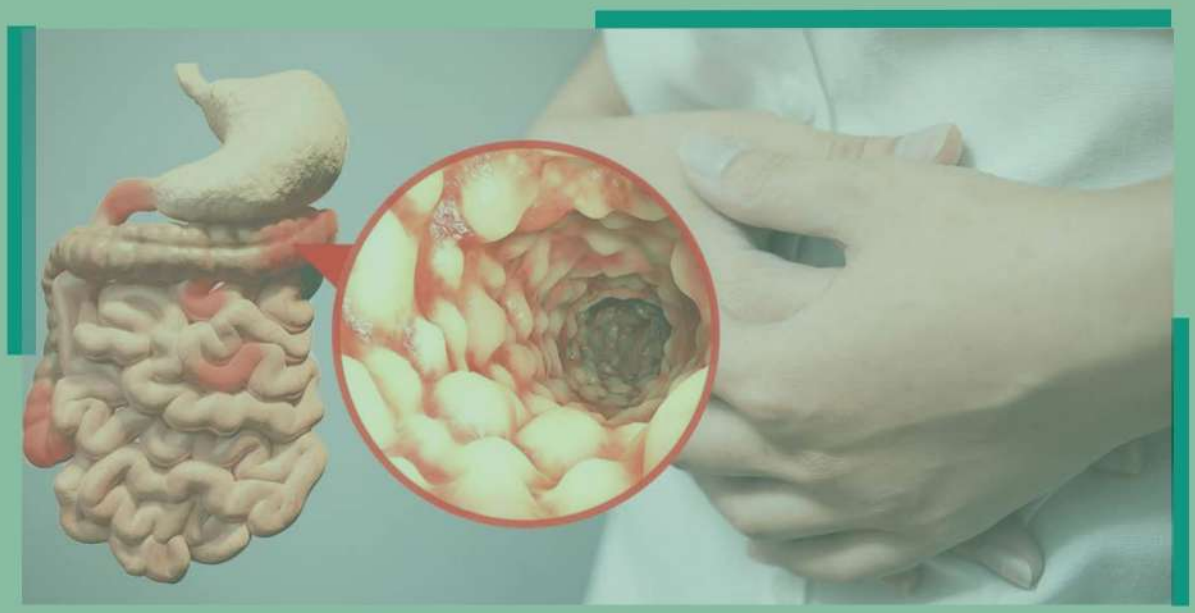
ISSN 2377-8369

Openventio PUBLISHERS

GASTRO

Open Journal

December 2019. Volume 4, Issue 1



ASSOCIATE EDITORS

Tatiana Goretsky (Zagranichnaya), PhD

Jacintha O. Sullivan, PhD

Shreyas Saligram, MD, MRCP

www.openventio.org

Copyright information. Openventio Publishers is licensed under a Creative Commons Attribution 4.0 International License. All the articles published under this license are open-access, which allows to copy, redistribute, remix, transform, and reproduce in any medium or format, provided the original work is properly cited.

ISSN 2377-8369

GASTRO
Open Journal

Openventio
PUBLISHERS

CONTENTS

Letter to the Editor

1. Endoscopic Treatment of Refractory Variceal Bleed 1-3

   – *Shreyas Saligram*, Marina Roytman, Helen Wong and ThimmaiahTheethira*

Letter to the Editor

2. Call Me Anything but Thoughtless or Misguided in IBD Management 4-6

   – *Nicholas V. Costrini**

Opinion

3. What IBD Physicians Can Learn from Major League Baseball Managers 7-8

   – *Nicholas V. Costrini*

Case Report

4. The Importance of Enzyme Substitution Therapy in Early Pancreas Exocrines of Insufficiency 9-10

   – *Biljana Petrovic**

ISSN 2377-8369

GASTRO
Open Journal

Openventio
PUBLISHERS

Letter to the Editor

Endoscopic Treatment of Refractory Variceal Bleed

Shreyas Saligram, MD, MRCP, FACG, FASGE[1*]; Marina Roytman, MD, FACP[1]; Helen Wong, MD[2]; ThimmaiahTheethira, MD, DM[1]

[1]*Department of Gastroenterology, Hepatology & Nutrition, 2823 Fresno Street, Fresno, CA 93721, USA*
[2]*VA Central California Health systems, 2615 E Clinton Ave, Fresno, CA 93703, USA*

[*]***Corresponding author***
Shreyas Saligram MD, MRCP, FACG, FASGE
Chief of Gastroenterology, Hepatology and Nutrition, Department of Gastroenterology, Hepatology and Nutrition, University of California San Francisco, Fresno, CA, USA; E-mail: drsaligram@yahoo.com

Article information
Received: February 19th, 2019; **Revised:** April 1st, 2019; **Accepted:** April 3rd, 2019; **Published:** May9th, 2019

Cite this article
Saligram S, Roytman M, Wong H, Theerhira T. Endoscopic treatment of refractory variceal bleed. *Gastro Open J.* 2019; 4(1): 1-3. doi: 10.17140/GOJ-4-128

