

ABSTRACT

Analysis of Irritable Bowel Syndrome and Fish Oil Supplements as a Potential Treatment

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Irritable Bowel Syndrome (IBS) is a gastrointestinal disorder of growing interest, both in the United States and globally. In this thesis, I discuss and analyze various aspects of IBS, including the symptomology, potential causes and risk factors, the diagnosing process, and clinical manifestations. Further discussion includes current treatment and management plans for IBS. Fish oil supplements are also another area of growing interest in the medical field, and discussions about relevant findings regarding fish oil that indicate that it may be beneficial to patients suffering from IBS will be included. Finally, recommendations include a study to test whether fish oil supplements could serve as a potential treatment for IBS.

ANALYSIS OF IRRITABLE BOWEL SYNDROME AND FISH OIL SUPPLEMENTS
AS A POTENTIAL TREATMENT

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TABLE OF CONTENTS

LIST OF FIGURES.....	iii
LIST OF TABLES.....	iv
ACKNOWLEDGMENTS.....	v
DEDICATION.....	vi
CHAPTER ONE: Introduction	1
CHAPTER TWO: Literature Review.....	9
CHAPTER THREE: Conclusion.....	20
BIBLIOGRAPHY.....	21

LIST OF FIGURES

Figure 1: Chromogranin A cells in control patients, IBS patients, plot of density.....	8
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LIST OF TABLES

Table 1: Comparison of general characteristics between two groups.....	4
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CHAPTER ONE

Introduction

The objective of this thesis is to analyze Irritable Bowel Syndrome (IBS), a multifaceted gastrointestinal disorder, and the potential effects of fish oil supplements in patients with IBS. This chapter will serve as an introduction to IBS, exploring the nature of the disorder, namely its symptomology, pathogenesis, and clinical manifestations.

Irritable bowel syndrome (IBS) is one of the most common gastrointestinal disorders in the United States (Sandler, 1990). It is estimated that 5-19% of men and 14-24% of women have IBS in the United States (Brandt, et al., 2009). 10-15% of the entire world population has been or will be diagnosed with IBS sometime during their life (Black, Manolakis, Di Palma, 2012). In the United States, about \$30 billion is estimated to be associated with IBS per year in both direct and indirect costs (Dean, Aguilar, Barghout, 2005). A study has reported that IBS has had a significant effect on society in terms of the workforce, as IBS patients showed a 20% loss in work productivity (Black, Manolakis, Di Palma, 2012).

IBS is a functional bowel disorder characterized by chronically recurring abdominal pain, discomfort, and altered bowel habits such as diarrhea, constipation, and general changes in stool consistency and frequency (Sandler, 1990). These occurrences are not readily explainable based on observing physiological or anatomical abnormalities. In population-based samples, only 25-50% of people who presented with typical IBS

symptoms seek medical care, although the symptoms are quite common (Mayer, 2008). Along with the physiological symptoms, psychological conditions are also common in patients who have IBS. These conditions include somatization, anxiety, and symptom-related fears (Whitehead, et al., 2003). An example of this would be a patient worrying about feeling extreme discomfort for the duration of the day if they do not completely empty their bowels in the morning.

Symptoms of IBS often date back to childhood, with childhood prevalence of IBS similar to that estimated in adult populations. Approximately 10% of adult patients develop symptoms similar to those of IBS after viral enteric or bacterial infections (Mayer, 2008). Usually patients with IBS begin having abdominal pain and gastrointestinal complaints that don't seem to have a specific cause. A good number of IBS patients just see their symptoms as part of their normal life and ignore them. Patients that are more likely to seek medical help for their IBS symptoms are those who already have conditions that they regularly see a clinician for, such as psychological disorders (El-Salhy, 2012).

IBS has a dynamic and multifaceted pathogenesis, and understanding this complex pathogenesis is key to the development of new treatments and management techniques for this disorder. Several factors play a role in the potential cause of IBS including but not limited to dietary practices, genetic disposition, heritability, and general environment (Mertz, 2003). The presence of a psychosocial factor such as severe stress at the time of infection is also a risk factor. It is clear from the aforementioned adult

prevalence statistics that females have a higher risk of development of post infectious IBS. Comparisons between IBS and psychological distress are often made, as both are predominant in women. Many clinicians view IBS as somewhat of a psychiatric disorder, a notion supported by various studies of IBS patients which indicated that IBS patients are not only more likely to be psychiatrically ill, but also more likely to have a history of abuse, whether sexual or physical (El-Salhy, 2012).

