



Article title: Impact of Mycobacterium Avium subspecies Paratuberculosis (MAP) on Crohn's disease and Effective Nursing Care

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Topic: Nursing care of Crohn's disease regarding MAP

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**Impact of Mycobacterium Avium subspecies Paratuberculosis (MAP) on Crohn's disease and
Effective Nursing Care**

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Abstract

Crohn's disease is a chronic inflammatory disease and is also an autoimmune disease (CDC, 2021; Johns Hopkins Medicine; NIH; Hinkle & Cheever, 2017). However, recent studies have found that John's Disease (JD) occurring in animals is very similar to Crohn's Disease (CD) appearing in humans. The *Mycobacterium avium* subsp *Paratuberculosis* (MAP) bacteria that causes JD has drawn recent attention (McNees et al, 2015; Pierce, 2010). Many studies have revealed that MAP bacteria have been found in many Crohn's disease patients and it's suspected that MAP bacteria may be the main cause of Crohn's disease. Crohn's disease nursing strategies are emerging that consider MAP bacterial infection (Rosenfeld & Bressler, 2010; Crohn's MAP Vaccine; Momotani et al., 2012). A recent study notes that various immunosuppressant medication treatments present with documented significant adverse effects that include but are not limited to dependency on steroids and hypersensitivity (Alcedo et al., 2016; Hinkle & Cheever, 2017). In most cases, patients need surgical intervention, including various abdominal surgeries such as laparoscopic surgery (Alcedo et al., 2016). These surgical procedures require the patient high cost, time consuming for recovery, and change their lifestyle, especially when the CD recurs (Alcedo et al., 2016). This study explores nutrition, patient education for self-management, nursing interventions, and lab results in order to provide better nursing care for Crohn's disease patients with focus on MAP bacterial infection. This study looks at possible patient's nutritional limitations with the consideration of MAP bacterial infection with the evidence of lab indicators and nursing interventions including patient isolation, patient education for self-care and adherence to continuous medication, based on the immunosuppressants the patient receives.

Introduction

Crohn's disease is a chronic enteritis disease. However, Crohn's disease has been known as an autoimmune disease, and complications such as intestinal stenosis, intestinal fistula, and intestinal obstruction caused by the unnecessary inflammation of the attacking of normal cells due to excessive activity of immune cells (CDC, 2021; Johns Hopkins Medicine; NIH). This not only causes

inconvenience to patients because of the need for continuous medication and frequent hospital visits, but also burdens in terms of medical expenses paid throughout their lives (Mayo Clinic, 2020). However, recent studies have found that the symptoms of John's disease in many animals are very similar to Crohn's disease, and based on this, recent studies have begun to examine the relationship between MAP bacteria and Crohn's disease. The John's disease (JD) is a chronic bowel inflammatory disease that appeared among livestock, especially in cows and goats, and many researchers have found the cause of John's disease is MAP bacteria infection (McNees et al, 2015; Swift, 2019; Honap et al., 2020). There is a suspicion that Mycobacterium subspecies Paratuberculosis (MAP) can infect humans and cause Crohn's disease (McNees et al, 2015; Swift, 2019; Honap et al., 2020). MAP bacteria are mainly found in pigs and cows, and are known to be transmitted to humans through milk or unripe meat (Crohn's MAP Vaccine; University of Wisconsin - Madison/ School of Veterinary Medicine; Koets & Gröhn, 2015; Steuer et al., 2018; Zwirzitz et al., 2020). It has been known that MAP can tolerate temperatures (about 72-75°C) in the milk refining process, and it can be transmitted to humans (University of Wisconsin - Madison/ School of Veterinary Medicine; Koets & Gröhn, 2015; Steuer et al., 2018; Zwirzitz et al., 2020). In many normal environments including human, MAP bacteria are detected by immune cells and can be eradicated during digestion, but immune cells in Crohn's disease patients fail to detect MAP bacteria, resulting in an immune response by attacking normal bacteria and normal intestinal cells, which are not accurate targets (University of Wisconsin - Madison/ School of Veterinary Medicine). This study also explores Lab results indicating MAP bacterial infection in patients with Crohn's disease such as what kinds of leukocytes counts appear to be increased in patient's blood sample test and examines types of additional Nursing interventions that may be required during hospitalization, regarding nutritional supports based on different immunosuppressive medications that patients have been taking, consideration of isolation, MAP bacteria transmission control in hospital setting, and family education in home residential setting, regarding MAP bacteria transmission. When examining the pathways that allow transmission for MAP bacteria between humans, the consideration of an isolation room for an arrangement during hospitalization is raised as a

necessary intervention. In addition, nutrition management that would minimize additional inflammatory responses in patients with Crohn's disease is discussed.