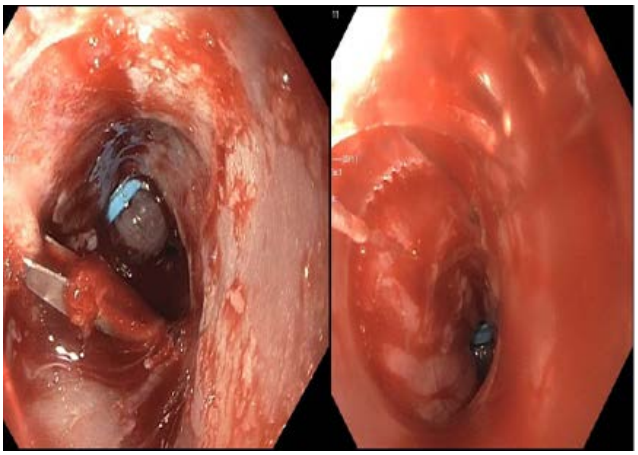
A 70-year-old man with history of end-stage liver disease due to alcohol misuse disorder was admitted to the hospital with hematemesis. He had at least 5 episodes of bright red hematemesis and was feeling dizzy. He complained of epigastric pain for 3 days prior to presentation. He had noticed progressive development of dark urine, pale stools and yellow sclera. He had not consumed any non-steroidal anti-inflammatory drugs recently.

His last consumption of alcohol was 3 months ago. He had a prior history of gastrointestinal (GI) bleeding and had undergone upper GI endoscopy that revealed large varices with high-risk stigmata (white nipple sign) requiring variceal band ligation. His last endoscopy was 6 weeks prior to presentation. He was non-compliant with prophylactic propranolol and was not on any other medications.

On physical examination, patient appeared chronically ill, pale with evidence of scleral icterus and spider nevi. He was alert and in apparent discomfort due to recent vomiting and retching. His BP was 90/50 mmHg with a pulse of 110/minute. He was afebrile. Pertinent laboratory studies revealed hemoglobin of 6 g/dL, platelets of 40,000 μL and INR of 2.2. His model for end-stage liver disease (MELD)-Na was calculated to be 25.

He was intubated and was transfused with 1 unit of blood, 1 unit of platelets and fresh frozen plasma. He was initially treated with intravenous proton pump inhibitors, Octreotide and Ceftriaxone antibiotics. He underwent emergent upper GI endoscopy. It revealed 4 large varices with high-risk stigmata for recent bleeding (red wale sign in the distal esophagus) and significant amount of prior scar tissue. There was no evidence of gastric varices. Decision was made to proceed with variceal band ligation to prevent further bleeding. At least 4 bands were placed, however some of the bands slipped immediately due to scarring from prior banding and there was sudden hemorrhaging from the varices (Figure 1). Patient became more hypotensive with the blood pressure of 70/30 mmHg requiring initiation of vasopressors.

Figure 1. *Active Hemorrhage Despite Endoscopic Therapy*

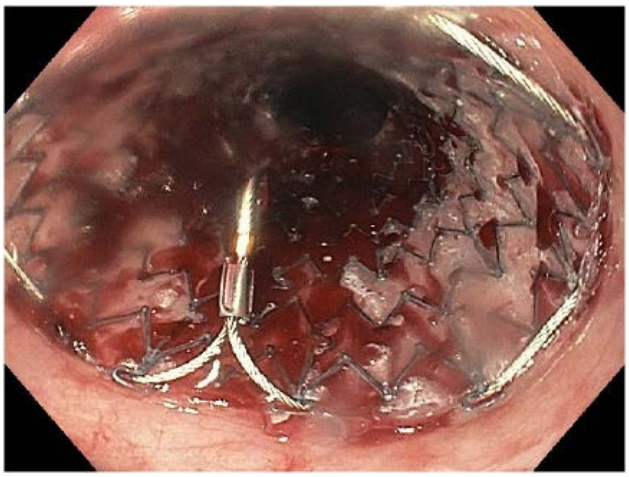


His MELD was more than 18 and he was therefore a relative contraindication for transjugular intrahepatic portosystemic shunt (TIPS). Decision was therefore made to tamponade the varices with an esophageal stent. A guidewire was placed into the stomach by upper GI endoscopy. The endoscope was then removed and a fully covered 23 mm×15 cm long, fully covered metal stent was introduced over the guidewire. This was followed by upper GI endoscopy. The gastroesophageal junction (GEJ) was noted to be at 40 cm. The distal end of the stent was placed 3 cm across the GEJ under direct visualization and proximal end at 28 cm of esophagus without the aid of fluoroscopy and under direct endoscopic visualization. Immediate tamponade of bleeding varices were noted (Figure 2). The patient was monitored for another 2 days in the hospital and remained stable without signs of recurrent

© Copyright 2019 by Saligram S. This is an open-access article distributed under Creative Commons Attribution 4.0 International License (CC BY 4.0), which allows to copy, redistribute, remix, transform, and reproduce in any medium or format, even commercially, provided the original work is properly cited.

bleeding, need for transfusions or hemodynamic instability. He was discharged home with twice a day high dose proton pump inhibitor to prevent acid reflux from the stent. Repeat upper GI endoscopy was performed 2 weeks later on the outpatient basis. Rat-tooth forceps was used to remove the esophageal stent. The endoscopy revealed 4 columns of large varices. The varices were than ligated by 4 bands to prevent future bleeding. He was followed regularly for another 3 months and had no further GI bleed and is doing well.