In a recent study of girls in middle school and high school, researchers found that there may be a link between IBS, worry, and stress (Song, S., et al., 2008). A questionnaire was used to survey 820 adolescent girls about dietary and lifestyle habits, such as amount and types of foods eaten, smoking and alcohol use, sleep patterns, and even socioeconomic status, all factors that can be used to evaluate stress and worry. The study authors reported that a significantly higher number of girls who averaged 6 hours of sleep or less, drank alcohol, and ate mostly fatty or salty foods were diagnosed with IBS than those who did not practice such habits. The group was divided into three cohorts based on stress score assessments. While 20.3% of the students in the severe stress group were diagnosed with IBS, a significantly smaller percentage of the mild stress group was diagnosed in comparison, only 6.3% as can be seen in Table 1 (Song, S., et al., 2008). Based on these findings, stress and worry are likely to be significant factors directly associated to the cause of IBS.

Another important risk factor that may be linked to the cause of IBS is heritability. Studies show that there is a correlation between being diagnosed with IBS

and having an immediate family member who has also been diagnosed. Statistics from a study in Olmsted County, USA showed that 33% of the IBS patients in the group had a family history of IBS (El-Salhy, 2012). There did not appear to be any links between spouses of those who had IBS.

Table 1: Comparison of general characteristics between two groups

Characteristics	Total No. (%)	With IBS No. (%)	Without IBS No. (%)	Chi-square	P value
Grade					
7th	148 (18.0)	8 (5.4)	140 (94.6)	20.20	< 0.001
8th	147 (17.9)	13 (8.8)	134 (91.2)		
9th	116 (14.1)	14 (12.1)	102 (87.9)		
10th	200 (24.4)	41 (20.5)	159 (79.5)		
11th	209 (25.5)	29 (13.9)	180 (86.1)		
BMI					
< 85th%	602 (91.8)	77 (12.8)	525 (87.2)	0.03	0.98
≥ 85th%, < 95th%	37 (5.6)	5 (13.5)	32 (86.5)		
≥ 95th%	17 (2.6)	2 (11.8)	15 (88.2)		
SES					
SES I	10 (1.5)	2 (20.0)	8 (80.0)	0.72	0.87
SES II	124 (18.3)	16 (12.9)	108 (87.1)		
SES III	434 (64.0)	51 (11.8)	383 (88.2)		
SES IV	110 (16.2)	13 (11.8)	97 (88.2)		
BEPSI-K					
Mild	318 (38.9)	20 (6.3)	298 (93.7)	32.28	< 0.001
Moderate	140 (17.1)	12 (8.6)	128 (91.4)		
Severe	360 (44.0)	73 (20.3)	287 (79.7)		

Study authors have also reported that there may be an association between diarrhea-predominant IBS and a functional polymorphism, that is the insertion or deletion of base pairs, in the *SERT* gene, while constipation-predominant IBS may be more closely associated with patients who have a long allele genotype of the *SERT* gene (El-Salhy, 2012). However these results are not conclusive and further research is needed in order to support this hypothesis.

One major area of research concerning IBS is the criteria that can be used to precisely diagnose the disorder (Thompson, 2006). Patients with IBS have been found to have similar psychological distress levels and health-related quality of life as Inflammatory Bowel Disorder (IBD) patients (Whitehead, et al., 2003). In the 1970s, scientists began to attempt developing a set of criteria for functional gastrointestinal disorders (FGID), particularly IBS. In 1991 the Rome I criteria was initiated, and improvements to these criteria led to the Rome II and finally to the more recent Rome III set in 2006 (Mikocka-Walus, A., et al., 2008). In order to meet the Rome II criteria, patients must have had at least 12 weeks of either consecutive or discontinuous abdominal pain or discomfort over a period of one year, accompanied with a combination of changes in stool frequency or consistency, and relief of pain after defecating. The revised Rome III diagnostic criteria is less stringent and requires only that patients have experienced recurrent abdominal pain or discomfort for no less than 3 days every month over the previous 3 months (Occhipinti, Smith, 2012), although still maintaining the Rome II criteria that these abdominal symptoms must be associated with a combination of changes in stool frequency or consistency, and relief of pain after defecating.