Research Background History

Crohn's disease (CD) is an autoimmune disease (CDC, 2021; Hinkle & Cheever, 2017; Silverthorn et al., 2019). Human immune cells in CD patients cause inflammation by misrecognizing and attacking resident bacteria that coexist with humans, including pathogens, or attacking normal human cells (University of Wisconsin - Madison/ School of Veterinary Medicine; Hinkle & Cheever, 2017; Koets & Gröhn, 2015; Silverthorn et al., 2019). Along with the inflammatory reaction, high fever occurs, and inflammation in the area physically blocks the intestinal pathway, which harms the human body by interfering with normal physiological activity (U.S. Department of Health and Human Services; Hinkle & Cheever, 2017; Koets & Gröhn, 2015; Silverthorn et al., 2019). Many Crohn's disease patients often must use immunosuppressants for life or in severe cases, there is intestinal resection (McNees et al, 2015; Hinkle & Cheever, 2017; Koets & Gröhn, 2015; Silverthorn et al., 2019). Recently, through the discovery that the symptoms of John's disease and the disease mechanism of human Crohn's disease are very similar, it has led to the belief that MAP bacteria, the cause of John's disease, are suspected to be the key cause of Crohn's disease (McNees et al, 2015; Pierce, 2010; Swift, 2019). A recent study revealed that MAP bacteria were detected in Crohn's disease patients, and based on this fact, the development of new drugs for Crohn's disease began (Pierce, 2010). In one study, mice were tested and demonstrated that MAP bacteria and Crohn's disease were closely related (Momotani et al., 2012). In this study, the incidence of various inflammatory-related diseases and the treatment method of human Crohn's disease were evaluated using the "2,4,6-trinitrobenzene sulfonic acid (TNBS)–induced murine colitis model" (Momotani et al., 2012). As a result of the experiment, it was found that the inflammatory response of mice used as a Crohn's disease model was very similar to that of Crohn's disease (Momotani et al., 2012). Another study noted that the first line of treatment is anti inflammatory drugs such as prednisone or prednisolone and can be used at the same time with other immunosuppressants such TNF- α inhibitor;

infliximab (Remicade) and adalimumab (Humira) until those immunosuppressants reach therapeutic level in the body (Alcedo et al., 2016).

Method

A search of the pertinent literature was used to examine MAP effects on Crohn's Disease and the best practices for nursing care. Evidence-Based Practice (EBP) is the core application of nursing research findings into nursing practice. This study examines nursing interventions for Crohn's Disease (CD). By examining the latest research for CD and MAP, we look at the latest possibilities for nursing interventions for Crohn's Disease

Research questions

- What effect does isolation have on the transmittal of MAP in Crohn's Disease patients ?
- How do optimal nutrition plans minimize recurrence of CD symptoms, when taking into consideration MAP growth ?
- What lab indicators show MAP bacterial infection in CD patients ?
- How do immunosuppressant medications affect nutritional care in CD patients ?
- What is the optimal nursing intervention for MAP infected CD patients?

Review of the literature

MAP Bacterial transmission pathway

MAP bacteria are one cause of Crohn's disease and have recently been suspected as playing a major role. The MAP bacteria mainly inhabit the intestines of cows and pigs. The main route of MAP bacteria is through dairy intake, and remains through the process of purifying milk at temperature of 72–75°C (University of Wisconsin - Madison/ School of Veterinary Medicine; Crohn's MAP Vaccine;

Koets & Gröhn, 2015). In addition, although very little of the cow's excrement is dumped along streaming rivers, it still may infect through general drinking water (University of Wisconsin - Madison/ School of Veterinary Medicine; Crohn's MAP Vaccine; Koets & Gröhn, 2015). However, if infecting through drinking water, it is highly likely to occur in developing countries that lack water purification facilities. In addition, the bacteria are also noted in ripe beef and pork in the US (University of Wisconsin - Madison/ School of Veterinary Medicine; Crohn's MAP Vaccine). Infection occurs by using cow feces as manure to grow crops (University of Wisconsin - Madison/ School of Veterinary Medicine). MAP infection is hosted in animals and only a small number of people are infected by the bacteria from eating infected meats (University of Wisconsin - Madison/ School of Veterinary Medicine; Koets & Gröhn, 2015; Steuer et al., 2018; Zwirzitz et al., 2020). As a result, most of the meat and dairy products produced from dairy are infected with MAP (Koets & Gröhn, 2015). However, one study reported that only about 10% of populations develop chronic inflammatory diseases even if most populations are exposed to MAP (Koets & Gröhn, 2015).

Nutritional triggers of inflammation for CD

The fundamental purpose of treating Crohn's disease associated with MAP bacterial infection is to eradicate bacteria. However, Crohn's disease patients, who are already vulnerable to this bacterial infection, will have continued exposure if they choose a diet with this type of bacterial inflow (University of Wisconsin - Madison/ School of Veterinary Medicine; Crohn's MAP Vaccine). Typically, periodic intake of undercooked meat and milk, such as steak, is the most severe exposure to MAP bacteria infection. This worsens the Crohn's disease condition and/or increases the frequency of Crohn's disease symptoms in patients (University of Wisconsin - Madison/ School of Veterinary Medicine; Crohn's MAP Vaccine). In addition, many studies have shown that patients with Crohn's disease have lactose tolerance (Szilagyi et al., 2016; Solis-Moreira et al., 2021; Reinshagen et al., 2002; Eadala et al., 2011) . Therefore, patients with Crohn's disease are restricted (and or should be restricted) from consuming dairy products containing lactose. As dairy intake is restricted in Crohn's disease patients, the intake of important key

ingredients such as B12, iodine, and vitamin D contained in dairy products becomes restricted (Solis-Moreira et al., 2021). Therefore, it is important for Crohn's disease patients to have daily supplements of those key ingredients.