Figure 2. *Stent Resulting in Hemostasis of Acute Variceal Bleed*



DISCUSSION

Cirrhosis of liver can be complicated by esophageal varices.[1] A bleeding esophageal varices can cause significant mortality and morbidity. The risk of recurrent GI bleed is very high if not treated. Endoscopic management along with pharmacotherapy is the current standard of care for management of esophageal varices. Bands placed through endoscopy can cause scarring of these varices and ligate it thereby preventing GI bleed. Bands can be placed either as a primary prophylaxis in large varices that have never bled before or as secondary prophylaxis in patients with history of bleed or who have high-risk features for bleeding such as nipple sign or red wale sign of varices. Banding of varices is highly successful in most cases. In minority of cases with repeated prior banding, scar formation will prevent successful band ligation. If this happens in the setting of acute GI bleed, the mortality is very high. The society practice guidelines suggest using a Minnesota tube, which is an esophageal balloon for immediate tamponade to control bleeding in refractory variceal bleed.[2] This can be in place for 24 hours and subsequently patients undergo TIPS.

Placement of a Minnesota tube is a complex procedure and can be cumbersome when needed acutely. It has a success rate of only 50% in controlling GI bleed and can have certain risks like mal-deployment and esophageal perforation especially if the gastric balloon is inflated in esophagus.[1] A multicenter randomized control trial of esophageal balloon tamponade *vs* stent in control of refractory variceal GI bleed showed that success was higher in stent group *vs* balloon group (66% *vs* 20%), control of bleeding was higher in stent group (85% *vs* 47%), Adverse events were lower in the stent group (15% *vs* 47%) and TIPS was used more frequently in the balloon group (4 *vs* 10).[3]

The TIPS is contraindicated in patients with right heart failure, pulmonary hypertension, severe renal failure, uncorrected coagulopathy, prior history of encephalopathy and high MELD.[4] TIPS, although is very effective in controlling variceal bleed, has some risks. About a third of patients can experience a debilitating encephalopathy even in patients without prior history of it.[4] Other risks are liver laceration, hematoma and procedure-related death.[4] Besides patients who undergo TIPS should be regularly followed with ultrasound of abdomen to evaluate its patency.

Self-expanding fully covered metal esophageal stents have been traditionally used for treatment of malignant esophageal strictures and esophageal perforation. The stent's large diameter and exact approximation to the lumen and mucosa of esophagus makes it very effective in treatment of refractory GI bleed either from varices or diffuse oozing from mucositis.[3] The ease of placing and removing the stent under direct visualization without the aid of fluoroscopy makes it safer than Minnesota tube.[5] Esophageal stents can have certain risks such as stent migration, which can be up to 30% of cases. This complication usually occurs after few days and the migrated stent is easily retrievable. The tamponade that is achieved in the initial 24-48 hours is crucial to controlling the hemorrhage which otherwise can be life-threatening. Other risks of esophageal stent are acid reflux, which can cause aspiration and this can be minimized by high doses of twice a day proton pump inhibitors. Stent-related esophageal perforation is very rare in expert hands, especially if caution is taken to ensure that guidewire is placed in the stomach. A recent meta-analysis of 155 patients from 12 studies showed success rate of achieving hemostasis within 24 hours in acute variceal bleed was 96%. The adverse events included rebleeding, ulceration and stent migration in 36% of patients. The 60 day survival rate was 64% in those undergoing the procedure.[6] Another meta-analysis of 80 patients from five studies showed success rate of 94% with no stent-related mortality. Number of patients with uncontrolled bleeding despite the stent placement was 12%, 21% of patients had stent migration and 34% died due to liver disease related cases.[7] We have described the technique of placement of Self-expanding fully covered metal esophageal stents under endoscopic guidance for treatment of refractory variceal bleed. However, some of the other kinds of stents like Denis Ella stent used in Europe for treatment of refractory variceal bleed does not need endoscopic visualization for placement of it.

There is a growing body of evidence suggesting that esophageal stents are safe and effective in treatment of refractory variceal bleeding and it should be the standard of care. This method is safer and more effective compared to Minnesota tube in controlling acute hemorrhage from refractory variceal bleed and can be used as either a bridge to TIPS or better as an alternate to TIPS.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

REFERENCES

1. Boregowda U, Umapathy C, Halim N, et al. Update on the management of gastrointestinal varices. *World J Gastrointest Pharmacol Ther*. 2019; 10(1): 1-21. doi: 10.4292/wjgpt.v10.i1.1

2. Garcia-Tsao G, Abraldes JG, Berzigotti A, Bosch J. Portal hypertensive bleeding in cirrhosis: Risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the study of liver diseases. *Hepatology*. 2017; 65(1): 310-335. doi: 10.1002/hep.28906

3. Escorsell À, Pavel O, Cárdenas A, et al. Esophageal balloon tamponade versus esophageal stent in controlling acute refractory variceal bleeding: A multicenter randomized, controlled trial. *Hepatology*. 2016;63(6): 1957-1967. doi: 10.1002/hep.28360

4. Fagiuoli S, Bruno R, Venon DW, et al. Consensus conference on TIPS management: Techniques, indications, contraindications. *Dig Liver Dis*. 2017; 49(2): 121-137. doi: 10.1016/j.dld.2016.10.011

5. Saligram S, Lim D, Pena L, Friedman M, Harris C, Klapman J. Safety and feasibility of esophageal self-expandable metal stent placement without the aid of fluoroscopy. *Dis Esophagus*. 2017; 30(8): 1-6. doi: 10.1093/dote/dox030

