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Crohn's Disease and Omega 3: Can it decrease CRP?

A Literature Review

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Crohn's Disease and Omega 3: Can it decrease CRP?

A Literature Review

The Crohn's and Colitis foundation of America estimates that 70,000 Americans are diagnosed with inflammatory bowel disease (IBD) each year (2021). Crohn's disease is an inflammatory bowel disease characterized by periods of remission and exacerbation triggered by an increase in stress (Mackner et al., 2020). Patients can experience debilitating abdominal pain, diarrhea, fatigue, blood in the stool, and reduced appetite during an exacerbation period, all of which can lead to life-threatening complications (Mayo Clinic, 2020). In most cases, patients are diagnosed in their late teens or early adulthood years, and are prescribed anti-inflammatory drugs (Mayo Clinic, 2020). As there is no true cure for Crohn's disease, medications are never guaranteed to work and patients are often forced to undergo many therapies before finding the right regimen for their condition. Currently, in hospitals, there has not been any added intervention with daily supplements for these patients to assist in treating the inflammation. In controlled clinical trials, omega-3 fatty acid supplements have statistically shown promise as an anti-inflammatory agent to aid in Crohn's disease treatment (Natto et al., 2019).

Clinical Problem

At the onset of a flare-up, patients will only take their anti-inflammatory medication. To date, there have been few to no supplements used together with prescribed Crohn's disease medications. Omega-3 fatty acid supplements are known to have an anti-inflammatory effect, and may help reduce inflammation associated with Crohn's disease (Natto et al., 2019). The following question is posed based on the knowledge that this literature review will evaluate the amount of inflammation in Crohn's disease patients using the C-reactive protein (CRP) level. Is the use of a daily omega-3 fatty acid supplement, as evidenced by a lower CRP level, effective in

reducing or eliminating inflammation in hospitalized Crohn's disease patients? This question is examined in the subsequent sections.

PICO Question

Following the Population, Intervention, Comparison, Outcome PICO formatting, the following question is posed. In hospitalized patients diagnosed with Crohn's disease, does implementing a daily 3,000mg omega-3 fatty acid supplement upon admission, compared to treatment with prescribed anti-inflammatories alone, decrease CRP levels? Does the literature support or refute this intervention?

Search Terms

The databases used for this literature review are EBSCO and PubMed. Search terms used for this literature review were: Omega-3, Crohn's Disease, Omega 3 supplement, and Crohn's Disease stress. Database research was completed on June 3, 2021. Appendix A displays the Individual Evidence Summary for each resource. Appendix B displays the Overall Evidence Summation for each resource that was graded using the Johns Hopkins Nursing Evidence-Based Practice Model for Evidence Rating Scales.

Literature Review

When a patient is diagnosed with Crohn's disease, most patient education consists of instructing them to rest and take the prescribed Crohn's medications. The most common medications prescribed are corticosteroids, oral 5-aminosalicylates, immunosuppressant's, or biologics (Mayo Clinic, 2020). As these medications are long-term, the patient must remain compliant, even when they are feeling well. The discontinuation of certain medications, including those of the biologic drug class, can cause antibodies to develop in the body against that drug (University of Michigan, 2021). If this occurs, the medicine may no longer be

beneficial (University of Michigan, 2021). In addition to the potential for developing antibodies against the medications, the majority of these medications come with undesirable side effects. Aminosalicylates have a number of common side effects, including muscle or joint pain, flu-like symptoms, slight hair loss, sweating, acne, vomiting, and heartburn (Crohn's and Colitis Foundation of America, 2020).

As prescribed medication is typically the topic of discussion, and alternative approaches are rarely discussed, many patients are left unaware of other alternatives for reducing flare-ups. A group of researchers conducted a study for a journal entitled *Digestive Diseases and Sciences* to determine the effectiveness of a specific carbohydrate diet, and it proved to be a promising treatment option (Suskind et al., 2016). An anonymous survey containing 45 questions was sent to multiple websites for patients to respond with ease (Suskind et al., 2016). Over half of the 417 individuals who responded to the survey reported that they began the diet to avoid medication (Suskind et al., 2016). After a period of twelve months on the diet regimen, most individuals reported a significant decrease in symptoms of IBD (Suskind et al., 2016). In order to achieve the highest quality of life, all treatment options should be thoroughly explained to patients, such as the use of diet, acupuncture, or omega-3 supplements rather than the use of simply prescribed Crohn's medications alone.