It has been reported that patients who meet the criteria for IBS usually present with symptoms for other FGID at the same time (Brandt, et al., 2009). Patients who present with more typical IBS symptoms do not usually require diagnostic testing. However patients who present with more alarming symptoms, also called red flags or warning signs such as rectal bleeding, fever, anemia, nocturnal symptoms, an age of over 50 years, weight loss, or have a family history of colon cancer are recommended for more

extensive testing. Scientist have debated the utility of diagnostic testing among such patients, as in one study where only 3% of patients with these alarm features accompanying their IBS symptoms presented with organic disease (Black, Manolakis, Di Palma, 2012).

Current clinical guidelines do not generally call for further testing beyond routine clinical procedures (Spiller, Campbell, 2006). Patients who have relatively stable symptoms without the aforementioned warning signs and meet the Rome criteria will have their history taken, a physical examination, and laboratory studies. Based on these procedures, patients are then classified into the subclasses of IBS. However, since the general symptoms of IBS are somewhat vague, the differential diagnosis allows for the possibility of other illnesses as well, such as colitis, celiac sprue, and atypical Crohn's disease (Mayer, 2008). The subclasses are namely constipation predominant IBS, diarrhea predominant IBS, and mixed bowel habits (Mertz, 2003).

While most doctors diagnose IBS solely based on the symptomology or Rome criteria and believe that this is sufficient, some gastroenterologists use a combination of Rome criteria and the red flags. Based on the nature of these symptoms, various tests may be used to eliminate the possibility of some of the more serious illnesses that have symptoms similar to those of IBS. Some of these tests include colonoscopies, ileocolonoscopies, and sigmoidoscopies (El-Salhy, 2012). In a study of 200 patients who met the Rome criteria, 139 presented with one or more red flag symptoms or warning signs. These patients were normally distributed between the various subclasses, with 38 mixed bowel habits patients, 105 diarrhea predominant IBS patients, and 57 constipation

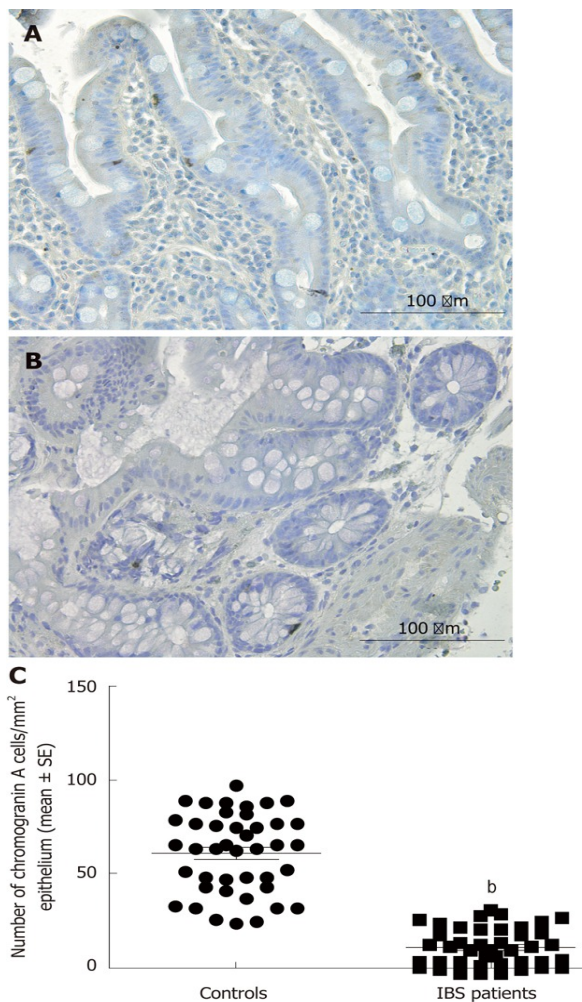
predominant IBS patients (Black, Manolakis, Di Palma, 2012). The study authors report that the majority of IBS patients have at least one red flag symptom. The study also indicates that diagnostic testing yields low results when carried out on patients exhibiting red flag symptoms. About 60-65% of the patients with alarm symptoms were given a colonoscopy, and less only about 10% of those tested showed abnormal results, such as adenomas (Black, Manolakis, Di Palma, 2012). These results support the general clinical practice of diagnosis from symptomology.

