Proctitis Workshop

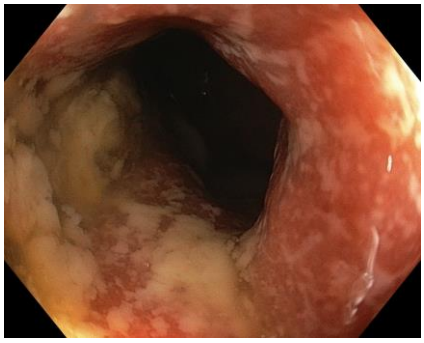
PD Dr Michel H. Maillard, MD-PhD[1,2]
[1]Crohn's and Colitis Center, Gastroentérologie Beaulieu SA
[2]CHUV, Lausanne

PD Dr Lukas Brügger, Universitätsklinik für Viszerale Chirurgie und Medizin, Inselspital Bern

Case n°1

- Chronic diarrhea and bloody discharge since 3 months
- Abdominal pain, weakness, no fever
- Lab: Slightly elevated CRP otherwise unremarkable
- Current medication: Irbesartan for arterial HT
- Stool tests: PCR positive for enteropathogenic E. Coli
- Trial of oral Ciprofloxacin+ metronidazole inefficient

Endoscopic aspect




Rectal swab negative for Chlamydia and gonoccoccus
Biopsies suggestive of ulcerative proctitis

What is your first-line therapy?

1. Oral 5-ASA.
2. 5-ASA suppositories
3. 5-ASA enemas
4. Topical steroids
5. Oral steroids
6. Antibiotics
7. Topical + oral 5-ASA combotherapy

What is your first-line therapy?

1. Oral 5-ASA.
2. 5-ASA suppositories
3. 5-ASA enemas
4. Topical steroids
5. Oral steroids
6. Antibiotics
7. Topical + oral 5-ASA combotherapy

Management of proctitis: ECCO guidelines

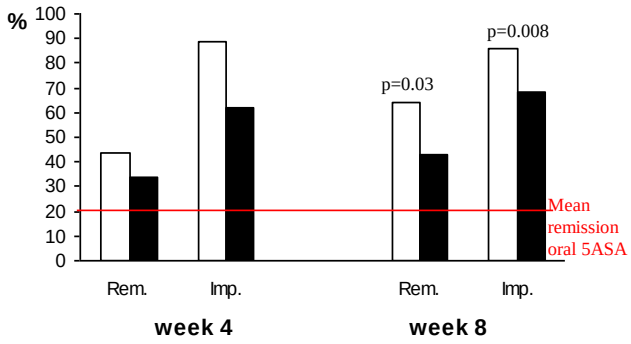
ECCO statement 11A

A mesalamine 1-g suppository once daily is the preferred initial treatment for mild or moderately active proctitis [EL1]. Mesalamine foam or enemas are an alternative [EL1], but suppositories deliver the drug more effectively to the rectum and are better tolerated [EL3]. Topical mesalamine is more effective than topical steroids [EL1]. Combining topical mesalamine with oral mesalamine or topical steroids is more effective [EL2]

Oral and topical 5ASA: PINCE

- Pentasa 4g + 1g enema vs 4g + placebo enema

  n = 116 (out of planned 250) Marteau et al *Gut* 2005;**54:**960-5



Refractory proctitis

- Only mild response to 5-ASA oral+ topical combotherapy
- No response to steroids
- Transabdominal ultrasound suggests extension to a left-sided colitis
- Stool PCR negative for C. Difficile and common enteropathogens

What is your next step?

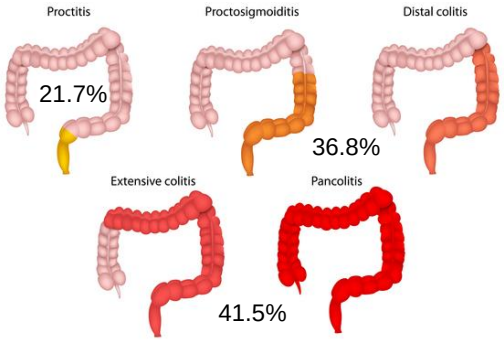
1. Iv steroids
2. Oral tacrolimus
3. Topical tacrolimus
4. Induction with anti-TNF
5. New drugs: Vedolizumab, Tofacitinib, Alicaforsen…
6. Surgery

What is your next step?

