NSAIDs, Gut Microbiota, and IBD – An Athlete Case Report
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A paper submitted to the faculty of the University of North Carolina at Chapel Hill in partial fulfillment of the requirements for the degree of Master of Public Health in the Department of Nutrition

Chapel Hill

December, 7th, 2017

Approved by:

MPH Paper Advisor (signature & date)
Abstract: Gastrointestinal (GI) distress is becoming increasingly common amongst the general population. Dysfunction of the gastrointestinal tract can also impact athlete populations at higher rates possibly caused by repetitive motions, physical impact on the GI tract, decreased flow of blood to the digestive system, and use of non-steroidal anti-inflammatory drugs (NSAIDs). NSAIDs have been linked to the onset of inflammatory bowel disease (IBD) and the disruption of the gut microbiota, which can be protective against IBD. This case report is based on a professional American football athlete and his experience with the irritable bowel disease ulcerative colitis. The athlete used NSAIDs extensively for years due to sport-related pain and developed abdominal pain, bloody stools, diarrhea, and experienced sudden urges to have a bowel movement leading to an ulcerative colitis (UC) diagnosis. After undesirable treatment outcomes and significant weight loss he underwent a total proctocolectomy and ileal pouch anal anastomosis. A combination of probiotics and FODMAP guidelines were used to minimize UC-similar symptoms and pouchitis. The patient was able to maintain new weight and had no symptoms of IBD. While NSAIDs are considered safe medications, precautions should be taken in regards to gut health or alternatives employed to possibly help prevent IBD onset.

Key words: non-steroidal anti-inflammatory drugs, inflammatory bowel disease; ulcerative colitis; gut microbiota; probiotics

Introduction:

NSAIDs and IBD Etiology: Pain killers are the most common over-the-counter medications and are taken at high frequencies among the general population, even amongst kids. This is no different in the athlete population where soreness and pains from sport occur frequently. One
study found 75% of high school football athletes had used non-steroid anti-inflammatory drugs (NSAIDs) in the last 3 months, with 15% of athletes describing daily use; that’s one-in-seven players [8]. Even amongst professional athletes NSAID usage is high with 30-46% of athletes using the drugs before an important event [9]. Contact sport athletes are more likely to be injured, and more likely to be taking NSAIDs since athletes feel compelled to play through aches, pains, and minor injuries [7]. The idea that NSAIDs can enhance physical performance by alleviating pain and thwarting off fatigue is common amongst this population [9]. Labels on these medications advise against daily usage, which also warn of gastrointestinal (GI) side effects experienced by greater than 50% of users [10]. However, the serious negative side effects are not considered by most, especially younger populations [8].

Inflammatory bowel diseases (IBD) are characterized by chronic inflammation of the bowels in the form of ulcerative colitis (UC) or Crohn’s disease (CD). Genetics, the GI immune system, gut microbiome and microbiota, and environmental factors including the usage of NSAIDs have all been postulated at contributors to IBD. The resulting symptoms of IBD, sores in the digestive tract, frequent urge to defecate, abdominal and pelvic pain, bloody stools, diarrhea, are associated with a change in the GI barrier and the GI microbiota [4]. NSAIDs have been shown to disrupt both the GI barrier tight junctions and the microbiota [1,15,18]. When exposing a mouse model with colonic inflammation to NSAID treatment rapid development of colitis occurs [5].

NSAIDs have been mentioned as a contributor to the onset or flare-up of IBDs. There are a few theories as to the pathology of how NSAIDs could disrupt the gut. NSAIDs function in part by the inhibition of cyclooxygenase (COX)1 and COX2, reducing prostaglandin production [4,10]. A study used this exact inhibition mechanism to induce relapse of IBD [14]. NSAIDs also
increase TNF-α which has been associated with ulcerative colitis as well. Newer treatments for UC involve the inhibition of TNF-α [13].

While there is a suggested avoidance of these drugs for those with already diagnosed IBD, this does not help those who have yet to develop the disease. Furthermore, those who already have the disease continue to take NSAIDs due to the pain caused by the disease and NSAIDs being seen as “safe” pain killers [1]. By better understanding the role of NSAIDs’ impact on the gut and how those effects can be minimized other than by avoidance, prevention of the onset of IBD or subsequent episodes becomes more possible.