Radio-isotope markers used to measure gut transit are the biomarkers chiefly used to diagnose IBS (Yantiss, Odze, 2009). Various biomarkers were thought to be factors usable to diagnose IBS at one point, but only radio-isotope markers meet the requirements needed for the most efficient means of diagnosis, such as availability and reproducibility (El-Salhy, 2012). This does not mean that these tests are readily reproducible and available, only relatively so. Radio-isotope tests are still limited in availability and fairly pricey. Researchers continue to search for a more affordable and available way to diagnose IBS, and one such way may be testing chromogranin A (El-Salhy, 2012).

Chromogranin A is a general marker for endocrine cells. Findings from a study indicate that IBS patients experience a reduction in endocrine cells located in their small intestine and that chromogranin A-containing cell densities are lower in the duodenum of IBS patients compared to controlled patients, as depicted in Figure 1 below (El-Salhy, 2012). From this study, researchers propose that the measurement of duodenal

chromogranin A cell density could be a new histopathological marker utilized for the diagnosis of IBS. Additional research indicates that gastroscopy with duodenal biopsies could possibly be used to exclude some of the more serious illnesses rather the more expensive and difficult procedures and tests. Hence, if accurate, these biopsies would be doubly efficient in that they could be used not only to exclude serious diseases but to confirm the diagnosis of IBS.

Figure 1: Chromogranin A cells in control patients (A) and IBS patients (B) and plot of density in both groups (C)



CHAPTER TWO

Literature Review

Introduction

As is true of most illnesses and disorders, IBS has a variety of treatment and management plans. This chapter will serve to highlight treatments that have been studied in relation to IBS as well as common ways that this disorder can be managed. Further in the chapter will be an analysis of fish oil supplements and their effects, later applied specifically to IBS and why fish oil supplementation may be a source of treatment and management for patients with this disorder.

Management of IBS can take various forms for patients who suffer from the disorder, due to the different subtypes of IBS (Braden, et al., 2009). Hence a patient with constipation dominant IBS would take different steps to manage the disorder than a patient suffering from diarrhea dominant IBS or mixed symptoms. The health-related quality of life can vary greatly among IBS patients depending on the nature and severity of their symptoms (Mathew, Bhatia, 2009).

Health Related Quality of Life

Health-related quality of life is used to gauge symptomology in the lives of patients, as well as the effect of any treatments or therapies (Rey, Talley, 2009). In IBS patients, abdominal pain, bloating, and bowel difficulties are symptoms that have the most negative influence on quality of life (Mathew, Bhatia, 2009). Since overall

discomfort is a factor in measuring patients' quality of life, symptoms that have a negative impact on quality of life are those that decrease their confidence and make them feel the need to avoid social settings (Lembo, et al., 2009). Patients do not feel comfortable being in environments where they can't easily access a bathroom at all times, so many choose to remain at home. These symptoms affect their sleep patterns, work habits, and overall lifestyle (Hertig, et al., 2007). In addition to these inconveniences, IBS can also significantly affect the financial habits of patients, either through healthcare costs or hours lost at work. All these factors serve as sources of stress and anxiety in the lives of IBS patients, which further decrease their quality of life (Mathew, Bhatia, 2009).

Another reason for the lack of uniformity in IBS management is that a large percentage of IBS patients are either never diagnosed or they tolerate the symptoms of the disorder for several years before eventually seeking medical help and receiving an IBS diagnosis. Over 75% of IBS patients go undiagnosed in the United States alone, and out of the 25% who receive a diagnosis, about 33% of patients maintained their symptoms for over 10 years before being diagnosed (Yoon, et al., 2009). Several more experience their symptoms for over 2 years before obtaining a diagnosis (Yoon, et al., 2009).