1. Iv steroids
2. Oral tacrolimus
3. Topical tacrolimus
4. Induction with anti-TNF
5. New drugs: Vedolizumab, Tofacitinib, Alicaforsen…
6. Surgery

Disease progression in SIBDCS

- Extent at diagnosis



Mean FUP: 9 years

- Progression: 15.8%
- Regression: 16.2%
- Risk factors: Steroid use (OR: 1.7); calcineurin inhibitor (OR: 2.7)

Safroneeva E et al. Aliment Pharmacol Ther 2015; 42: 540-8

Topical tacrolimus is effective

Tacrolimus 0.5mg/ml (3ml 2x/d total) n=11
Placebo n=10

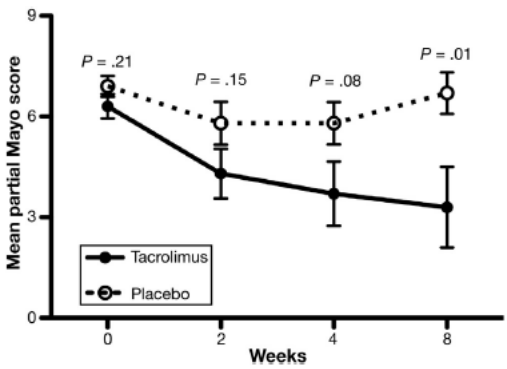
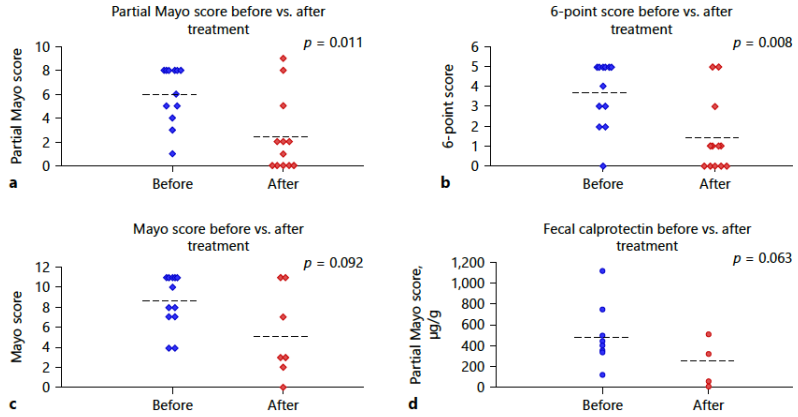


Figure 3. Mean partial Mayo score.

Lawrance, I. C. *et al. Clinical Gastroenterology and Hepatology* **15,** 1248–1255 (2017).

Alicaforsen in distal UC

N=12 patients



Greuter, T. *et al*. *Dig Dis* **36,** 123–129 (2018).

Biologic agents

- No specific study on proctitis. Few subgroup analyses
- Small case studies with infliximab suggestive similar efficacy than for more extensive disease

Case n°2

- Male, 38 years, HIV pos since 4/2013
- Recurrent anal HSV infection since 2008
- 2014/15 2x Op for anal condylomata

- 4/2016 routine follow up:
  - 1 month treatment for fissure (diltiazem)
  - Small fissure 6 o`clock
  - Linea dentata 3 o`clock Biopsy: chronic inflammation

15

Case n°2

- 5/2016 follow up
  - after improvement symptoms → pain after going to toilet
  - Hyperemic mucosa

Next steps

1. Continue Diltiazem
2. BOTOX
3. Symptomatic: topic Lidocain+
4. Surgery
5. Physiotherapy
6. other

Next steps

1. Continue Diltiazem
2. BOTOX
3. Symptomatic: topic Lidocain+
4. Surgery
5. Physiotherapy
6. other

Case n°2

- 9/16 much better…until 1 week ago
  - pain (tearing, when moving → left inguina)
  - Diltiazem pos. effect
  - Sphincter pressure↑, normal mucosa
- 8/17 still Diltiazem, happy patient, normal examination
- 10/17 planned journey, patient wishes BOTOX

Next steps

1. BOTOX yes
2. BOTOX no
3. other

➢BOTOX in LA (signs of healed fissure 6 o`clock)

Case n°2

- 12/17 symptoms slightly better
- Anal pain especially when sitting

Next steps

1. Mesalazin supp 2x500 mg
2. Smear

Bakterien/Pilze		
Nukleinsäuresequenzen		
Chlamydia trachomatis		
1)2)DNA Nachweis (PCR)	POSITIV	
Chlamydia trachomatis Genotyp		
Diese Untersuchung wird am Centre Hospitalier Universitaire Vaudois (CHUV) in Lausanne durchgeführt.		
Leider steht uns zu wenig Material zur Verfügung, um diese Analyse durchführen zu können.		
Gonokokken		
DNA Nachweis (PCR)	negativ	
Viren		
Antigene		
Herpes simplex Viren 1+2	negativ	

Next steps

- Azithromycin 1g po, single dose
- Mesalazin supp 1g/die
- Physiotherapy (trigger points Pelvis, Lumbovertebral Syndrome)

➢ 2/2018 Clamydia trachomatis neg.

