pts who required surgery. Surgical combined with medical was superior to endoscopic treatment in grade 4 while local agents were ineffective. Preventive strategies prior to radiation were associated with lower grade of injury.

Conclusion: Radiation proctocolitis causes significant morbidity requiring prolonged treatment and hospitalization. Dose and duration of radiation had direct relation to the severity of injury. Concurrent chemotherapy had no effect on severity of injury. Our study showed acute proctocolitis required predominantly supportive medical treatment. Chronic form from grade 1 to 3 required predominantly endoscopic treatment with prolonged duration of treatment but less morbidity. Grade 4 required surgical and intensive care and local therapy was ineffective.

INTRODUCTION

Gastrointestinal injury may occur following irradiation of thoracic, abdominal, and pelvic malignancies limiting radiation doses that can be delivered as well as causing significant morbidity requiring intervention [(1)]. Radiation proctocolitis, both acute and chronic, is one such complication required multidisciplinary management for good outcomes. We analyzed the injury with respect to spectrum of injury, severity, morbidity and compared endoscopic vs combined medical and surgical modalities of treatment.

MATERIALS AND METHODS:

All patients presenting to Department of Digestive Health and Diseases, Kilpauk medical college, Chennai, with acute and chronic radiation proctocolitis defined as illness presenting before and after 3 months respectively, of radiation treatment were included in the study. The study period was five years.

Parameters analyzed- Primary diagnosis, Dose and duration of radiation, Concurrent chemotherapy if given, grading of radiation proctocolitis caused, severity of injury, Time of presentation of injury, endoscopic findings and the treatment required. Treatment modalities were Medical- local therapies like sucralfate enema, short chain fatty acid enema, mesalamine enema, Hydrocortisone enema, Drug therapy- estrogen/progesterone, Anti VEGF Bevacizumab, Antioxidants, Iron supplements, Endoscopic- 4% formalin application, Argon plasma coagulation, endo therapy for bleeding wherever required. Surgical was resection anastomosis, partial colectomy, total colectomy.

EXCLUSION CRITERIA:

Patients who underwent surgery prior to radiotherapy, patients with recurrent malignancy, patients with unknown primary malignancy, patients with prior Inflammatory bowel disease.

RESULTS

Total number of patients studied were 75. Most common primary disease was carcinoma prostate in men and was carcinoma cervix in women. Radiation proctocolitis was the most common injury with abdominal irradiation others being partial gastric outlet obstruction, radiation duodenitis, small bowel obstruction, jejunal ulceration, colovesical fistula and anal canal stricture.

Radiation proctocolitis:

Mean duration of presentation – 9 months
Most common cause- Carcinoma cervix
Other causes – Ca prostate, Sarcoma
All pts had bleeding PR
All pts had anemia at presentation.
Total patients- 75

Acute proctocolitis- 5, mean duration of presentation- 2 weeks
Chronic proctocolitis- 70 patients.

Mean dose of radiation given was 75Gy.
Grade 2 injury was most commonly seen. Pharmacotherapy was equally effective in grade 1 injury whereas Endoscopic treatment was superior to pharmacotherapy in Grade 2,3. Surgery offered lesser rates of rehospitalization in grade 3 but was associated with higher complications. There were no deaths in endoscopic arm while there were 2 deaths in pts who required surgery. Surgical combined with medical was superior to endoscopic treatment in grade 4 while local agents were ineffective. Preventive strategies prior to radiation were associated with lower grade of injury.

DISCUSSION:

A variety of symptoms and signs can be seen following radiation treatment which constitute the syndrome of radiation induced GI injury. Altered physiology manifests in the form of increased stool frequency, decreased bile acid and vitamin B12 absorption, increased fecal fat excretion, lactose malabsorption, rapid small-intestinal and whole-gut

transit[2]. Although most of these changes improve with time, at 1 to 2 years after the completion of irradiation, at least 1 parameter of gastrointestinal function was abnormal many patients.

In a rat model changes in dose-rate had profound effects on the intensity of the inflammatory response elicited by abdominal irradiation, with HDR (180 Gy/h) inducing a significantly higher recruitment of rolling, adherent and emigrating leukocytes than irradiation with an equal total dose at a lower dose-rate of 59 Gy/h[1].

Radiation proctitis according to the 'common toxicity criteria', version 4- Grade CRP 1- Rectal discomfort; intervention not indicated, grade 2-Symptoms (rectal discomfort, passing blood or mucus); medical intervention indicated, grade 3-Severe symptoms; fecal urgency or stool incontinence; limiting self-care grade 4- Life-threatening consequences; urgent intervention indicated, grade 5- Death.