6. McCarty TR, Njei B. Self-expanding metal stents for acute refractory esophageal variceal bleeding: A systematic review and meta-analysis. *Dig Endosc*. 2016; 28(5): 539-547. doi: 10.1111/den.12626

7. Shao XD, Qi XS, Guo XZ. Esophageal stent for refractory variceal bleeding: A systemic review and meta-analysis. *Biomed Res Int*. 2016; 2016: 4054513. doi: 10.1155/2016/4054513

ISSN 2377-8369

GASTRO
Open Journal

Openventio
PUBLISHERS

Letter to the Editor

Call Me Anything but Thoughtless or Misguided in IBD Management

Nicholas V. Costrini, MD, PhD, MBA*

Gastroenterology Associates of Big Bend, Tallahassee, Florida, USA

Corresponding author
Nicholas V. Costrini, MD, PhD, MBA
Gastroenterology Associates of Big Bend, Tallahassee, Florida, USA; E-mail: drcostn@gmail.com

Article information
Received: September 7th, 2019; **Accepted:** September 19th, 2019; **Published:** September 26th, 2019

Cite this article
Costrini NV. Call me anything but thoughtless or misguided in IBD management. *Gastro Open J.* 2019; 4(1): 4-6. doi: 10.17140/GOJ-4-129

I read with interest the open access, original article, by S.K. Murthy, et al, *Introduction of anti-tumor necrosis factor (TNF) therapy has not yielded expected declines in hospitalization and intestinal resection rates in inflammatory bowel diseases: a population-based interrupted time series study* appearing in Gut 12 June 2019.[1] It must first be stated that the authors are to be congratulated for the magnificent demonstration of the benefits of the Canadian healthcare system in terms of collection of healthcare data. That said, I take issue with their explanation and hypothesis: "misguided use and failure to optimize use of infliximab, particularly among patients with Crohn's Disease (CD), as well as possible underuse of infliximab among patients with ulcerative colitis (CUC)…." In the follow-up press release, one summary recommendation was that "*doctors should be more thoughtful in managing inflammatory bowel disease (IBD).*" It is unfortunate, indeed, that the term "misguided use" would appear and then be translated into perhaps a deeper, and unwarranted, criticism that doctors managing IBD have been "less than thoughtful or misguided" in the use of biologics. I think the authors actually intended to report that the academic community has collected clinical trial data and offered practicing clinicians a plan for use of biologics only to find in retrospect that those recommendations were not likely to be effective given the general IBD patient population and the less than complete effectiveness of the biologics. Nonetheless, the message was certainly blurred.

Beyond the social implications of the article and its interpretations, there are numerous clinical areas of concern in this publication. The basic premise of the conclusions is that since the anti-TNF agent infliximab has been demonstrated to reduce hospitalizations and surgeries in controlled trials and observational studies, one should expect, for the price and deep intrusion into the marketplace, similar effectiveness to be demonstrable in population studies. Because such effectiveness was not demonstrated in this elegant study, the conclusion offered is that the fault must lay with the physicians. I believe the authors are quite mistaken and I offer more likely explanations for consideration.

The infliximab 2002 ACCENT I[2] and 2004 ACCENT II[3] trials reported clinical remission rates of twenty-two percent. The adalimumab 2007 CHARM trial[4] reported similarly less than spectacular remission rates. For the first decade after anti-TNF entry into the marketplace, practicing gastroenterologists were "guided" by the academic community to treat IBD patient with either "top-down or the bottom-up" programs based upon clinical parameters. The 2015 REACT trial[5] provided enough "real world" evidence to support treating patients with early introduction of combined immunomodulator plus biologic agent. While combined treatment (i.e. top-down) did not offer a statistically significant improved clinical remission rate compared to a conventional treatment program (i.e. bottom-up), early combined treatment was associated with a lower two-year aggregate rate of hospitalizations, surgeries, and serious infections. We can extrapolate from the clinical remission rates that the endoscopic remission rates would be in the twenty-five percent range. Hence, in clinical trials and in "real world" experience, the anti-TNF agents are rather weak in providing endoscopic remission and by extension a weak tool in altering the natural history of IBD. In fact, it was not until 2012, the year the study ended, that the EXTEND trial[6] was published. This was the first study to use endoscopic healing as the primary endpoint in a CD treatment trial. Mucosal healing was recorded in only twenty-four percent of patients treated with adalimumab for two years. In patients with a less than a two-year history of CD, endoscopic remission reached thirty-three percent at two years. I was very surprised by your explanation since it is agreed that while these agents provide gratifying clinical relief for an interval, anti-TNF agents have the power to alter the natural history of CD in only a small proportion of patient. That is why additional more tightly designed trials have been completed. In 2018, the CALM

© Copyright 2019 by Costrini NV. This is an open-access article distributed under Creative Commons Attribution 4.0 International License (CC BY 4.0), which allows to copy, redistribute, remix, transform, and reproduce in any medium or format, even commercially, provided the original work is properly cited.