Immunosuppressant for CD - “drug mechanism & food interaction” related patient teaching

Corticosteroid/Glucocorticoid (Prednison/Prednisolon)

Corticosteroid for treating Inflammatory Bowel Disease (IBD) including CD is the first line of anti-inflammatory medication used in order to decrease inflammation (Puckett, 2022). Corticosteroid inhibits vasodilation which decreases emigration of leukocytes out of the blood vessels and also increases glucose level in the bloodstream (Coutinho & Chapman, 2011). Corticosteroid drugs are injected into the cytoplasm bound to the receptor, forming a hormone-receptor complex that enters the nucleus of the cell and interacts with DNA (Coutinho & Chapman, 2011; Puckett, 2022). And because of this interaction, certain proteins are synthesized (Coutinho & Chapman, 2011; Puckett, 2022). This steroid easily permeates the lipophilic cell membrane and binds to the glucocorticoid receptor in the cytoplasm and transitions into the cell nucleus to act on the nucleus's chromatin receptor. As a result, certain genes are activated, followed by the transcription of mRNA (Coutinho & Chapman, 2011; Puckett, 2022). Eventually, the synthesis of proteins increases, greatly changing the function of the cells, and the receptors do not differ between cells, but the resulting synthesis of proteins varies greatly from cell to cell, resulting in two unusual reactions depending on the cell (Coutinho & Chapman, 2011; Puckett, 2022; Akalestou et al., 2020). First, in transaction, the steroid binds to the glucocorticoid receptor and the cell substrate, so that the form of the receptor is activated by ligand binding (Coutinho & Chapman, 2011; Puckett, 2022; Akalestou et al., 2020). After the hormone binds to the receptor, the newly formed receptor-ligand complex binds to a glucocorticoid response element at the site that metastasizes into the cell nucleus and raises the target gene when regulating gene expression (Coutinho & Chapman, 2011; Puckett, 2022; Akalestou et al., 2020; Cruz-Topete & Cidlowski, 2014). As a result, activated hormone receptors interact with special transcriptional elements and have a "transpression" effect that prevents

transcription of target genes (Coutinho & Chapman, 2011; Puckett, 2022; Chourpiliadis, 2021).

Glucocorticoid can prevent transition of pro-inflammatory genes such as IL-4, IL-5, IL-8, chemokine, and cytokine that cause inflammation (Coutinho & Chapman, 2011; Puckett, 2022; Cruz-Topete & Cidlowski, 2014).

Weight gain is a significant predictor of side effects of the corticosteroids (Schipani et al., 2021; Wahl, 2016; Tresca, 2020). The corticosteroid causes weight gain through fluid retention from electrolyte imbalance, increasing appetite, and fat deposition (Tresca, 2020). Corticosteroids act as cortisol, which is attributed to increase aldosterone II and result in water retention by absorbing sodium and water (Ayari et al., 2014; Alan & Alan, 2017). Lipolysis in peripheral adipose tissue occur by elevated cortisol level via corticosteroids, which cause increased blood glucose level by breaking down fat and adipogenesis occurs at the same time in the central adipose tissue around intestines and central digestive organs (Ayari et al., 2014; Alan & Alan, 2017). Corticosteroids also inhibit the action of insulin, which increases appetite (Ayari et al., 2014; Alan & Alan, 2017; Tresca, 2020) by stimulating the liver to release glucose into the bloodstream (Alan & Alan, 2017; Tresca, 2020). The accumulation of adipose tissue in the intestines result in the mesenteric issue called “creep fat”, which is a distinguished characteristic of CD (Karaskova et al., 2021; Peyrin-Biroulet et al., 2007; Smith & Bénézech, 2020). The creep fat also introduces promotes the innate immune response by physical barrier through more induced bacterial translocation from gut to adipose tissue, which potentially increase the rate of inflammation (Karaskova et al., 2021; Peyrin-Biroulet et al., 2007; Smith & Bénézech, 2020).