The endoscopic classification of CRP is usually analyzed by the Vienna Rectoscopy Score (VRS) to describe rectal mucosa [18]. The VRS divides the inner rectal mucosa into 12 mucosal areas. Furthermore, each area is scored on the presence and grading of telangiectasia (Grade 0–3), congested mucosa (Grade 0–3), ulceration (Grade 0–4)

The method of delivery and dose of radiation has significant impact on occurrence of adverse effects of radiation. It was conclusively proved from studies that, compared to conventional method, Conformal techniques significantly lowered the risk of late radiation-induced proctitis after radiotherapy for prostate cancer[4].

Concurrent chemotherapy is associated with significantly increased acute gastrointestinal, genitourinary, dermatological toxicities when conventional radiation therapy techniques are used[5]. Use of radio-sensitizing drugs further exacerbates the toxicity[6].

The evidence base for current therapies is limited, but nutrition, anti-diarrhoeals, anti-inflammatories, antibiotics, probiotics, pentoxifylline, tocopherol, cholestyramine, hyperbaric oxygen, endoscopic and surgical therapies have all received attention. Given the significant morbidity and mortality associated with chronic radiation enteritis, current available preventative strategies are reviewed, including tissue-sparing radiotherapy techniques[10].

Acute radiation colitis is mostly self-limited, and usually, only supportive management is required. Chronic radiation colitis, a poorly predictable progressive disease, is considered as a precancerous lesion; radiation-associated malignancy has a tendency to be diagnosed at an advanced stage and to bear a dismal prognosis[8].

Sucralfate enemas have been used to treat bleeding from CRP [27–28]. Kochhar et al. [27] studied 37 patients with radiation-induced proctosigmoiditis randomized to receive a 4-week course of oral sulfasalazine plus 20 mg BID rectal prednisolone enemas or 2.0 g BID rectal sucralfate enemas plus oral placebo. At 4 weeks, both groups showed significant improvement in symptoms and endoscopic healing.

5-Aminosalicylic acid (5-ASA) is the active compound found in sulfasalazine. 5-ASA compounds are established and well tolerated for the treatment of inflammatory bowel disease . Its anti-inflammatory mechanisms include inhibition of biosynthesis of prostaglandins, inhibition of the transformation of leukotriene A4 to leukotriene B4, and promotion of endogenous cytoprotective prostaglandins Formalin is a solution of formaldehyde gas used for glues, embalming, and fire proofing. Application of formalin covalently bonds proteins, causing cell necrosis. In animal studies, administration of formalin enemas result in formic acid levels detectable in the serum. Formic acid toxicity includes acidosis, coma, and renal failure[9]. Formalin has been applied topically as an enema or "dab" from a cotton swab in several clinical studies in patients with bleeding from CRP. Enema treatment is often administered in the operating room with general or spinal anesthesia. Although formalin enemas have been demonstrated to reduce the severity of rectal bleeding in patients with CRP, significant and serious complications of formalin instillation including anal pain, fissure formation, rectal strictures, and rectal fistulas have been described. In addition, chemical proctosigmoiditis as a direct toxicity of topical formalin has been described.

APC consists of high frequency monopolar electrosurgical generator, an argon gas source, a foot switch for energy and gas delivery, flexible delivery catheters, a gas flow meter, and a grounding pad. Monopolar current travels from an electrode in the probe tip through the argon plasma to the tissue. The technique usually requires several sessions for adequate obliteration of rectal telangiectasias. Preparation for colonic APC[9] treatment always requires a full colonoscopy preparation. Side effects include luminal distension with argon gas, rectal pain, and tenesmus. Serious complications are rare (< 1 %) and include APC-induced ulcerations, rectal strictures, and rectal fistula formation, often requiring surgery such as a diverting colostomy. Several cases of explosions in the colon due to the ignition of methane gas from inadequate colon preparation have been reported.

CONCLUSION:

Radiation proctocolitis causes significant morbidity requiring prolonged treatment and hospitalization. Dose and duration of radiation had direct relation to the severity of injury. Concurrent chemotherapy had no effect on severity of injury. Our study showed acute proctocolitis required predominantly supportive medical treatment. Chronic form from grade 1 to 3 required predominantly endoscopic treatment with prolonged duration of treatment but less morbidity. Grade 4 required surgical and intensive care and local therapy was ineffective.

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