Omega-3 fatty acids are an essential fat because the body cannot manufacture it on its own, so they must be consumed through food or supplements in order to survive (Cleveland Clinic, 2019). The anti-inflammatory properties of omega-3 fatty acid supplements are attributed to the fact that it decreases the production of inflammatory molecules, such as cytokines, leading to improved levels of inflammatory biomarkers (Natto et al., 2019). Studies have not yet been performed to determine whether omega-3 supplements are effective in helping patients with

Crohn's disease; however, studies have shown promise for its effect on other conditions. A recent study looked at patients with chronic kidney disease to determine whether omega-3 supplementation helped in "general characteristics, nutrition, renal disease markers, and inflammatory markers C-reactive protein, interleukin (IL)-6, IL-10, and tumor necrosis factor alpha (Valle Flores et al., 2020). The study found that patients taking omega-3 supplements for twelve weeks showed a significant decrease in CRP, IL-6, IL-10, and tumor necrosis factor levels (Valle Flores et al., 2020). However, the placebo-controlled group showed no significant difference in these measurements (Valle Flores et al., 2020).

Marine omega-3 supplementation was investigated in a meta-analysis to determine its effects on coronary heart disease, cardiovascular disease, and myocardial infarction risk (Hu et al., 2019). Marine omega-3 supplements were found to lower the risk of myocardial infarction, coronary heart disease, and cardiovascular disease, as well as reduce the risk of death from these conditions (Hu et al., 2019). Aside from omega-3 supplements, certain foods also contain omega-3 fatty acids. The three main types of omega-3 fatty acids are known as "alpha-linolenic acid, eicosapentaenoic acid, and docosahexaenoic acid" (NIH, 2021). The most abundant omega-3 fatty acid in western diets is alpha-linolenic, as it is found in flaxseed, canola, and soybean oils (Harvard University, 2019). Eicosapentaenoic acid and docosahexaenoic acid, on the other hand, can be found in seafood like shrimp or salmon (Harvard University, 2019; NIH, 2021).

In order to measure the effectiveness of these interventions, CRP levels should be monitored. Serum CRP is, "an acute-phase protein exclusively synthesized by the liver largely under transcriptional control of IL-6" (Coelho, 2009). CRP begins to secrete within four to six hours of an inflammatory stimulus being released by the body, and it can remain elevated for long periods of time in patients with chronic inflammatory diseases (Coelho, 2009). In a CRP

blood test, C-reactive protein levels are measures with a normal level of less than 10 mg/L and a level over 10mg/L indicating a high degree of inflammation in the body (Mayo Clinic, 2017). In inflammatory bowel disease, a CRP test is more closely associated with disease activity than a complete blood count alone (Chen et al., 2020).

Practice Recommendations

Upon the completion of this literature review, the following three practice recommendations have been identified. First, patients with Crohn's disease should have labs drawn upon admission to the hospital, specifically the CRP level needs to be monitored and compared to the patient's primary care CRP labs. While Crohn's disease cannot be diagnosed through a CRP blood test, it gives the health care providers a closer look at the degree of disease activity occurring in the patient. (Crohn's and Colitis Foundation of America, 2021). Initially, the patient's CRP may appear to be at a normal level, however, it can change within four to six hours of a stimulus making it an important value to closely monitor (Coelho, 2009). This test, while simple, can indicate how the patient is responding to the treatment allowing the provider to adjust the treatment plan as necessary.

Second, every patient over the age of 18 that is admitted with Crohn's disease should be started on a daily Omega-3 fatty acid supplement of 3,000mg, unless otherwise contraindicated, along with their prescribed Crohn's medications. Initially, when providing care to a patient with Crohn's disease, physicians will prescribe medications such as corticosteroids or immunosuppressants, without recommendation for omega-3 supplements (Mayo Clinic, 2020). According to a study performed by Calder, "studies in healthy human volunteers suggest that an intake of >2g EPA+DHA/day is required to affect inflammatory processes" (Calder, 2010, p.365). The high levels of stress associated with hospitalization can trigger a Crohn's disease

exacerbation, if the patient not already experiencing one. Adding a daily omega-3 supplement along with prescribed anti-inflammatory medication in these hospitalized patients with Crohn's disease can leading to a decrease in CRP and assist in treating the exacerbation.

Third, nurses can encourage foods high in Omega-3 such as flaxseed oil, canola oil, and salmon. In addition, patients should receive education regarding an anti-inflammatory diet such as a specific carbohydrate diet and avoiding a diet high in fiber (Suskind et al., 2016). Treating Crohn's disease involves a well-rounded approach by including every aspect of the individual's life. This can be done by, decreasing inflammatory foods, adding in foods high in omega-3, and using omega-3 supplements to, in combination, decrease the patient's CRP.