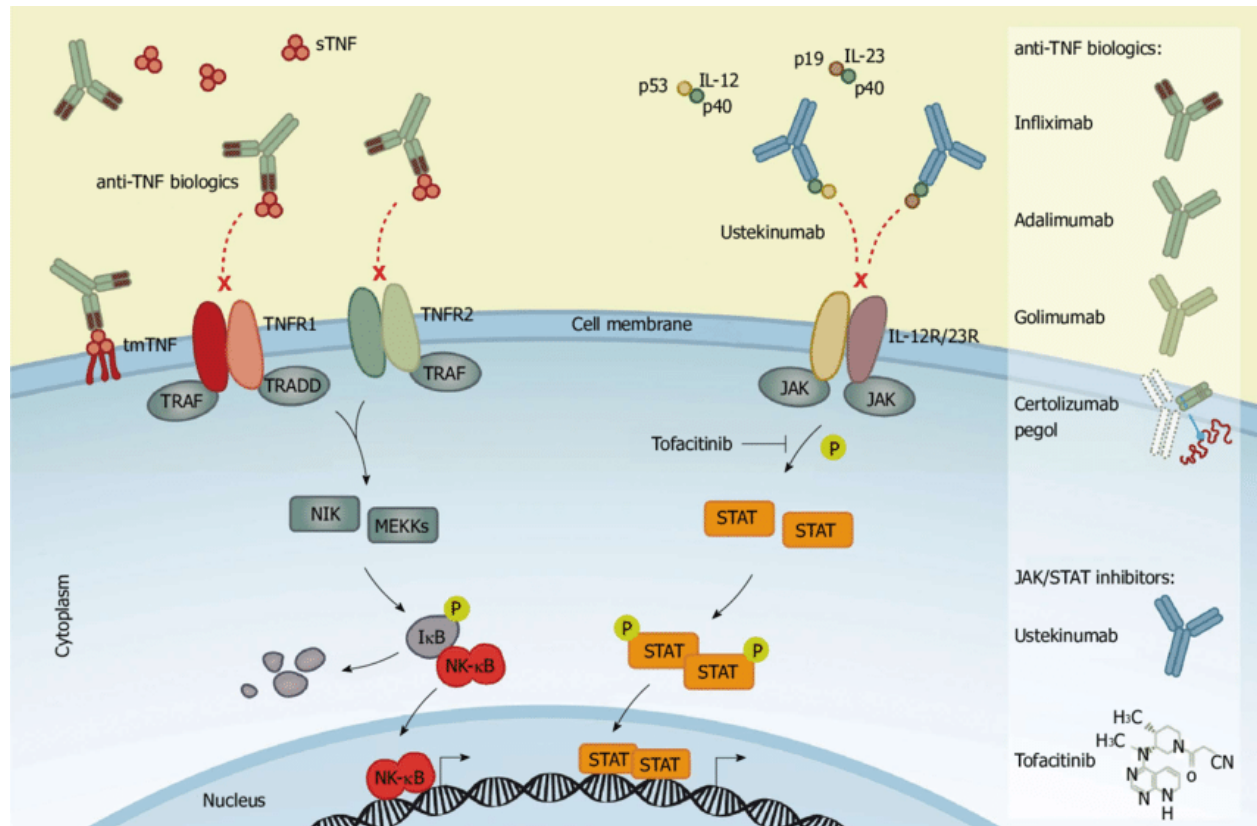
The nutritional support to manage health status under corticosteroid is crucial in nursing care with Crohn’s disease (CD) patients. A low fat diet is primarily offered to decrease glucose level in blood stream to prevent hyperglycemia issues such as diabetes and also to decrease adipose tissue deposition (e.g. creep fat) in the central digestive organ system (Schipani et al., 2021; Wahl, 2016; Tresca, 2020; Karaskova et al., 2021; Peyrin-Biroulet et al., 2007). Also a high protein diet is highly recommended to improve recovery from any scar tissue within the intestines (Schipani et al., 2021; Wahl, 2016; Tresca, 2020). Vitamin support is important to prevent blood clot formation at scar tissue sites with vitamin K and

recover less absorbed vitamins due to intestinal inflammation (Schipani et al., 2021; Wahl, 2016; Tresca, 2020).

Immunosuppressant

TNF- α blocker such as Certolizumab (Cimzia), Adalimumab (Humira), and Infliximab (Remicade) bind to either TNF- α molecule or its receptors to inhibit inflammation responses (Pedersen et al., 2014; Goel & Stephens, 2010; Creative Biolabs Recombinant Antibody). TNF- α molecule is a cytokine produced by macrophages or monocytes binds to the target cells' receptors in order to make inflammatory responses by vasodilation for other leukocytes to emigrate out of blood vessels (Pedersen et al., 2014; Goel & Stephens, 2010; Creative Biolabs Recombinant Antibody). According to some research, TNF- α contributes to the alteration of bone density by “Decreased physical activity, inflammation-related bone resorption, multiple intestinal resections, dietary malabsorption of minerals and vitamin D deficiency, genetic factors, gut-bone immune signaling interaction, steroid treatment, microbiota and pathogenic microorganisms interaction, and dietary malabsorption of minerals”, which leads to low bone density disease such as osteoporosis (Ali et al., 2009; Sgambato et al., 2019). So, research shows the “metabolic bone alteration” is at high risk of Inflammatory Bowel Disease (IBD) such as Crohn's Disease (Ali et al., 2009; Sgambato et al., 2019). A research result shows osteoporosis is the most common disease from IBD due to TNF- α (Ali et al., 2009). In the physiological aspect, the inflammation caused by TNF- α leads to malabsorption of calcium and vitamin D, which drives weak bone formation. Also, TNF- α acts as “key regulators of bone remodeling” by inducing differentiation of osteoclast, causing osteolysis (Ali et al., 2009). Therefore, TNF- α enhances absorption of calcium and vitamin D in the diet and regulates osteoclast to prevent osteoporosis. However, long term TNF- α inhibitor use potentially leads to liver damage or liver cancer (Rossi et al., 2014; Tran-Minh et al., 2017). Based on research, 30% IBD patients who have been taking anti-TNF- α medication are found to have abnormalities of the liver function tests (LFT) (Rossi et al., 2014; Tran-Minh et al., 2017). The effects on the liver from using