➢ Symptoms resolved completely

Case n°3

- Male, 53 years, HIV pos since 2015
- 3x bariatric surgery, BMI 52→23
- Recurrent perianal abscesses
  - 5x incision before 2011
  - 2x antibiotic treatment (Dalacin) 2016

➢ 4.10.2018 incision perianal abscess 7 o`clock
- 7.10.2018 incision perianal abscess 7 o`clock
- 16.10.2018 incision perianal abscess 6 o`clock
- 25.10.2018 wounds produce much pus

25

Next step

1. Back to OR
2. Endosonography
3. Watch and wait
4. other

Next step

1. Back to OR
2. Endosonography
3. Watch and wait
4. other

Bakterien/Pilze

Mikroskopie

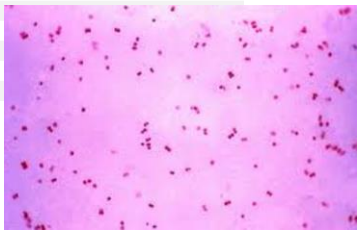
Gramfärbung		+++ Leukozyten
		++ gramnegative Diplokokken

Kultur allgemein

Bakterien	Keim 1	+++ Neisseria gonorrhoeae
		+ aerobe Mischflora, 3 Keimarten

Resistenzprüfung

	Keim 1
Ceftriaxon MHK (E-Test)	sensibel
	0.004 mg/l
Azithromycin MHK (E-Test)	
	2.000 mg/l



- Ceftriaxon 500 mg i.m.
- Follow up eneventful

Tab. 2 Ursachen infektiöser Proktitis mit Diagnostik und Therapie.

Krankheit	Erreger	Diagnostik	Therapie
Syphilis	*Treponema pallidum*	Multiplex-PCR Serologie, (Dunkelfeld)	Benzathinpenicillin 2,4 Mio. I.E. i.m.
Herpes-simplex-Infektion	*Herpes-simplex-Virus* Typ 1 und 2	PCR, Viruskultur	Valacyclovir 2×500–1000 mg oder Famaciclovir 3×250 mg für 7–10 Tage
Gonorrhö	*Neisseria gonorrhoeae*	Grampräparat, Kultur, PCR	Rocephin 250–500 mg i.m. und Azithromycin 1 g p.o.
Lymphogranuloma venereum (LGV)	*Chlamydia trachomatis* Serotypen L1-L3	PCR, (Serologie)	Doxycyclin 2×100 mg pro Tag für 3 Wochen
Chlamydieninfektion (Nicht-LGV-Chlamydien)	*Chlamydia trachomatis* Serotypen D-K	PCR	Azithromycin 1 g p.o.

I.E. internationale Einheiten, *i.m.* intramuskulär, *p.o.* per os, *PCR* Polymerase-Kettenreaktion.

Vavricka SR, Der Gastroenterologe 2015[29]

Case n°4

- Female, 71 years
- 2006 Laparoscopic Anterior Rectal Resection/TME, Adeno-CA in situ
- 1/18 uT3 Adeno CA distal Rectum
- Infiltration prox M. sphincter ani internus
- 2/2018 neoadjuvant RCHT 49 Gy
- 3/2018 stop RCHT/Hospitalisation due Diarrhea/Proctitis (ulcers)

30

Next steps

1. Continue Topic (Mesalazine, Budenoside, Metronidazole, Sucralfate)
2. Resection Tumour
3. Protective Ileostomy
4. other

Next steps

1. Continue Topic (Mesalazine, Budenoside, Metronidazole, Sucralfate)
2. Resection Tumour
3. Protective Ileostomy
4. other

Lieber Lukas

Danke für Deine Mail.
In der Regel wird eine radiogenbedingte Proktitis mit der Zeit geheilt, aber falls es um eine schwere Proktitis mit starken Symptomen handelt dann braucht eine Therapie.
Bezüglich der Therapie kommt es darauf an, ob das eine blutende- oder entzündliche Proktitis ist. Da die blutende, das häufigste Form ist, besteht die lokale Therapie aus:

- Mesalazin oder Kortikosteroiden (als Zäpfchen oder Einlauf, eventuell kombiniert mit Metronidazol), Sucralfat-Einläufen, Butyrat-Zäpfchen und/oder Formalin (eventuell kombiniert mit Retinol oral). Retinol oral könnte auch eine positive Wirkung haben. Bei persistierenden Blutungen kann der Einsatz von koagulierenden Methoden sinnvoll sein.

Ich würde die Prednisolone-Zäpfchen plus Sucralfat-Einläufe empfehlen, die andere Medikamente/Therapien können in Reserve behalten werden.