Conclusion

Over 70,000 people are diagnosed with Crohn's disease every year, which results in many painful symptoms and can end in life-threatening complications (Crohn's and Colitis Foundation of America, 2021; Mayo Clinic, 2020). Therefore, it is imperative that the healthcare system meets the needs of this population. Since, according to Mackner et al. (2020), stress is a trigger for inflammation, all patients with a history of IBD should undergo routine CRP testing upon admission. As a result of this literature review, it can be concluded that anti-inflammatory medications alone have been the standard treatment for Crohn's disease. Additionally, supplements have rarely been used in conjunction with prescribed Crohn's disease medications to date. Omega-3 fatty acids have been shown to lower inflammatory biomarkers in patients with conditions like chronic kidney disease and coronary heart disease (Hu et al., 2019; Natto, 2019; Valle Flores et al., 2020). Thus, suggesting that diets high in omega-3 supplements and supplements, along with prescribed Crohn's medications, may be beneficial in treating patients with Crohn's disease.

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Appendix A

Individual Evidence Summary

Databases Used: EBSCO; PubMed			Search Terms Used: Omega 3; Crohn's Disease; Omega 3 supplement; Crohn's Disease stress			Filters Used: Years 2016-2021 Peer-Reviewed Article	
Article #	Author(s)	Year	Evidence Type	Sample Size	Results Recommendations	Limitations	Strength & Quality
1	Natto, Yaghmoor, Alshaeri, Van Dyke	2019	Meta-Analysis of RCT	N/A	Omega-3 fatty acid supplements may be associated with improvements in inflammatory biomarkers and lipid profiles.	Researchers used 16 studies to analyze when 696 studies were found relating to the topic due to the exclusion criteria they identified.	Level I B
2	Mackner et al.	2020	Empirical & Quantitative	23	Pediatric patients with Crohn's Disease who report high levels of stress show greater disease activity in their intestinal microbiota than patients who report low stress levels.	Smaller sample size	Level II C
3	Chen, et al.	2020	Retrospective	876	In individuals with Inflammatory Bowel Disease, CRP and ALB are strongly correlated with disease activity.	The patients participating in the study are only from southeast China, may not represent larger population and it is a retrospective single-center study.	Level III B

Article #	Author(s)	Year	Evidence Type	Sample Size	Results Recommendations	Limitations	Strength & Quality
4	Valle Flores, et al.	2020	RCT	93	In patients with CKD it is essential to begin them on an omega-3 supplement. The results of the investigation showed a significant decrease in concentrations of inflammatory markers of the participants.	Cost effectiveness of the trial	Level I A
5	Suskind, et al.	2016	Survey	417	Dietary therapy, specifically specific carbohydrate diet (SCD) are promising in the treatment of Inflammatory Bowel Disease but further studies need to be performed.	The majority of internet sites the survey was sent to are SCD-specific so there was the likelihood of response bias.	Level II B
6	Hu, et al.	2019	Meta-analysis of RCT	127,477	Omega-3 supplementation is associated with a lower risk of MI, CHD, CVD, and death from CVD or CHD	Unable to perform a subgroup analysis and the analysis did not include small trials.	Level I A

Note: n/a= not applicable, RCT= randomized control trial, CRP= C-reactive protein, ALB= albumin, CKD= chronic kidney disease, MI= myocardial infarction, CHD= coronary heart disease, CVD=cardiovascular disease, SCD= specific carbohydrate diet

Appendix B

Overall Evidence Summation

Level of Evidence	# of Journal Articles	Summary of Findings	Overall Quality
I	3	Oral Omega-3 fatty acid supplements lead to a decrease in inflammatory markers in individuals with CKD on hemodialysis. It is essential that Omega-3 become regular protocol of diet for CKD. Marine Omega-3 supplementation leads to lower risk of MI, CHD, and CVD. High doses of marine omega-3 supplementation is needed to see these results. Omega-3 fatty acids lower triglycerides from reducing VLDL secretion. Omega-3 may affect insulin metabolism and lipids by reducing LDL synthesis, working on receptor activity in the liver, improving glucose tolerance, and increasing AMPK expression.	A
II	2	Pediatric patients with Crohn's Disease who report high levels of stress have greater amounts of disease activity in their intestinal microbiota. Microbiome difference between high and low stress patients is independent from prescribed medication use. A specific carbohydrate diet has shown decreased clinical symptoms of Crohn's disease and positive effects on laboratory values. Diet should be maintained long term for maximum effectiveness.	B
III	1	In individuals with Inflammatory Bowel Disease, the CRP and ALB ratio is strongly correlated with disease activity. The CRP/ALB ratio should be used over a CBC to determine disease activity in IBD patients.	B
IV	0	N/A	N/A
V	0	N/A	N/A

Note: CKD= chronic kidney disease, n/a= not applicable, IBD= inflammatory bowel disease, CRP= C-reactive protein, ALB= albumin, CBC= complete blood count, MI= myocardial infarction, CHD= coronary heart disease, CVD= cardiovascular disease, VLDL= very low-density lipoprotein, LDL= low density lipoprotein, AMPK= activated protein kinase