TNF- α inhibitor potentially leads to hepatotoxicity, hepatocyte proliferation, and liver regeneration with risk of infections and malignancies (Rossi et al., 2014; Tran-Minh et al., 2017).



<Figure 1. Mechanism of Anti-TNF- α ; (Pedersen et al., 2014) >

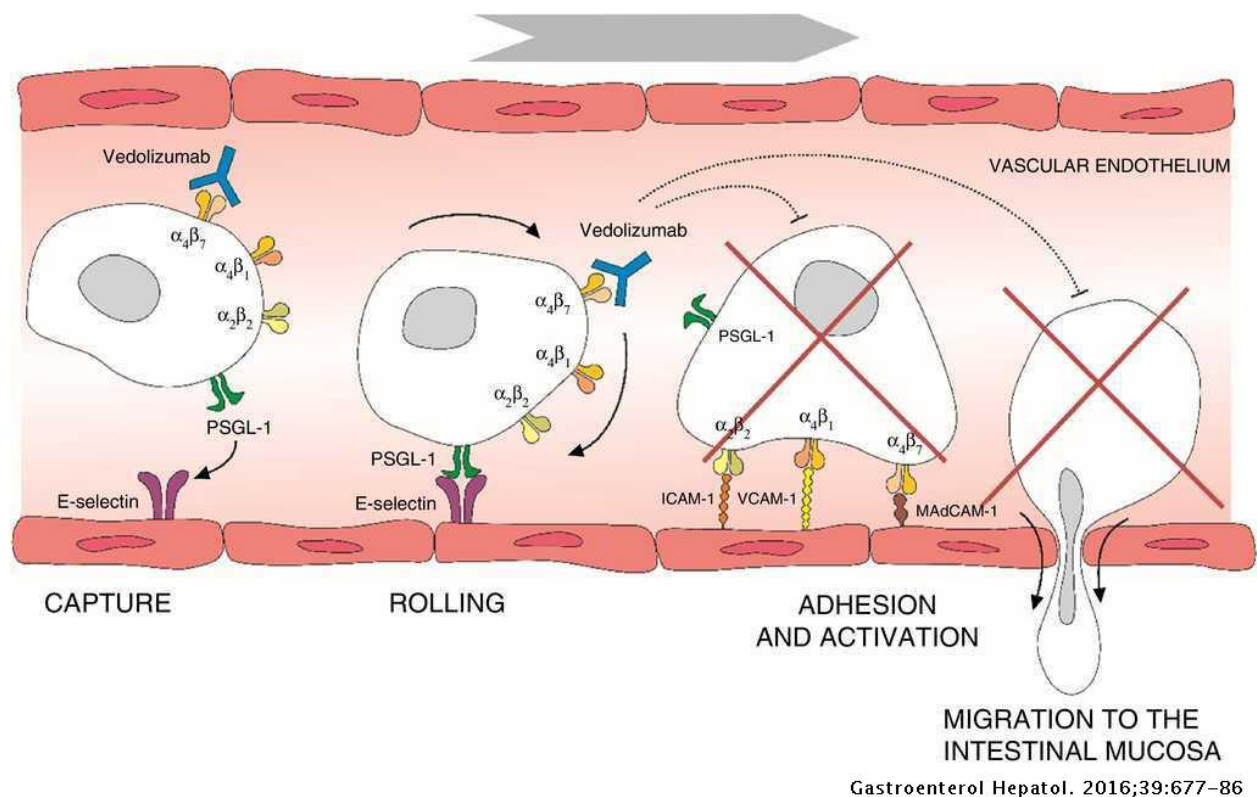
The diet of Crohn's disease patients while using anti-TNF- α therapy may be limited (Andersen et al., 2017; Reddavid et al., 2018). One study notes that typical calories and excess of some macronutrients in Western dietary patterns increase intestinal inflammation (Reddavid et al., 2018). In addition, immune nutrient consumption, which plays the role of trace elements such as vitamins A, C, E, and D, folic acid, beta-carotene, zinc, selenium, manganese, iron, etc., has emerged as a "new concept" that has the potential to control intestinal inflammation (Reddavid et al., 2018). One animal study found that when the development of colitis was observed in IL-10-deficient mice, a high-milk fat diet promote change in the bile acid composition in host's body, which leads to the changes in intestinal microbiota assembly