Pharmacological Treatments

Pharmacological treatments for IBS are divided into the IBS subtypes because of the variety of symptoms that patients experience. These medications target certain

functions associated with gastrointestinal motility, therefore their effects are symptom specific (Braden, et al., 2009).

Many patients suffering from diarrhea dominant IBS also experience nausea and vomiting due to serotonin stimulation in the intestinal tract (Hertig, et al., 2007) which affects 5-HT₃ receptors (Braden, et al., 2009). The use of medications, such as alosetron and cilansetron, which antagonize these receptors helps to alleviate the nausea and vomiting that IBS patients experience (Krueger, et al., 2009). Loperamide is also an effective medication for diarrhea dominant IBS patients. It acts locally to reduce gastrointestinal spasms and motility (Krueger, et al., 2009). Codeine can also be used, acting in the same way to reduce abdominal pain (Rey, Talley, 2009).

For patients with constipation dominant IBS or mixed symptoms, laxatives can be prescribed to alleviate the symptoms as with non-IBS patients who suffer from constipation. Polyethylene glycol can be used to this effect, and similarly docusate, which acts as a stool softener (Lembo, et al., 2009). Prokinetic medications can also be prescribed, although the use of these drugs should be limited due to certain cardiovascular implications. Lubiprostone is a prokinetic drug that acts on chloride channels and aids in the increase of water secretion in the intestines, which decreases constipation (Krueger, et al., 2009).

The most common medications used to manage all subtypes of IBS are antispasmodics, such as cimetropium, hyoscine, and pinaverium (Braden, et al., 2009). These drugs act on cholinergic receptors to reduce gastrointestinal contractions and have

been reported to aid in the alleviation of IBS spasms that cause severe discomfort for IBS patients. Antispasmodics can be used with laxatives and prekinetics (Rey, Talley, 2009).

Alternative Treatment

Aside from the conventional pharmacological treatments for IBS, the majority of IBS patients choose to actively manage their symptoms rather than seek treatment for the disorder (Yoon, et al., 2009). This is largely based on the lack of a definite cure for IBS. Patients with IBS rely on a number of non-prescribed treatments and therapies, all under the scope of complementary and alternative medicine. One of these management techniques that almost all IBS patients utilize is dietary restriction and modification.

Dietary Modification

Diet management is the primary method used to control IBS symptoms, both by patients who have not been diagnosed and by clinicians (Mathew, Bhatia, 2009).

Patients often discover that certain foods greatly increase their discomfort and aggravate their symptoms, and they in turn find great relief from their symptoms when they cut these foods out of their diet. These results may be related to disturbances in GI motility and intestinal permeability (Krueger, et al., 2009). Eating habits can have a major influence on the severity of the symptoms that patients experience in a manner that can be compared to food allergies or intolerances, such as lactose intolerance.

Difficulties with lactose intolerance have been found to be more prevalent in IBS patients when compared to the general population (Lahmann, et al., 2010). Upon lactose intake, IBS patients tend to experience bloating, distention, and diarrhea, all in

connection to lactose malabsorption. This may be a result of the production of hydrogen gas which follows lactose ingestion (Lembo, et al., 2009). This gas release in the stomach causes distention which can be further aggravated due to the fermentation of the unabsorbed lactose by various intestinal bacteria, however most IBS patients tested negative for hydrogen breath tests, which are used to diagnose lactose intolerance (Yoon, et al., 2009). Nevertheless, IBS patients seem to experience some relief of their symptoms by decreasing their regular intake of lactose products or cutting these foods out of their diet completely, such as milk and cheese.

Study authors have reported that there may be a proportional relationship between fat intake and diarrhea in IBS patients, with fatty foods that patients incorporate into their diet being more likely to increase stool and aggravated diarrhea symptoms (Braden, et al., 2009). A similar connection has been made between certain carbohydrates and more severe symptoms (Lembo, et al., 2009). These carbohydrates are present in a number of packaged products, such as breakfast cereals, soft drinks, and baked goods. Researchers believe that items containing fructose, sorbitol, and even sugar-alcohols found in sugar-free products may not be efficiently absorbed in the intestines of patients and result in amplification of their typical IBS symptoms like discomfort, diarrhea, and flatulence (Rey, Talley, 2009).