Grüsse und schönes WE,
Hossein

33

International Journal of Radiation Oncology biology • physics

www.redjournal.org

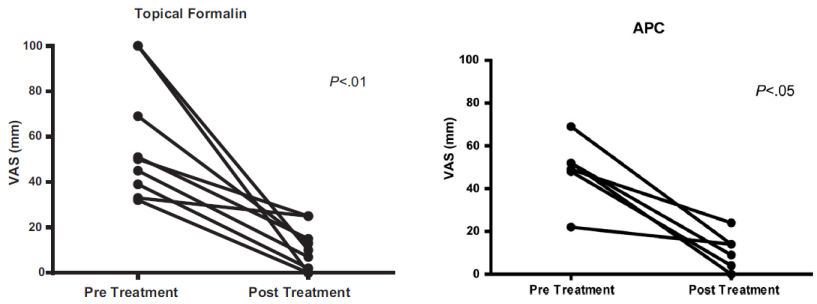
Clinical Investigation: Genitourinary Cancer

Argon Plasma Coagulation Therapy Versus Topical Formalin for Intractable Rectal Bleeding and Anorectal Dysfunction After Radiation Therapy for Prostate Carcinoma

Eric Yeoh, MD, FRCP(Edin), FRCR, FRANZCR,[*,§] William Tam, PhD, FRACP,[§,†] Mark Schoeman, PhD, FRACP,[§,†] James Moore, MD, FRACS,[§,‡] Michelle Thomas, PhD, FRACS,[§,‡] Rochelle Botten, BSc(Hons),[*] and Addolorata Di Matteo, BSc(Hons)[*]

*Departments of *Radiation Oncology, †Gastroenterology, and ‡Colorectal Surgery, Royal Adelaide Hospital, Adelaide, Australia; and §School of Medicine, University of Adelaide, Adelaide, Australia*

Received Jun 8, 2013, and in revised form Aug 23, 2013. Accepted for publication Aug 25, 2013.



CLINICAL PRACTICE GUIDELINES

The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Treatment of Chronic Radiation Proctitis

Ian M. Paquette, M.D.[1] • Jon D. Vogel, M.D.[2] • Maher A. Abbas, M.D.[3]
Daniel L. Feingold, M.D.[4] • Scott R. Steele, M.D., M.B.A.[5]

On behalf of the Clinical Practice Guidelines Committee of The American Society of Colon and Rectal Surgeons

- Formalin application 1B
- Sucralfate enemas 1C
- Hyperbaric Oxygen Therapy 1B

Not recommended:

- Butyrate enemas 1B
- Mesalazine, Ozone Therapy, Metronidazole 1C
- Bipolar Coag, Nd-YAG laser, Cryotherapy 1C

Diseases of the Colon and Rectum 2018

Eur Rev Med Pharmacol Sci. 2018 Nov;22(21):7562-7572. doi: 10.26355/eurrev_201811_16298.

Hyaluronic acid for treatment of the radiation therapy side effects: a systematic review.

Cosentino D[1], Piro F.

Author information

Abstract

OBJECTIVE: The main limit of radiation therapy is the dose-dependent toxicity to healthy tissues. The 36% of patients exposed to radiotherapy for pelvic malignancies reporting gastrointestinal symptoms as incontinence, pain, mucus discharge, and bleeding (radiation proctopathy). In the cervix cancer, healthy tissues exposed to radiations easily develop inflammation of vaginal mucosa, bleeding and pain and to improve these symptoms, some medical devices were developed. One of the most interesting for its features is undoubtedly the hyaluronic acid. Considering the histological similarity between the vaginal and the rectal mucosa, the application of hyaluronic acid for the radiation proctopathy represents an interesting opportunity.

MATERIALS AND METHODS: We performed a literature search of MEDLINE, EMBASE, PubMed, and Research Gate for studies published up to March 2018. The following combination of medical subject headings, terms and free text words were used: 'hyaluronic acid', 'hyaluronate', 'topical application' and 'radiation proctitis'.

RESULTS: After the screening of titles and abstracts, and using the established criteria, 7 studies were selected for inclusion in the systematic review.

CONCLUSIONS: The clinical use of hyaluronic acid for topical administration in patients with inflammatory conditions at the level of the vaginal and anal mucosa, following radio and chemo-therapies, resulted an innovative approach to help patients in managing the AEs. Hyaluronic acid confirmed its totally safety profile and resulted effective in the inflammation decrease, improving the tissue health and the symptoms related. For all these reasons, we can easily promote the clinical application of hyaluronic acid on inflamed tissues though a substantial work is necessary to investigate more deeply the hyaluronic acid role on this context.

PMID: 30468506 DOI: 10.26355/eurrev_201811_16298