conditions (Andersen et al., 2017; Reddavid et al., 2018). It is said to cause a biological disorder that can disrupt immune homeostasis and cause colitis (Andersen et al., 2017; Devkota et al., 2012; Ejlsing-Duun et al., 2008). It was also found that vitamin D deficiency promotes diarrhea, as it has been confirmed that vitamin D inhibits the TNF- α pathway (Andersen et al., 2017; Cantorna et al., 2000 ;Zhu et al., 2005). Next, they found that a low dietary intake of fiber decreased the mucus layer and thus increased susceptibility to colitis (Andersen et al., 2017; Desai et al., 2016). Finally, it was found that a high-salt diet can promote colitis, as sodium chloride was found to induce TH17 cells characterized by upregulation of TNF- α (Andersen et al., 2017; Kleinewietfeld et al., 2013; Wu et al., 2013).

Vedolizumab (Entyvio)

Drug mechanism

Vedolizumab (Entyvio) is now considered the safest drug on the market (Domènech & Gisbert, 2016; Entyvio® (vedolizumab) official HCP Site). Unlike other immunosuppressants, Vedolizumab is a molecule that sticks directly to the immune cell to prevent the immune cell from migrating out of the blood vessel (Domènech & Gisbert, 2016; Luzentales-Simpson et al., 0001). As shown in [Figure 3], immune cells need to go through several steps to escape the blood vessels, and proteins on the surface of the immune cells must bind to a protein called Selectin on the endothelial cell of the blood vessel, which is called capture and rolling. After that, migration is carried out through Adhesion and Activation, in which Vedolizumab molecules attach to one of the adhesion proteins on the immune cell surface to inhibit the immune cell migration by preventing the binding of endothelial cells to activate immune cells (Domènech & Gisbert, 2016; Entyvio® (vedolizumab) official HCP Site; Luzentales-Simpson et al., 0001).



<Figure 2. Mechanism of Vedolizumab; (Domènech & Gisbert, 2016) >

Effect on Immunity to Crohn's Disease

The immunity of Crohn's disease involves a lot of neutrophils (Wéra et al., 2016; Zeissig et al., 2018). In one study, a large increase in the number of neutrophils was found around the intestine in the inflammatory region of Crohn's disease patients (Wéra et al., 2016). Therefore, this is more closely related to change in innate immunity than to adaptive immunity in patients with Crohn's disease (Wéra et al., 2016; Zeissig et al., 2018). Therefore, the effect of Vedolizumab is immunosuppressive on innate immunity in patients with Crohn's disease, but Entyvio (Vedolizumab) is not systemic, which means it does not affect whole body blood circulating neutrophils and the entire body immune system (Brewer, 2016; 2017). Since Entyvio (Vedolizumab) is not a systemic immunosuppressant, it is considered as a biologic therapy for both Crohn's disease (CD) and ulcerative colitis (UC) (Brewer, 2016; 2017; Zeissig

et al., 2018). Therefore, the Vedolizumab is currently considered as the most safe immunosuppressant in terms of immunity/inflammation control and infection (Brewer, 2016; 2017; Zeissig et al., 2018). However, the medication still has side effects in severe levels for liver problems such as tuberculosis, giardiasis, cytomegaloviral colitis, and listeria meningitis, sepsis, progressive multifocal leukoencephalopathy (PML), and allergic reaction (Brewer, 2016). Among these severe side effects of Entyvio, the most considered side effect is associated with liver problems, since it has the possibility of liver toxicity and injury (Kowsika et al., 2017; MediLexicon International; U.S. National Library of Medicine, 2020).

Liver toxicity & Injury

Vedolizumab has reported low rates of serum ALT elevations (lower than 2%) (National Library of Medicine, 2020). However, it still has potential adverse effects for severe hepatitis B without specific detailed reason by reporting 6.5% of CD patients got liver injury (Kowsika et al., 2017; National Library of Medicine, 2020). The theoretical approach for possible reason of liver toxicity by reactivation of hepatitis B is that the injury appeared to be an immunological response to newly expressed viral antigens, considering that immunosuppressive therapy typically occurs after discontinuation or between treatment processes (Kowsika et al., 2017; MediLexicon International; U.S. National Library of Medicine, 2020). Therefore, patients who already have liver problems are at high risk of further liver damage and worsening liver problems by the administration of Vedolizumab, so patients with HBsAg or anti-HBc in the serum should be careful to observe evidence of reactivation and screen HBV infection markers before treatment begins (MediLexicon International; U.S. National Library of Medicine, 2020).