trial[7] was completed. In this trial patients with CD of less than one-year duration and naïve to immunomodulators and biologics, were entered into programs in which the treatments were escalated on the basis of regularly measured biomarkers and endoscopy as well as clinical symptoms. In this highly selected, intensely investigated group of patients, endoscopic remission rates with adalimumab reached its zenith of forty-six percent, well above the remission rate of thirty percent in their patients managed conventionally. We have yet to learn if we have found a way to use anti-TNF agents in a manner that alters the natural history of the disease in the majority of patients and capable of deflecting adverse event curves. The population of CD patients exposed to anti-TNF agents between 2000 and 2012 were managed conventionally as directed by the controlled trials of the time. Hence, remission occurred in only a quarter of CD patients treated with infliximab (and for an unknown duration). It is not surprising that the population curves were not deflected. I offer that the fault lies not in "misguided" clinicians but in the fact that anti-TNF agents are only modestly effective in promoting endoscopic healing when used as they were in the years of the study. Comment is made that drug trough levels were not used regularly. It was not until well after the study was completed that the academic community embraced such testing as meritorious. The fact that we have spent a fortune on the drugs for IBD and have so little to show for it, as you so vividly demonstrate, is evidence enough of the frailty of this class of drugs in the mission of changing the natural history of the disease. This limited anti-TNF impact on CD natural history is justification for the aggressive search for new drugs and the design of studies such as CALM in order to find how to better select and manage patients and employ the drug. Regarding surgery for strictures in CD, anti-TNFs would not likely affect the rate of surgery as the expected remission rate in this study interval was simply too low to have a measurable population impact on CD natural history. Any contention that the failure of anti-TNFs is the fault of misguided physicians, is not supported by the literature or your data.

Turning to the impact of anti-TNF agents in the course of CUC, it is difficult to make much of the fact that adverse event incidences were not changed over time for the entire group since only 2.1% of the CUC group was exposed to anti-TNF agents. The authors suggest that doctors did not use the biologics often enough. It was surely effective, however, as hospitalization rates were reversed and declined "markedly" with an Odds Ratio of 0.515, 95% CI 0.342 to 0.777. I would offer the explanation that CUC has many more options for maintenance of remission (i.e. mesalamine and immunomodulators), has very commonly a limited disease profile (i.e.proctosigmoiditis); and as a hemorrhagic mucosal disease, is less likely to progress silently to dangerous fistulae or strictures. Thoughtful clinicians are aware of all this. The two-fold increase in drug costs was highly effective in CUC management. That surgery rates were unaffected in the anti-TNF subgroup is expected as the drug will not reduce cancer and resistant-to-treatment rates until we have drugs that produces high proportions of long-lasting endoscopic remissions. Is it possible that many more CUC patients should have been treated with anti-TNF drugs? That is difficult to say. If many more were treated, the cost for any incremental benefit would have been higher. Additionally, fifty to eighty percent of patients would have failed to benefit at all given the defined rate of remission with the conventional care practiced during 1995-2012 interval.

In closing, I offer my personal experience. I studied two hundred CD patients in my private practice as a very early adopter of anti-TNF treatment. The incidences of surgery and steroid use in the interval of 2000 to 2010 with and without exposure to anti-TNF agents were identical to those parameters in the decade of 1990 to 2000. I was disappointed by the results to be sure. The patient demographics in my study group and in this publication were identical. The explanation for the elegant study results and for my small office results rests in the fact that as far as anti-TNFs are concerned, IBD patient groups with long-standing disease (five years or more), prior exposure to other agents (biologics and immunomodulator), and managed principally by clinical measures cannot be expected to generate a substantial proportion of patients with long-term endoscopic remissions. Without long-term endoscopic remissions with mucosal healing, we cannot expect to change the natural history of IBD. As we consider new drugs in the pipeline and aggressive management programs now being promoted, we can hope for better directions and more appealing curves along the road leading to a cure for IBD. I thoughtfully offer my explanations for this data. The explanations, sir, resides in the potion and not in the physician.

REFERENCES

1. Murthy SK, Begum J, Bechamel EL, et al. Introduction of anti-TNF therapy has not yielded expected declines in hospitalization and intestinal resection rates in inflammatory bowel disease: A population-based interrupted time series study. *Gut.* 2019; 1-9. doi: 10.1136/gutjnl-2019-318440

2. Hanauer SB, Feagan BG, Lichtnestein GR, et al. Maintenance infliximab for Crohn's Disease: The ACCENT I randomized trial. *Lancet.* 2002; 4: 1541-1549. doi: 10.1016/S0140-6736(02)08512-4

3. Sands, BE, Anderson FH, Bernstein CN, et al. Infliximab Maintenance Therapy for Fistulizing Crohn's Disease. *N Engl J Med.* 2004; 350: 876-885. doi: 10.1056/NEJMoa030815

4. Colombel JF, Sandborn WJ, Rutgeerts P, et al. Adalimumab for maintenance of clinical response and remission in patients with Crohn's Disease: The CHARM trial. *Gastroenterology.* 2007; 132: 52-65. doi: 10.1053/j.gastro.2006.11.041

5. Khanna R, Bressler B, Levesque BG, et al. Early combined immunosuppression for the management of Crohn's Disease (REACT): A cluster randomized controlled trial. *Lancet.* 2015; 386: 1825-1834. doi: 10.1016/S0140-6736(15)00068-9

6. Rutgeerts P, VanAssche G, Sandorn WJ, et al. Adalimumab induces and maintains mucosal healing in patients with Crohn's

disease: Data from the EXTEND trial. *Gastroenterology*. 2012; 142: 1102-1111. doi: 10.1053/j.gastro.2012.01.035