Research also indicates that there is an inversely proportional relationship between IBS symptoms and the intake of fiber (Hertig, et al., 2007). This includes both natural fiber from fruits or vegetables and external fiber sources. Study authors found that when psyllium fiber was added to the diet of IBS patients, they experienced a

reduction in their uncomfortable symptoms (Lahmann, et al., 2010). It seems that patients classified under the subtype constipation dominant IBS experienced the greatest relief in symptoms, which correlates with the general practice of using fiber to regulate bowel movements (Rey, Talley, 2009).

Another factor that determined the extent of relief that patients experienced was the amount of soluble and insoluble fiber that the patients were given to add to their diet (Lembo, et al., 2009). Overall, general symptoms were seen to decrease with the addition of soluble fiber with less relief of symptoms when insoluble fiber was added to the diet. Yet, both forms of fiber were ineffective in relieving abdominal pain in patients. From these results, authors believe that additional soluble fiber should be recommended for patients with constipation dominant IBS (Rey, Talley, 2009). However these results cannot be rules as conclusive because of the relatively small sample size (Yoon, et al., 2009).

Probiotics

Probiotics are ingestible additives that has been found to have an effect on the health-related quality of life and symptoms that IBS patients experience (Lahmann, et al., 2010). Probiotics have been extensively researched in relation to IBS symptoms. The main species that are used in studies are Streptococcus, Lactobacillus, and Bifidobacterium strains. Several study authors using these bacteria reported less symptoms of bloating, bowel movements, flatulence, abdominal pain, and inflammatory cytokines (Rey, Talley, 2009).

Acupuncture

Another alternative source of management that has been studied in IBS patients is acupuncture (Braden, et al., 2009). Acupuncture has been known to affect various neurotransmitter systems in the body which lead to physiological changes (Lembo, et al., 2009). Hence acupuncture can be used to influence the processes of the cholinergic and serotonergic neurotransmission systems which play a role in the interactions between the brain and the digestive system. In a controlled study, 30 IBS patients were divided into two groups (Lembo, et al., 2009). One group received standard clinical treatment while the other group received routine acupuncture treatments. These respective treatments were continued for 3 months, and at the end of the time, patients who underwent the acupuncture reported a significant decrease in several of their symptoms and their overall quality of life. Study authors have demonstrated that a combination of acupuncture and moxibustion, which is a variation of the acupuncture technique, can be very effective at combating IBS symptoms (Yoon, et al., 2009).

Additional Alternative Therapies

Several other contemporary and alternative techniques have been reported to be effective at relieving IBS symptoms. Hypnotherapy could potentially increase the health-related quality of life in IBS patients, however research in this technique as an IBS treatment is limited and there is need for further study (Lembo, et al., 2009). Another technique that is of interest in relation to IBS management is relaxation. Relaxation techniques have been presented in positive correlation among some of the more

psychological factors relating to IBS such as stress and worry (Lahmann, et al., 2010). Since study authors have reported a connection between psychological distress and the onset of IBS, researchers believe that relaxation training may be beneficial to these patients (Yoon, et al., 2009). Various herbal therapies are also of interest in managing IBS.

Fish Oil

Research has indicated that along with these other contemporary and alternative treatments for IBS, fish oil supplements may also be an important source of managing and treating IBS.

Fish oil supplements are composed of fatty acids from fish, namely omega-3 polyunsaturated fatty acids (PUFA) (DeFilippis, Sperling, 2006). PUFA can be classified as omega-3 or omega-6 based on the locations of the double bonds in their chains (Wall, et al., 2010). PUFA play an essential role in all cell membranes, which makes them necessary for life since all living things are composed of cells. They also aid in the regulation of several important brain and blood processes, as well as inflammatory responses in the body through the production of inflammatory mediators called eicosanoids (DeFilippis, Sperling, 2006).