**NSAIDs, Microbiota, and IBD:** The gut microbiota is a heavy influencer of the GI immune system, having the ability to induce pro- and anti-inflammatory responses. The GI immune system helps regulate inflammatory responses to harmless stimuli such as food or host bacteria of the gut microbiota. GI epithelial and the microbiota communicate using receptors to help recognize friendly vs. harmful bacteria. Without this constant communication and updating of the GI immune system, the gut can lose immune tolerance, tolerance of harmless antigens, resulting in hypersensitivity. The hypersensitization of the gut can result in the chronic inflammation seen in IBD [1,17]. One theory, known as the Hygiene hypothesis, states that any disturbance in the balance between the microbiome and mucosal immune system will lead to GI barrier impairment. As mentioned previously, IBD is heavily associated with changes in the GI barrier and dysbiosis, or alteration of the gut microbiota [4,18]. Some probiotic strains, microorganisms ingested for the purpose of a health benefit, have modeled anti-inflammatory effects but the bacterial genetics must be very specific to the issues faced by the host [21].

NSAIDs have been shown to cause dysbiosis by an unknown mechanism. A study using mice monitored commensal microbiota changes after the administration of the NSAID
indomethacin. After the drug was given and changes in microbiota composition were measured, one group of mice was given antibiotics while another only water. The group given antibiotics had a higher mortality rate and suffered from more severe bowel damage. In a second experiment, mice were given fecal transplants either from control mice or from indomethacin-treated mice. The mice with transplants from indomethacin-treated mice had lesser injuries and decreased expression of pro-inflammatory cytokines such as TNF-α. Both results point to an adapted microbiota protective effect against NSAID-induced IBD [16].

**Case Relevance:** What is specifically interesting about this case is the environment under which the athlete possibly developed ulcerative colitis. He was admittedly taking large amounts of NSAIDs like many college athletes do, particularly in football, for years prior to disease diagnosis [7-10]. While it cannot be said that NSAIDs solely or outright caused the onset of disease in this particular case, they can certainly be implicated and have been associated to IBD onset in other studies by the mechanisms above [14].

The development of disease in this case stuck out for one reason - three of the athlete’s college teammates at the time consuming NSAIDs at the same rate also developed the disease along the same timeline as the subject of this case study, suggesting this specific mechanism of IBD development could be more common than previously thought [9]. To have such a widely consumed over-the-counter medication, often used incorrectly, causing serious health outcomes raises some questions about how we educate patients, what we ask them, and how we can prevent such behaviors from leading to GI distress. Upper GI disorders have been thoroughly investigated amongst athletes given the high prevalence of GERD in endurance athletes. Lower GI issues have been studied but usually in the context of the sport directly influencing the digestive tract through blood flow changes or physical forces [2,3]. In walking through this case
and discussing its pathogenesis and complications, hopefully new insight into prevention of NSAID-related IBD, treatment, and the potential role of probiotics can be made.