7. Colombel JF Panaccione r, Bossuyt P, et al. Effect of tight control management on Crohn's Disease (CALM): A multicenter, randomized, controlled phase 3 trial. *Lancet*. 2018; 390: 2779-2789. doi: 10.1016/S0140-6736(17)32641-7

ISSN 2377-8369

GASTRO Open Journal

Openventio PUBLISHERS

Opinion

What IBD Physicians Can Learn from Major League Baseball Managers

Nicholas V. Costrini, MD, PhD, MBA*

Gastroenterology Associates of Big Bend, Tallahassee, FL, USA

***Corresponding author**

Nicholas V. Costrini, MD, PhD, MBA

Gastroenterology Associates of Big Bend, Tallahassee, FL, USA; E-mail: drcostn@gmail.com

Article information

Received: November 1st, 2019; **Accepted:** November 4th, 2019; **Published:** November 6th, 2019

Cite this article

Costrini NV. What IBD physicians can learn from major league baseball managers. *Gastro Open J*. 2019; 4(1): 7-8. doi: 10.17140/GOJ-4-130

Yogi Berra philosophized, "*You can observe a lot by just watching.*" Physicians managing inflammatory bowel disease (IBD) patients are constantly exposed to the recent literature, the visiting pharmaceutical representatives, and to the valuable presentations by the academic experts at the annual meetings. In my opinion, these presentations too often are advanced in a vacuum of unconvincing compartmentalization rather than as a well-choreographed management strategy that considers both the impact of any IBD drug and the nearly certain likelihood of a patient's failed response or eventual relapse. Stated another way, what is most often missed, only mentioned as an aside, and almost never clearly defined is an agent's place within the context of management of the entire course of the disease. Twenty years into the new century with the current and evolving list of IBD drugs, it would be valuable to much more often and with authority present specific management algorithms that offer the highest likelihood of remission.[1,2] Having a progressively enlarging menu of partially effective drugs is no longer satisfactory. I give you Major League Baseball (MLB).

We appropriately view the physician's role as that of the manager of the IBD case and particularly as manager of the medications employed. As an instruction, I offer what we can learn from MLB managers as we observe the well-defined strategy in calling Starting and Relief Pitchers to the mound.[3]

1. Great Pitching (i.e. The first IBD drug employed) beats Great Hitting (i.e. moderate to severe IBD). Both starting and Relief Pitching are necessary. In IBD, we have good but not great drugs at the present time. Follow-up (i.e. relief) medications are an essential part of the strategy for IBD. Any discussion of a specific drug must include a recommendation for use in an over-all strategy leading to remission and change in the natural history of IBD.

2. Starting Pitchers seldom hold the mound past six innings.

3. Starting Pitchers' inning-by-inning earned run averages (ERA) rise after the fourth inning.

4. Managers monitor the Starting Pitcher effectiveness (ERA per inning); in IBD, clinical status and fecal calprotectin require intense monitoring[3] which has been lack-luster for decades.

5. In MLB managers know the bullpen expertise and prior work; in IBD, physicians must know the classes of drugs in the IBD armamentarium.

   a. Mesalamine/Steroids/Immunosuppressants/Biologics/Small molecules

   b. Make decision based upon disease/activity/urgency of need/prior drugs exposure

6. Starting Pitchers wins 90% of Cy Young (best pitcher of the year) Awards even though they seldom pitch a complete game. Similarly, the starting biologic should be expected to bring about complete remission in only a quarter of the cases.[4-6] Discuss a total medication strategy with patients. Advise that non-responsiveness and relapse are likely and the management strategy provides for these eventualities.

7. The Relievers have lower ERAs than the Starting Pitchers and promote winning seasons. Consider Anti-TNFs, T-Cell Migration Inhibitors, IL 12/23 Inhibitors, JAK inhibitors as essential management choices which should be outlined in the course management from the outset. To be clear, do not cling to the idea that the first biologic will secure long-term remission. Rather, plan with the patient that a change will be re-

© Copyright 2019 by Costrini NV. This is an open-access article distributed under Creative Commons Attribution 4.0 International License (CC BY 4.0), which allows to copy, redistribute, remix, transform, and reproduce in any medium or format, even commercially, provided the original work is properly cited.

quired and seek the ideal time and agent for the change.

8. For a Quality Start in Baseball, the pitcher goes six innings allowing less than three runs. For the first biologic drug used in IBD, expect a response in 40-50% of patients by 2-10 weeks.[7]

9. In the prior century, Starting Pitchers commonly pitched complete games. In this century, they are not expected to and do not always win. Indeed, the three best starting pitchers of the past twenty years (Randy Johnson, Pedro Martinez, and Roger Clemens) had a *combined* winning percentage of only 66%. Current starting IBD drugs fare only half as well in maintaining remission. In IBD, in this century, do not expect the starting biologic to go the distance. Rather, prepare all involved for an expeditious change as the expected failure or relapse arrives.

10. Relief Pitchers (middle inning and closers) have won 9 Cy Young Awards. MLB managers decide upon the reliever based upon the batters coming to the plate, the inning, and the score. The all-important closer may be the most reliable pitcher on the staff, i.e., Mariano Rivera. In IBD, follow-up medications can be expected to be moderately effective when starting drugs have become ineffective. Perhaps an augmented 15-20% remission rate can be expected from follow-up drugs.[8] Hence, when the second drug is started, begin to consider your closer as there is an eighty-percent chance it will be needed.