Linoleic acid, an omega-6 fatty acid, and alpha-linolenic acid, an omega-3 fatty acid, are two fatty acids that must be present in the human diet because the body cannot produce them on its own (Das, 2006). Unfortunately, the prevalent dietary habits in developed Western countries encourage the consumption of food products that are rich in

only linoleic acid (Kris-Etherton, et al., 2009). A largely unbalanced ratio of the intake of these two acids to each other leads to the production of eicosanoids derived from an omega-6 PUFA in the body which promote inflammation such as prostaglandin E2 and leukotriene B4 (DeFilippis, Sperling, 2006).

Fish oil supplements serve to correct this imbalance because they are rich in omega-3 fatty acids such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) which have anti-inflammatory properties and help to stop the production of omega-6 eicosanoids (Wall, et al., 2010). Marine fish such as salmon, trout, and herring contain a high EPA and DHA content, which can not only alleviate inflammation, but can help protect patients from developing further inflammation (Calder, 2006).

Omega-3 fatty acids from fish supplements can also regulate and control inflammation by altering the expression of inflammatory genes through their influence on various transcription factors (DeFilippis, Sperling, 2006). EPA and DHA can block transcription factors that coordinate inflammatory signaling pathways on cell membranes (Das, 2006).

There have been numerous studies carried out to test the effect of omega-3 fatty acids on patients with chronic inflammatory disorders, such as arthritis and inflammatory bowel disease (IBD), a disease which shares several similarities symptomatology-wise with IBS (Calder, 2006). Study authors report that the fatty acids were successful in decreasing the number of inflammatory cytokines and led to a net production of anti-inflammatory eicosanoids by suppressing the production of inflammatory eicosanoids (Kris-Etherton, et al., 2009).

Inflammation that remains unsuppressed plays a key role in several important diseases and disorders, for example cancer, heart disease, obesity, Alzheimer's disease, and even Crohn's disease (Das, 2006). In a study that lasted for a year, a group of Crohn's patients in remission were placed into two groups and regularly received either a placebo or a dose of omega-3 fatty acids in the form of fish oil (Wall, et al., 2010). At the end of the study, only 28% of the group who had been receiving fish oil supplements suffered a relapse, while 69% of patients in the placebo group relapsed, over twice as many (Wall, et al., 2010). In this same study, 26% of patients in the placebo group remained in remission, compared to the 59% of patients in the fish oil group who remained in remission.

Study authors have also reported that omega-3 fatty acids have other general health benefits for patients suffering from illnesses. Another study showed results that indicate that patients who are given omega-3 fatty acids after surgery have a shorter hospital stay because of the modulating effect that the fatty acids have on immune responses (Calder, 2006). Based on these numerous studies, researchers recommend that dietary intake of omega-3 fatty acids should be encouraged due to overall health benefits and effects (Wall, et al., 2010).

With these results and recommendations, it is reasonable to conclude that fish oil supplements could serve as a potential treatment and management option for patients with IBS by possibly alleviating discomfort, inflammatory symptoms, and increasing their health-related quality of life.

CHAPTER THREE

Conclusion

This chapter will serve as a proposal for a study to further investigate the effect of omega-3 fish oil supplements as a potential treatment for IBS based on the findings highlighted in the previous chapter. To date, few studies have been conducted that measure the effects of fish oil on IBS symptomology. Future research should attempt to see what attenuating effects may occur in IBS when supplementing their diet with fish, fish oil supplements, or both.

A reliable study to test the effects of omega-3 fish oil supplements in patients with IBS must meet several basic requirements. The sample size of the study should be large enough that conclusive results can be ascertained at the end of the study. This study group should be divided into at least two cohorts, with one cohort receiving a suitable placebo and the other receiving fish oil supplements.

If there are more than two groups, then one group should receive the placebo while the others receive various amounts of fish oils supplements. There should be an equal distribution of males and females participating in the study and distributed among the groups. It must also cover a suitable duration of time, no less than two months, in order to ascertain that the effects of the fish oil supplements are fairly consistent.

Patients should undergo a routine full physical exam, be tested for inflammation factors and evaluated for their health-related quality of life at the start of, conclusion of,

and at various time intervals during the study. Patients should also be asked to record all dietary intakes so that these records can be used to analyze the results of the study.

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