Food interaction:

Currently, there have been no reports of interactions with any food related to vedolizumab, so there are no dietary restrictions (Westphalen, 2021). However, considering negative effects of alcohol on the liver and the potential side effects associated with vedolizumab on liver even if there is no direct

interaction with alcohol, the chronic alcohol consumption is likely to lead to high risk of Hepatitis B virus (HBV) infection and liver damage (Westphalen, 2021; Winn, 2014).

Conclusion (Answer the research question)

- What effect does isolation have on the transmittal of MAP in Crohn's Disease patients ?

MAP bacteria found to be the cause of Crohn's disease are parasitic during human digestion and cause inflammation due to immune responses (McNees et al, 2015; Pierce, 2010). Currently, the MAP infection route is transmitted in the process of processing the livestock product from livestock where MAP is mainly parasitic (University of Wisconsin - Madison/ School of Veterinary Medicine; Crohn's MAP Vaccine). In other words, the temperature used in refining dairy products such as milk processed from cattle has been shown to be tolerable and indeed MAP bacteria have been found in several processed foods (University of Wisconsin - Madison/ School of Veterinary Medicine; Crohn's MAP Vaccine; Koets & Gröhn, 2015). In addition, it has been revealed that bacteria and parasites on livestock such as cows infect humans through ingestion of undercooked meat (University of Wisconsin - Madison/ School of Veterinary Medicine; Crohn's MAP Vaccine; Koets & Gröhn, 2015). However, even if humans are exposed to MAP bacteria, only 10% of the population experience inflammation in the body (CDC, 2021; Johns Hopkins Medicine; NIH; Koets & Gröhn, 2015). Also, although it does not directly affect humans, many studies have shown, it is generally known that MAP bacteria have oral and fecal transmission, given that livestock are infected from the soil on feed and potentially by drinking water in which they are excreting their feces (CDC, 2021; Johns Hopkins Medicine; NIH; Koets & Gröhn, 2015). Therefore, when this process is applied to humans, it is assumed that bacterial infections can occur sufficiently through human feces. Therefore, patient isolation in hospitals can reduce the risk of potentially infecting other patients by using the same toilet. However, considering studies showing that exposure to MAP bacteria infects only 10% of the population, clean sterile toilets are required if patients share rooms and

toilets. In addition, families of Crohn's disease patients are tentatively more likely to have Crohn's disease easily due to exposure to MAP bacteria genetically. Therefore, it is necessary to educate families living with Crohn's disease to clean and sterilize the toilet that is shared.

- How do optimal nutrition plans minimize recurrence of CD symptoms, when taking into consideration MAP growth ?

Considering the inflow path of MAP bacteria, it is most desirable to inhibit the inflow of additional MAP bacteria by avoiding ripe meat and dairy products (University of Wisconsin - Madison/ School of Veterinary Medicine; Crohn's MAP Vaccine; Koets & Gröhn, 2015). MAP bacteria are parasitic mainly on livestock such as cattle and pigs (University of Wisconsin - Madison/ School of Veterinary Medicine; Crohn's MAP Vaccine). Therefore, when eating beef or pork, it is recommended to cook it in full to eliminate the possibility of MAP bacteria (University of Wisconsin - Madison/ School of Veterinary Medicine; Crohn's MAP Vaccine). There is no research on the possibility of MAP infection due to chicken consumption yet. However, given the possibility that MAP bacteria can be infected through cattle and pig feces, it can be inferred from previous studies that if the chickens is close to beef or pork livestock and if the chicken that eats insects that live on the land where cow and pig feces exist, it is also likely to be exposed to MAP bacteria (University of Wisconsin - Madison/ School of Veterinary Medicine; Crohn's MAP Vaccine). The exacerbation of Crohn's disease symptoms due to *C. difficile* infection, commonly known as the most common cause of food poisoning, has been found in many studies (Binion, 2012; Hsu et al., 2012; Nitzan et al., 2013; Zhang et al., 2016). In particular, Crohn's disease patients belong to a high-risk group to *C. difficile* infection (Binion, 2012; Hsu et al., 2012; Nitzan et al., 2013; Zhang et al., 2016). Crohn's disease patients are taking immunosuppressants, so *C. difficile* infection is fatal to Crohn's disease patients (Binion, 2012; Hsu et al., 2012; Nitzan et al., 2013; Zhang et al., 2016). Therefore, it is best to avoid spoiled food in terms of food intake (Nitzan et al., 2013; Zhang et al., 2016). In general, it is recommended to avoid high-fat foods for Crohn's disease patients because fat accumulation worsens Crohn's disease symptoms (Schipani et al., 2021; Wahl, 2016; Tresca,

2020; Karaskova et al., 2021; Peyrin-Biroulet et al., 2007). In particular, among patients with Crohn's disease, taking steroids increases their appetite, which can lead to a sharp increase in fat output due to excessive food intake (Ayari et al., 2014; Alan & Alan, 2017; Tresca, 2020). In addition, high protein intake is recommended to quickly heal intestinal wounds due to immune cell attacks and inflammatory reactions (Haskey & Gibson, 2017; Vidal-Lletjós et al., 2017).

- What lab indicators show MAP bacterial infection in CD patients ?