11. Know when to face a loss. Finish; review the runs, hits, errors and strategy as there is another game tomorrow. Consider hiring another premier reliever. In IBD, know when to prepare for surgery, review the course of responses and remissions. Seek the better drug on the horizon.

The above list of comparisons is designed in a lighthearted way to stress the too-often over-looked reality that no current, single-agent is likely to alter the natural history of the disease in the IBD population as a whole.[9] It may be effective in only ten to twenty percent of patients. A facile understanding of the evolving classes of IBD drugs is paramount; their timely and strategic introduction should promote a greater proportion of long-term remissions. That is a winning strategy. We cannot, however, win them all. Ted Williams said it best. "*Baseball is the only endeavor where a man can succeed 3 times in 10 and be considered a good performer.*" That is about where we are in IBD management.

REFERENCES

1. Colombel JF, Panaccione R, Bossuyt P, et al. Effect of tight control management on Crohn's disease (CALM): A multcentre, randomized, controlled phase 3 trial. *Lancet*. 2018; 390: 2779-2789. doi: 10.1016/S0140-6736(17)32641-7

2. Ungaro R, Colombel JF, Lissoos T, et al. A treat-to-target update in ulcerative colitis: A systematic review. *Amer J Gastro*. 2019; 114: 874-883. doi: 10.14309/ajg.0000000000000183

3. Baseball-Reference. MLB stats, scores, history, and records, 2019. Web site. Baseball-Reference.com. Accessed October 31, 2019.

4. Sandborn WJ, Feagan BG, Rutgeerts P, et al. Vedolizumab as induction and maintenance therapy for Crohn's disease. *N Engl J Med*. 2013; 369: 711-721. doi: 10.1056/NEJMoa1215739

5. Hanauer SB, Feagan BG, Lichtenstein GR, et al. Maintenance infliximab for Crohn's disease: The ACCENT I randomized trial. *Lancet*. 2002; 359: 1541-1549. doi: 10.1016/S0140-6736(02)08512-4

6. Colombel JF, Sandborn WJ, Rutgeerts P, et al. Adalimumab for maintenance of clinical response and remission in patients with Crohn's disease. *Gastroenterology*. 2007; 132(1): 52-65. doi: 10.1053/j.gastro.2006.11.041

7. Vasudevan A, Gibson PR, vanLangenberg DR. Time to clinical response and remission for therapeutics in inflammatory bowel diseases: What should the clinician expect, what should patients be told. *World J Gastroenterol*. 2017: 23(35): 6385-6402. doi: 10.3748/wjg.v23.i35.6385

8. Sandborn WJ, Rutgeerts P, Gasink C, et al. Long-term efficacy and safety of ustekinumab for Crohn's disease through the second year of therapy. *Aliment Pharmacol Ther*. 2018: 48(1): 65-77. doi: 10.1111/apt.14794

9. Murthy SK, Begum J, Benchimol EL, et al. Introduction of anti-TNF therapy has not yielded expected declines in hospitalization and intestinal resection rates in inflammatory bowel diseases: A population-based interrupted time series study. *Gut*. 2019; pii: gutjnl-2019-318440. doi: 10.1136/gutjnl-2019-318440

ISSN 2377-8369

GASTRO
Open Journal

Openventio
PUBLISHERS

Case Report

The Importance of Enzyme Substitution Therapy in Early Pancreas Exocrines of Insufficiency

Biljana Petrovic, PhD*

Health Center Kraljevo, JUG BOGDANOVA BB, Kraljevo 560313, Serbia

Corresponding author
Biljana Petrovic, PhD
Health Center Kraljevo, JUG BOGDANOVA BB, Kraljevo 560313, Serbia; Tel. +381648056169; E-mail: biljanapetrovic576@yahoo.com

Article information
Received: November 3rd, 2019; **Revised:** December 2nd, 2019; **Accepted:** December 11th, 2019; **Published:** December 31st, 2019

Cite this article
Petrovic B. The importance of enzyme substitution therapy in early pancreas exocrines of insufficiency. *Gastro Open J.* 2019; 4(1): 9-10. doi: 10.17140/GOJ-4-131

ABSTRACT

Introduction
Functional disorders of the digestive tract are a common occurrence in the doctor's office. In addition to functional dyspepsia, 35% of dyspepsia are unresolved dyspepsia, which are a symptom of the early stage of pancreatic exocrine insufficiency.

Aim
Based on clinical experience, we can suspect and detect chronic pancreatic insufficiency at an early stage, which is the aim of this paper.

Method
To demonstrate the efficacy of enzyme replacement therapy in the early stage of pancreatic exocrine insufficiency using the case report of the patient.

Results
Results confirms significance and effectiveness of creon as an enzyme replacement therapy in the treatment of malabsorption and maldigestion.

Conclusion
Creon (pancreatin) showed great effect in the treatment of dyspepsia and anorexia nervosa, body mass index (BMI) for 30 days increased from 15.9 to 17.4, which leads us to the conclusion that unrecognized chronic pancreatic insufficiency can be expected in long-term dyspepsia.

Keywords
Chronic pancreatic insufficiency; Enzyme; Body mass index (BMI); Digestive tract.

INTRODUCTION

Functional disorders of the digestive tract are a common occurrence in the doctor's office. In addition to functional dyspepsia, 35% of dyspepsia is unresolved dyspepsia, which is a symptom of the early stage of pancreatic exocrine insufficiency in the abdomen.[1] Maldigestion is usually followed by malnutrition. Every fourth patient with functional dyspepsia and epigastric pain have chronic panreatitis and malasbsorption-it has been reported in the literature. Also, dyspepsia is one of the most common diagnosis in doctors practice.[2] At the same time, early pancreatic insufficiency is not common diagnosis in general doctors practice. Based on clinical experience, we can suspect and detect chronic pancreatic insufficiency at an early stage, which is the aim of this paper.[3] To demonstrate the efficacy of enzyme replacement therapy in the early stage of pancreatic exocrine insufficiency.

CASE PRESENTATION

History

Female patient, 52-years-old, unemployed, unmarried, uneducated, poor socioeconomic status. In the region of the epigastrium, lack of appetite, weight loss, malaise, discomfort, negates other problems. Treated several times with gastroenterologists and psychiatrist, saw multiple times Ipp-pantoprazol (nolpase, controloc) and

© Copyright 2019 by Petrovic B. This is an open-access article distributed under Creative Commons Attribution 4.0 International License (CC BY 4.0), which allows to copy, redistribute, remix, transform, and reproduce in any medium or format, even commercially, provided the original work is properly cited.

antidepressant therapy. Helicobacter pylori negative, non-smoking, no alcohol addiction. She had financial, social and family problems.[4]

Family medical history: Negative for digestive organ diseases.

Present Status

The present status of patients' health was conscious, well-oriented, agitated, depressed, poorly nourished and furthermore indicated the impression of being in the midst of severe pain. During the treatment, the weight, height and BMI of the patient were 43 kg, 1.64 m and 15.9 respectively. After performing the tests of the heart and the lungs, the therapeutic reports and ECG test were found to be normal. The abdomen of the patient was palp (Palpable) soft, with little pain, and with painful sensitivity in the epigastrium. We performed echo of the abdomen and the result was normal. Laboratory test showed mild hypochromic anemia. Examination of stool for bacteria, parasites and fungi showed normal results. Test for a hidden blood in stool was negative which is said to be a normal result.

In this case, during the diagnosis of the patient K30 dyspepsia, F32 anorexia nervosa and sy depressivum were used. The therapy was given by Controloc 40 mg (pantoprazole), Kreon 25000 ij (pancreatin), Ksalol 0.5 mg (anxiolytic). The dosage of, Controloc 40mg (pantoprazole) was 2 times for first 7 days and then reduced for 1 time a day and dosage of Kreon 25000 ij (pancreatin), Ksalol 0.5 mg (anxiolytic), was carried out for 3 times per day for a month.

The patient was advised to maintain a healthy lifestyle, according to his current poor social conditions. Also, the Social Work Center was involved in solving social, financial and family problems.

Checkup After 30 days

Subjective: The patient was shown with less problems, no digestive problems, nervousness dominated (under control/has dominated/dominates?), insomnia, expresses concern for the ongoing problems. After treatment, the weight, height and BMI of the patient were 47 kg, 1.62 m and 17.4 which are improved greatly.

After the 30 days checkup the therapy was given by Kreon25000ij (pancreatin), Zoloft (antidepressant), Ksalol 0.5 mg (anxiolytic). The dosage of Kreon25000ij (pancreatin) was 3 times for another 5 months and dosage of Ksalol 0.5mg (anxiolytic), was carried out for 2 times per day for a month.

CONCLUSION

Creon (pancreatin) showed great effect in the treatment of dyspepsia and anorexia nervosa, BMI for 30 days increased from 15.9 to 17.4 -for a short time, which leads us to the conclusion that unrecognized chronic pancreatic insufficiency can be expected in long-term dyspepsia. Excellent effect on the general condition of the patient, including an increase in BMI, but in this case previous antidepressant therapy without enzyme replacement therapy did not give a satisfactory effect, which confirms-significance and effectiveness of creon (pancreatin) as an enzyme replacement therapy in the treatment of malabsorption and maldigestion as a symptoms of dyspepsia with pancreatic insufficiency.

In the family practice it could be useful conclusion to remember that in the case of chronic dyspepsia we may suggest to think to detect and treat chronic pancreatic insufficiency. It exist more common than we expect and this short report of the case in my practice was just an effort to demonstrate that we could treat problems better thinking for a place for a pancreatic insufficiency in dyspepsia.

REFERENCES

1. Summary of Product Characteristics. Creon® 25000. Data Health. Web site. https://data.health.gov.il/drugs/alonim/Creon_25000_dr__Pancreatin_300mg_1437031539160.pdf. Accessed November 2, 2019.

2. Demir K. Pancreatic dyspepsia: A place for pancreatic insufficiency in dyspepsia. *Eur J Surg Sci.* 2012; 3(1): 1-4.

3. Löhr JM, Hummel FM, Pirilis KT, Steinkamp G, Körner A, Henniges F. Properties of different pancreatin preparations used in pancreatic exocrine insufficiency. *Eur J Gastroenterol Hepatol.* 2009; 21(9): 1024-1031. doi: 10.1097/MEG.0b013e328328f414

4. Zigic D, Janosevic-Dotlic S, Ivankovic D, Pertot V, Konstantinovic D. *Methodology of Scientific Research.* Belgrade, Serbia: Department of General Medicine SLD, Department of General Medicine, Faculty of Medicine; 1992.