**Description of the case:**

The patient is a 29 year old Caucasian male professional football athlete. Presents at 6’3”, 236 pounds, with a body composition of 5.8% body fat.* Currently the athlete is post-total proctocolectomy and ileal pouch anal anastomosis (IPAA) in which his colon and rectum were removed and a new rectum was formed using the small intestine. The patient has no known genetic predisposition to the disease when looking at family history suggesting environmental factors may have played a larger role in disease development. Physical examination shows him to be otherwise healthy. The main concern of the athlete was to avoid pouchitis, inflammation of the pouch forming the new rectum. Symptoms for pouchitis are very similar to those of ulcerative colitis and occur in up to 50% of those with UC – frequent urge to defecate, increased true bowel frequency, abdominal pain, blood in stool, pelvic discomfort, and rectal bleeding [6]. In addition to pouchitis, the athlete was also concerned about absorption post-total colectomy since he was experiencing some abdominal pain and undigested food in his stool when eating certain foods as well as maintaining his weight and strength. He was very vocal about fears of certain foods which he avoided to prevent GI issues – spicy foods, gas-producing foods, raw vegetables. In addition to food avoidance, the athlete was taking psyllium husk before each meal and a probiotic once a day. Since the athlete was concerned about eating high-fiber foods that had previously caused him issue he substituted obtaining fiber from food with psyllium husk, a common fiber supplement for stool-bulking. Probiotics had been recommended by a previous dietitian to prevent inflammatory symptoms and pouchitis.
The athlete has been playing a high-impact sport for over ten years and has sustained several injuries including two ACL tears and one shoulder injury. Aside from injuries, American football is a high impact sport that causes athletes many pains, aches, and bruises regularly [7]. These aches and pains are often treated with self-administered NSAIDs by athletes [7-10]. The athlete described his use of NSAIDs as multiple times a day, almost every day, for a few years. The height of his NSAID usage was in alignment with the timeline of his injuries during college football. During this time, he also experienced abdominal pain, frequent bowel movements, diarrhea, blood in stool, and tenesmus. At the end of his college career the athlete was diagnosed with the IBD ulcerative colitis. He then entered the National Football League and was placed on corticosteroid therapy for treatment of UC. During this period, he said he did stop using NSAIDs stating he knew he could not have them under his condition, which often left him in pain. After years of steroid treatment with undesirable side effects, persistent UC symptoms, and significant weight loss the athlete spoke with his physicians and decided surgery was the next best course of action. The athlete underwent three separate surgeries in order to completely remove the colon and rectum and to then form a new rectum from the ileum. The athlete reached a low weight of 180 pounds post-op down from his usual 243 pounds over the course of months. After surgery recovery, he worked with a dietitian to regain weight bringing him back to 236 pounds through diet and supplements. Now being seen at 8 months post-op 3rd surgery.

The athlete was diagnosed with malabsorption related to proctocolectomy and (IPAA) as evidenced by undigested food in stool. The athlete is also considered to likely have dysbiosis, or an impaired microbiota due to ulcerative colitis and the recent surgeries disrupting gut absorption.
The environment of intervention should be pointed out. The athlete was at an athletic treatment facility all day long Monday-Friday. This allowed most meals, snacks, and supplements to be controlled and overseen by staff. As to not disturb the athlete’s nutritional routine, and considering probiotics had helped him heal in the past, under plan of care the athlete was given *Lactobacillus acidophilus* 3.6 billion and *Bifidobacterium bifidum* 3.6 billion as a probiotic once a day in the form of Athletic Greens®. Probiotics have been utilized in the treatment and relief of IBS and IBD, however, results are inconsistent [20]. In an animal model of colitis, pro-inflammatory cytokines were suppressed in the presence of *Lactobacillus* and *Bifidobacterium* [21]. In addition, these two types of bacteria have been shown to diminish growth of harmful bacteria found in rats with bowel ulcers [16]. The medical probiotic VSL3 has been proven to prevent chronic pouchitis and maintain remission. It contains eight strains of a blend of *Streptococcus, Bifidobacteria, and Lactobacillus* [12]. The brand of probiotic used in this case was a form in which the athlete was comfortable using; keep in mind he was very hesitant to change for fear of pouchitis or experiencing pain like at the height of his ulcerative colitis. In order to help ease fears about increasing his variety of intake low FODMAP guidelines were used to choose foods to slowly add back in to his diet. At the same time, he continued use of psyllium husk for comfort even though he could be getting the same fiber from foods at this stage of recovery. This was not started until the athlete’s second week at the facility and was increased over time adding 1-2 new foods each week that he was previously afraid of. In order to build trust and reduce hesitation there needed to be a mechanism in place for choosing new foods. FODMAP has been shown to reduce IBD symptoms and prolong remission including those who had had bowel surgery [22]. A low FODMAP diet can reduce irritation of a hypersensitive bowel by eliminating foods that are harder to digest or are common irritants.
High calorie, nutritious meals and snacks were given throughout the day to ensure he was meeting his needs and to prevent weight regression of the athlete since he was now training.