Crohn's disease with MAP bacterial infections has elevated levels of many lymphocytes, including the WBC count as common bacterial infections (Wéra et al., 2016; Zeissig et al., 2018). However, based on Crohn's disease studies, the most prominent feature was the high level of neutrophil in the inflammation area of Crohn's disease patients (Wéra et al., 2016; Zeissig et al., 2018). Therefore, as a characteristic of Crohn's disease, the overall elevated inflammatory level, WBC count, and lymphocytes, as well as the particularly high level of the neutrophile, are recorded (Wéra et al., 2016; Zeissig et al., 2018).

- How do immunosuppressant medications affect nutritional care in CD patients ?

The Nutritional Care effect of adalimumab and infliximab as anti-TNF is weight gain (Lutf & Hammoudeh, 2012; Tan et al., 2013; Patsalos et al., 2020; Lepp et al., 2020; Wiese et al., 2008; Hepatology, 2007). Many studies show weight gain and BMI gain for adalimumab and infliximab (Lutf & Hammoudeh, 2012; Tan et al., 2013; Patsalos et al., 2020; Lepp et al., 2020; Wiese et al., 2008; Hepatology, 2007). One study observed changes in weight gain over 12 months in 20 patients with Crohn's disease taking Adalimumab, and showed that more than 73% of the participants gained weight (Patsalos et al., 2020). In addition, in this study, 3.3% of the participants reported hair loss (Patsalos et al., 2020). In addition, another study reported that 60% of Crohn's disease patients in participants taking infliximab gained weight over 6 weeks (Lepp et al., 2020). As a cause of this weight gain, infliximab improve "inflammatory markers and disease activity" (Wiese et al., 2008; Hepatology, 2007).

Physiologically, there are no clear effects of adalimumab and infliximab on weight gain or on increasing or inhibiting certain nutritional intake (Lutf & Hammoudeh, 2012; Tan et al., 2013; Patsalos et al., 2020; Lepp et al., 2020; Wiese et al., 2008; Hepatology, 2007). However, the two drugs increase patients' appetite, leading to increased food intake (Lutf & Hammoudeh, 2012; Tan et al., 2013; Patsalos et al., 2020; Lepp et al., 2020; Wiese et al., 2008; Hepatology, 2007). Therefore, when taking these two drugs, appropriate diet management and systematic diet planning are needed in consideration of the possibility of weight gain.

- What is the optimal nursing intervention for MAP infected CD patients?

Currently, the most ideal nursing intervention is the prevention of Crohn's disease and the alleviation of symptoms in patients with Crohn's disease. Therefore, if anyone in the family is sensitive to colon-related cancer, colon-sensitive syndrome, Crohn's disease, and other intestinal diseases, taking the Crohn's vaccine as a precaution can prevent various symptoms caused by getting Crohn's disease and prevent financial spending on drugs for life (Crohn's MAP Vaccine; Johnston et al., 2010; Rostami-Nejad et al., 2020). Diet-related patient education is important for patients with Crohn's disease. Like beef and pork, it is safer to avoid livestock meat, but it is important to cook it fully when you eat it (University of Wisconsin - Madison/ School of Veterinary Medicine; Crohn's MAP Vaccine; Koets & Gröhn, 2015). Also, restricting dairy intake, such as milk, can prevent the possibility of additional MAP inflow and prevent additional Crohn's disease symptoms (University of Wisconsin - Madison/ School of Veterinary Medicine; Crohn's MAP Vaccine; Koets & Gröhn, 2015). In addition, it is safest to give Crohn's disease patients a solitary room, but it is also imperative to educate others and family members about cleaning and sterilizing the toilet when sharing with other people with Crohn's disease. If it is impossible to prepare a toilet that can be used separately by Crohn's disease patients, it is emphasized that family members should clean and sterilize the toilet whenever possible.

Discussion

As MAP bacteria have been discovered as one of the causes of Crohn's disease, MAP bacterial infection management is being considered as a major part of the Crohn's disease management methods . This bacterial infection limits the diet of Crohn's disease patients. The main purpose of these patients' diet is to minimize bacterial activity and additional bacterial infections. In addition, Crohn's disease symptoms are controlled by using anti-inflammatory inhibitors such as steroids and immunosuppressants.

This study has addressed patient care, nutrition management, and quality of patient education that can minimize Crohn's disease symptoms in consideration of bacterial infection by examining new causes of Crohn's disease through nursing research. As MAP bacterial infection is recognized and commonly viewed as a cause of Crohn's disease to improve the quality of nursing care. Also, this study contributes to the future nursing intervention improvement by suggesting diet changes considering MAP bacteria and current CD medications in order to prevent liver and kidney potential damage from corticosteroid and other immunosuppressant and arranging patients in a solitary room in order to minimize the bacterial transmission by using the same toilet with other non-infected patients. It is hoped that future studies will also focus on further mapping of the bacteria and look at the effectiveness of the nursing interventions based upon the new findings.

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