The patient was under the care of the facility for 5 weeks. In that time he was able to eat most anything from the menu without digestive issue. His reservations on what he could eat seemed to subside considering he expressed no problems with too frequent stooling, blood in stool, abdominal pain or undigested food in stool. His weight was mostly maintained, losing 4 pounds at the end of 5 weeks but maintaining most muscle mass with a BF% of 4.7. Since he is a professional athlete with high caloric needs his meal plan was set very high, but often the athlete said the volume of food was too much to finish. Under care he was exercising intensely 4 days a week, an increase from what he was doing previously which could have attributed to weight loss.

*Disclaimer – some patient characteristics that are not key to the case have been changed to ensure patient confidentiality

Discussion:

NSAIDs are generally safe medications, or at least thought of as such since they can be purchased over the counter [7]. Though they can offer short-term relief, using them frequently over long periods of time can be associated with serious health concerns including GI issues [10]. While the prescription and education of proper drug usage falls under the scope of physicians and pharmacists, dietitians must be prepared for the nutrition- and digestion-related consequences of patients who use these drugs. Presenting this case study and the evidence surrounding NSAIDs, gut microbiota, and IBD sheds light on prevention, not simply treatment, of IBD and what follows.
Probiotics and diet therapy were used to help prevent symptoms and the development of pouchitis post-IPAA. Treatment was guided by the concerns of the athlete and the nature of his job in an attempt to help him return to the same quality of life and athleticism prior to surgery. Literature supports the success of the treatments seen in this case when looking at the proposed mechanism of distress caused by NSAIDs and the role of gut microbiota in IBD. However, some success could have been partially attributed to overcoming mental food fears as opposed to physiological changes. While the athlete was seen after surgery that generally resolves ulcerative colitis, the disease often transforms leaving patients with similar symptoms seen in pouchitis or Crohn’s like symptoms elsewhere in the gut post-IPAA [6]. Considering the success he had with diet therapy changes, the athlete questioned himself as to whether the surgery was necessary in the first place. Teammates who followed the same timeline of disease were able to control IBD through diet therapy without resorting to extreme measures such as surgery. It’s possible there were other factors contributing to his severity of disease such as genetics. Though he has no known family history of disease and ulcerative colitis is less likely to be genetic than Crohn’s disease, extensive genetic testing could illuminate a predisposition to disease [11].

**Precautions for NSAIDs:** Well-known side effects including GI distress and GI bleeding suggest some precautions should be taken when a person is regularly using NSAIDs [1,8]. Patient guidelines when it comes to NSAIDs should be formed as a result of interdisciplinary work with dietitians and physicians talking about who is at risk – those who suffer from chronic pain, migraines, young athletes, etc. Considering the GI toxicity that NSAIDs can cause, better patient surveying to uncover NSAID usage habits and patient education on side effects could help with IBD prevention [4]. When performing initial assessments, medications are traditionally asked for as well as supplements. NSAIDs can be forgotten since they are generally self-administered as
needed. It is important for dietitians, or whoever is performing initial assessments, to probe further so this information isn’t missed and proper medical advisement on their usage and side effects can be provided [7,10].

**Alternatives to NSAIDs:** There are pain relief alternatives to NSAIDs that do not result in the same unnecessary GI distress. While NSAIDs work by inhibiting COX1 and COX2, COX2 selective inhibitors have been shown to result in less GI toxicity [4]. Non-NSAID acetaminophen does not inhibit COX1 or COX2 and does not result in IBD relapse [14]. Topical or transdermal ibuprofen has been shown to be comparable to the oral NSAID in pain relief [19]. On the nutrition side, curcumin, a naturally-occurring molecule in the spice turmeric, carries anti-inflammatory properties when taken as a concentrated supplement but does not produce negative GI side effects [25,26].

**Further Research:** Probiotics have been routinely used to treat or subside GI distress symptoms as seen in IBD. While success is sometimes seen, the specific mechanism by which they work and which strains work best for which conditions are still up for debate [20,21,25]. Probiotics, such as VSL3, have been proven to be effective in the prevention of pouchitis, whereas treatment for pouchitis is successful with antibiotics [6,12]. While positive effects of high-potency probiotics like VSL3 are seen in regards to disease management and prevention, 40-50% of patients still develop pouchitis after IPAA. Further research of such probiotics and their potential reach in health benefits for other conditions could help make their suggested usage more widespread and offer another method of treatment and prevention.
References:


