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CASE REPORT

Enteral nutrition with medium-chain triglyceride compared to total parenteral nutrition in patient with chylothorax: an evidence based case report

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Abstract

Introduction: Chylothorax is associated with longer length of stay, higher morbidity, mortality, and hospitalization cost. The main principle of chylothorax therapy is to reduce the chylous flow. The current nutritional management of patients with chylothorax are a low fat diet with long chain triglyceride (LCT) restriction, enteral nutrition with high medium chain triglyceride (MCT), and total parenteral nutrition. However, low fat diet with LCT restriction takes quite a long time (around 3 weeks) and requires close monitoring due to risk for malnutrition, essential fatty acid, and micronutrient deficiencies. The nutritional management determines the success of conservative therapy in chylothorax patients. The aim of this study was to determine whether a high MCT enteral diet is more superior than total parenteral nutrition regarding the resolution of chylothorax.

Method: Literature searching was conducted using advanced searching in three large databases: Pubmed, Science Direct, and ProQuest using eligibility criteria determined by the authors. Quality of evidences were assessed based on GRADE Guidelines. Level evidence was determined based on Oxford Center of Evidence-based Medicine (CEBM).

Result: Three systematic reviews and one cohort met the PICO and eligibility criteria that had been set. Two studies concluded that enteral nutrition was better than parenteral nutrition. One study concluded that parenteral nutrition could be considered first and one study could not conclude which kind of nutrition was better.

Conclusion: Administration of high MCT enteral nutrition can be the first line therapy in patients with chylothorax and still need close monitoring during the administration. One of the factors that need to be monitored is the daily production of chylothorax volume. The results shown by these studies are inconsistent and warrant further research of high-quality studies regarding the treatment of chylothorax.

Keywords: total parenteral nutrition, enteral nutrition, low fat diet, MCT, chylothora

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Case Scenario

Mr. A, 53 years old, has been admitted to the hospital with chief complaint of severe shortness of breath one day before admission. The patient was then using water seal drainage (WSD) and the initial production was 1200 mL in 24 hours-serous. Two days later, the color of the WSD became white like milk with daily production reaching 1500 mL per day. The laboratory results showed total cholesterol in the pleura was 76 mg/dL, pleural triglyceride was 713 mg/dL, total blood cholesterol was 179 mg/dL, and serum triglycerides were 161 mg/dL. Pleural fluid analysis showed positive rivalta test, count cell 3834 with PMN 1717 and MN 2117, protein ratio 0.61, LDH ratio 0.96, with the conclusion chylous effusion. The patient was diagnosed with chylothorax. The thoracic and cardiovascular surgeon then consulted to a clinical nutrition specialist regarding the diet for this patient with chylothorax. The doctor asked whether enteral nutrition with high MCT is better than total parenteral nutrition.

Introduction

Chylothorax is a condition where there is accumulation of chyle in the pleural cavity. Chyle is the milky bodily fluid formed in the lacteal system of the intestine. The etiology of chylothorax can be classified into traumatic and non-traumatic. Non-traumatic chylothorax can be caused by congenital, neoplasms (lymphoma, leukemia, lung cancer, or esophageal cancer), infection which is a complication of tuberculous lymphadenitis, and several other rare cases such as cattleman's disease, sarcoidosis, or Kaposi's sarcoma. Malignancy is the most common cause of non-traumatic chylothorax.[1] Traumatic chylothorax can be caused by postoperative, blunt, or sharp trauma. Postoperative chylothorax is the most common cause of chylothorax. Incidence of chylothorax ranges from 0.5 to 2%, but mortality rate is up to 50% due to nutritional deficiency, dehydration, and immunosuppression. It is also associated with a longer duration of hospitalization, higher morbidity and mortality rates, and higher hospitalization cost.[2]

The diagnosis of chylothorax can be obtained from the result of pleural fluid analysis, pleural triglycerides >110 mg/dL and total pleural cholesterol <200 mg/dL.[1,3] Management of chylothorax can be therapeutic or surgical. Surgical treatment is considered invasive meanwhile conservative treatment is effective especially for low flow-rate chylothorax (<800 mL/day).[4] One of the important factors in conservative therapy in patients with chylothorax is the nutritional management used.[5] The principal treatment of the chylothorax is to reduce the chyle outflow so that the leak resolves on its own. Consequently, the conventional management of the chylothorax is to put the patient in a fasting state. If the patient puts in fasting state for quite long time, this can lead into malnutrition. Therefore, studies are looking for the best option for nutrition in chylothorax. Current nutrition management strategies for chylothorax patients are long chain triglyceride restriction diet, high medium chain triglyceride enteral nutrition, and total parenteral nutrition. However, low fat diet with LCT restriction takes quite a long time (around 3 weeks) and requires close monitoring due to risk for malnutrition,

essential fatty acid, and micronutrient deficiencies. Long chain triglyceride restriction diet is highly unpalatable, hence lowering the adherence of the patients. Enteral formulas containing MCT can provide macronutrients and micronutrients needed. TPN contains provides nutrients through the veins, thus avoiding the absorption of LCT into the lymphatic through the intestine and in other hand still provide essential fatty acid needed. However, long term PN would weaken the intestinal function and lead to further complications.[2]

The most ideal nutritional strategy including the duration of nutritional administration is one of the components that determine the success of conservative therapy in patients with chylothorax. Considering the difficulty of dietary adherence, the risk of infectious malnutrition, and essential fatty acid deficiencies, the provision of nutrition

to patients with chylothorax must be given appropriately and efficiently.[2]

Clinical Question

P : Patients with chylothorax
I : High MCT enteral nutrition
C : Total parenteral nutrition
O : Resolution of chylothorax

Clinical question: Is a high MCT enteral diet compared to total parenteral nutrition better for resolution of chylothorax?

Methods

Literature searching was performed using combination of MeSH terms and Title/Abstract on three large databases: Pubmed, Science Direct, and ProQuest. Search was carried out on June 5, 2023. The keywords used were "total parenteral nutrition", "enteral nutrition", "MCT", "medium chain triglyceride", "chylothorax", "chyle leaks", "chylous leaks", "chylous thorax", "parenteral nutrition". Critical assessment tools and levels of evidence are based on the Oxford Center for Evidence-Based Medicine.

Eligibility criteria

Inclusion criteria including subjects between 18 to 65 years of age with chylothorax, study design was cohort, systematic review/meta-analysis, and one of the outcomes is the resolution of the chylothorax, published between year 2019 to 2023, and was written in English. Exclusion criteria including animal study and article not available in full text.

Results

The author found 164 articles in Pubmed, 357 articles in Proquest and 171 articles in Science Direct. Duplicate removal was performed using Zotero. The articles were assessed for eligibility criteria based on PICO, resulting in the selection of four articles as shown in **Figure 1**. There are three systematic review and one cohort that met the eligibility criteria. The study characteristics of these articles were listed in **Table 2**. The level of evidence for these articles is presented in **Table 3**, and all the articles were found to be relevant for answering the clinical question **(Table 4)**

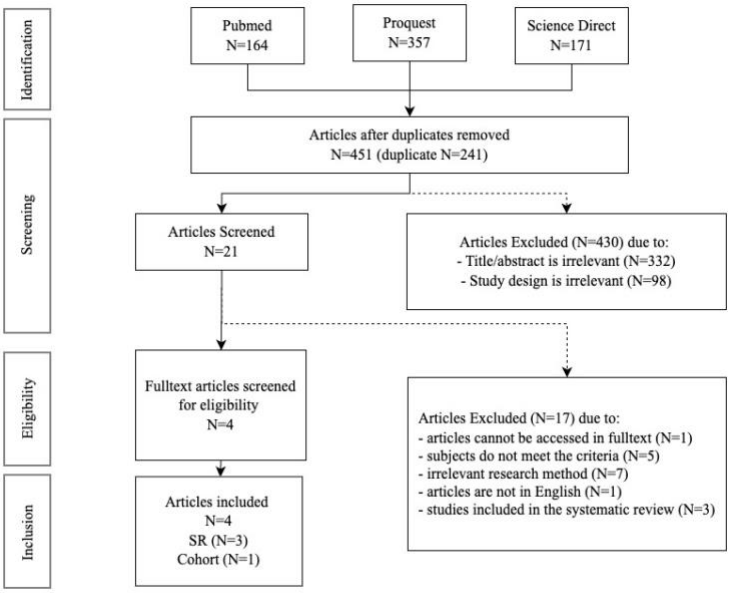

Figure 1. Prisma's flowchart

Table 1. Resources and search strategy

Database	Terminology	Hits	Eligible
Pubmed	("total parenteral nutrition" [MeSH Terms] OR "parenteral nutrition" [MeSH Terms] OR "enteral nutrition" [MeSH Terms] OR "MCT" [MeSH Terms] OR "medium chain triglyceride" [MeSH Terms]) AND ("chylothorax" [MeSH Terms] OR chyle leaks" [MeSH Terms] OR "chylothorax" [MeSH Terms])	164	1
Proquest	(total parenteral nutrition OR parenteral nutrition OR enteral nutrition OR MCT OR medium chain triglyceride) AND (chyle leaks OR chylothorax OR chylous leaks)	357	2
Science Direct	(total parenteral nutrition OR parenteral nutrition OR enteral nutrition OR MCT OR medium chain triglyceride) AND (chylothorax OR chyle leaks OR chylous thorax)	171	1

Table 2. Study characteristic

Author	Study Design	Population Characteristic	Total Participants	Outcome	Key Results
Power R, *et al*[7] (2021)	Systematic review	Postoperative patients with chylothorax	726 (N=16 studies)	Technical success rate, clinical success rate, resolution time after chyle leaks, complication from procedure	• 3 studies using enteral nutrition (EN) • 16 studies using parenteral nutrition (PN) • Clinical success rate of PN 11-100% • Clinical success rate of EN 38-83% • Resolution time using PN has median 5-35 days • Resolution time using EN has median 9 days.
Zheng J, et al[8] (2020)	Cohort Retrospective	Postoperative patients with chylothorax, got at least three days of nutritional management	38	Nutrition cost, treatment cost, time of resolution, duration of drain installation, length of stay, duration until surgery, duration from surgery to diagnosis of chylothorax.	• Enteral nutrition + MCT was significantly less expensive than total parenteral nutrition (p=0.00) • The cost of hospitalization in patients with enteral nutrition + MCT was significantly less expensive compared to total parenteral nutrition (p=0.001) • Resolution time for chylothorax in patients with enteral nutrition + MCT compared with total parenteral nutrition was not significantly different (p=0.260) • The duration until surgery in patients with

Author	Study Design	Population Characteristic	Total Participants	Outcome	Key Results
					enteral nutrition + MCT compared with total parenteral nutrition was not significantly different (p=0.654) • Duration from surgery to diagnosis of chylothorax in patients with enteral nutrition + MCT compared to total parenteral nutrition was significantly different (p=0.01)
Smith R, et al.[9] (2022)	Systematic Review	Postoperative patients with chylothorax	30 (N =10 studies)	Resolution of chylothorax	• 7 cases resolved after receiving non-nutritional or surgical treatment • 7 cases resolved after receiving TPN • 15 cases resolved after given MCT-based enteral diet • 1 case resolved after given low-fat diet • The average duration of TPN use was 3 weeks • The average duration of MCT enteral diet was 15 days.
Robinson AV,et al.[10] (2022)	Systematic review	Postoperative patients with chylothorax and undergo conservative therapy	838 (N= 21 studies)	Resolution of chylothorax	• Success rate using MCT as a nutritional intervention is 57.9% • Success rate using TPN as the main nutritional intervention 51.5%.

EN: Enteral Nutrition; MCT: Medium Chain Triglyceride; PN: Parenteral Nutrition, TPN: Total Parenteral Nutrition

Table 3. Validity criteria

	PICO	Review Strategy	Study Design	Study Quality Assessment	High Quality	Results in Tables/ Forest Plots	Similarity of Study Results	Quality of evidence*	Level of evidence**
Power R, *et al*[7]	+	+	+	+	-	+	+	Low	1
Zheng J, et al[8]	+	+	+	+	+	+	+	Low to Moderate	3
Smith R, et al. [9]	-	+	+	+	-	+	+	Low	1
Robinson AV, et al. [10]	+	+	+	+	+	+	+	Low to moderate	1

* Quality of evidence according to GRADE guidelines, https://www.ncbi.nlm.nih.gov/pubmed/21208779
**Level of evidence according to Oxford Center of Evidence-based Medicine (CEBM), http://www.cebm.net.
+ clearly mentioned in the article; - not done; ? Not stated clearly

Table 4. Relevance criteria

Authors	Similarity Population	Similarity determinant/intervention/indicators	Similarity Outcome
Power R, *et al*[7]	+	+	+
Zheng J, et al[8]	+	+	+
Smith R, et al. [9]	+	+	+
Robinson AV, et al. [10]	+	+	+

+ clearly mentioned in the article; - not done; ? not stated clearly

Discussion

There are four articles reviewed in this paper. Two of four articles reviewed stated enteral nutrition was better than parenteral nutrition. One study stated that parenteral nutrition can be considered first, and one study cannot conclude which nutrition was better.

Nutritional management plays an important role in chyle leak cases to maintain adequate caloric intake and minimize the volume of chyle passing through the thoracic duct, giving time for the lymphatic system to heal and close. There are several approaches to providing nutritional therapy in patients with chylothorax. Modifying a low-fat oral diet is one of the preferred options using a high protein and low fat (<10 grams of fat per day) diet. By reducing the amount of fat absorbed, it is hoped that there will be a decrease in chylous flow and in the accumulation of chylous in the pleural space. Patients are also advised to avoid consuming long-chain triglycerides (LCT). [11] However, low fat diet with LCT restriction takes quite a long time (around 3 weeks) and requires close monitoring due to risk for malnutrition, essential fatty acid, and micronutrient deficiencies.[6] Enteral nutrition can also be given as supplement for patients with chylothorax. High-MCT enteral nutrition will be transported directly through the liver to the portal vein without crossing the thoracic duct. Another option is total parenteral nutrition containing carbohydrate, protein, and fat. In total parenteral nutrition, no fat restriction is needed because the fat will be given intravenously.[11]

Systematic review from Power R et al.,[7] compared conservative therapy and surgery in patients with chyle leaks post esophagectomy. This study is the largest study that evaluates the therapy in cases of post-operative chyle leaks. The outcomes assessed in the study were success rate, clinical success, time required to resolve the chylous leak, and complications from the procedure. Sixteen out of 25 studies (726 patients) in the systematic review underwent conservative therapy.

Conservative therapy is by giving total parenteral nutrition and enteral diet modification. Twelve out of 16 studies undergoing conservative management provided total parenteral nutrition with success rates ranging from 11-100%. The rest of the studies used an enteral feeding approach with high MCT, with the percentage of success rate ranging from 38-83%. However, study from Power R et al.[7] did not conclude which type of nutrition was better.

A systematic review from Smith[9] assessed proper nutritional management in chyle leaks cases. The options were giving a low triglyceride diet with MCT supplementation, enteral feeding with MCT, or total parenteral nutrition. This study assessed 31 cases related to chyle leakage. Seven cases were resolved after the administration of total parenteral nutrition, 15 of them were resolved after the administration of enteral nutrition, one resolved after the administration of a low-fat diet, and the rest were by non-nutritional intervention.

Study from Smith[9] explained the discrepancy between the duration of the therapy from two types of nutrition administration. The average duration of total parenteral nutrition was three weeks, while using the enteral MCT diet was 15 days. The heterogeneity in this study was high; therefore, the meta-analysis cannot be carried out. Smith[9] concluded that nutritional management is the main therapy for chyle leaks. Reducing chylous production can be decreased by restricting fat intake and supplementation with MCTs. Oral intake can still be given in the

rehabilitation process. Based on this study, the administration of enteral nutrition with high MCT is still the mail and first choice in patients with chylothorax. However, this study acknowledges the need for more high-quality evidence regarding chylothorax.

A retrospective study from Zheng J et al.,[8] analyzed patients with chylothorax in 2014- 2018 at the West China Hospital of Sichuan University. The strength of this study is that the researchers included specific inclusion criteria for the nutritional intervention given. All patients must receive nutritional management for at least three days and if the patient receives total parenteral nutrition, it has to be given with total calories above 60% of daily needs, and oral nutrition must meet at least 400 kcal/day. Nutrition received by patients can be divided into four classifications: a group of those who received MCT enteral nutrition (MCT being the only source of lipids), patients on the MCT diet (low-fat diet cooked with oil sourced from MCT), MCT enteral nutrition and the MCT diet (enteral nutrition high MCT being the supplementation of the additional diet obtained), and total parenteral nutrition. This study compared the group receiving enteral nutrition with MCT (group E) and total parenteral nutrition (group T). It was found that there were significant differences in the aspect of nutritional costs and overall medical costs between the two groups. The group that received parenteral nutrition had a higher total cost than the other groups. Interestingly, there was no significant difference between the two groups regarding resolution time and length of hospital stay. Zheng et al., [8] recommend giving enteral nutrition with high MCT as the first line therapy before giving total parenteral nutrition considering the risk of giving total parenteral nutrition, such as venous infection and liver disorder, so enteral nutrition is considered safer and more natural.

A systematic review from Robinson[10]assessed 21 studies consisting of 814 chyle leak cases with different therapeutic approaches. One study by Weijs et al.,[12] showed a success rate of up to 65.6% in the population given a low-fat diet for seven days in patients with chyle leaks <500 mL/day. Meanwhile, the total parenteral nutrition approach was used in at least 378 cases (47.5% of the population).[12] Based on the review of these studies, treating chyle leaks is highly variable, and it is difficult to determine the most optimal therapeutic strategy. Three clinical trials in this study stated fat restriction is the last option, preferred in cases with a low volume of drain (<500 mL/day). Based on a study from Robinson[10], if the initial production is higher than 500 mL per day, total parenteral nutrition is preferred.

There is a limited available study in this systematic review. Of 21 studies obtained, 20 were with level II evidence, and only one was a clinical trial. However, the clinical trial needed to state the method of randomization and blinding used clearly. Therefore, the validity was doubtful. It should be considered that the decision to perform surgery or end the conservative therapy in most studies still uses clinical judgment. There are no benchmarks that determine the failure of conservative therapy.[10]

A systematic review from Steven and Carey[13] highlighted the role of nutrition in patients with chylothorax. This study concluded that the MCT diet had a success rate of 77.3% which was higher than total parenteral nutrition, which was 68.5%. The combined administration of the MCT diet and total parenteral nutrition had a slightly higher success rate, namely 77.6%. However, it cannot be concluded that total parenteral nutrition is more ineffective in patients with chylothorax because the population with the administration of total parenteral nutrition has a higher amount of drain production.

In determining the type of nutrition that should be given, the volume of chylothorax needs to be considered. The Esophagectomy Complications Consensus Group (ECCG) classification also classifies chyle leaks into three types and two severities. Type I only requires modification of enteral diet, type II requires total parenteral nutrition, and type III requires intervention or surgical therapy. Based on the severity level, level A is those with chyle production less than one liter per day, and level B is those with chyle production of more than one liter per day.**[14]** However, until now, there is no definite consensus on which

states the main therapy for each type and severity of chyle leaks.

One of the studies in the systematic review of Robinson[10], Weijs, et al.,[12]. explained that an enteral diet can be given if drain production is less than 500 mL per 24 hours, but if the production is 500-1000 mL per 24 hours, it is recommended to give total parenteral nutrition for at least seven days. Weijs, et al.,[12] shows that the production of chylothorax fluid also influences the decision to choose nutritional therapy.[8]

Based on the protocol from Smith[7], the chylous volume, whether it is less than or more than 1000 mL, will still be given the enteral nutrition with high MCT as the first-line treatment. Nevertheless, if the response afterward needs to be revised, the next step approach will be different. In a population with chylous production of less than 1000 mL per day and not reduced after administration of the MCT diet, it is recommended to combine with octreotide first, whereas in patients with daily production of more than 1000 mL per day and not responding to MCT diet, it is suggested to start parenteral nutrition.

Study characteristic from Zheng[8] shows that the volume of chylothorax in the study population ranges from 171.86 mL to 639.24 ml. This study cannot be classified as high-output chylothorax. Therefore, this might be why giving enteral or total parenteral nutrition in this study did not have a significant difference.

Assessment, analysis, and conclusion from these studies are difficult due to the lack of studies with high levels of evidence. Chylothorax is a rare event with high potential to cause complication, morbidity, and mortality.[13] The difficulties in conducting studies related to chylothorax are: (1) low incidence (0.3-2.3%), (2) the definition of chyle leaks and high output chylothorax are different in each center, (3) it is difficult to determine the timing of chylothorax occurred, and (4) rapid change of condition that requires modification of dynamic management.[4,7] These are the factors why studies related to chylothorax have low quality. All the SRs found cannot make a meta-analysis due to the heterogeneous study population.

Making conclusions from these studies has become more difficult due to various choices of therapy that have been given as a part of conservative therapy in patients with chylothorax. Therapies that have been given are ocreotide, ethylenephrine, and pleurodesis.[8,15] In addition, there are many variations of nutritional therapy, making it more difficult to make a protocol.[2]

Palatability and patient nutritional compliance are considerations that need to be made when carrying out low-fat or high MCT enteral diet. Studies shown that feed tolerance and palatability of low LCT diet is one of the main barrier to manage chylothorax.[2] Enteral formula containing MCT are easier to use, but patients may not accept the taste. It is usually used for tube-fed patients. However, other kinds of food can still be given, such as clear fluid, water, fruit juice, or drinks without milk. [11]

Since chylothorax is a rare case, we can use the Delphi approach to determine appropriate nutritional management in patients undergoing conservative therapy.[8] In this case, the patient was a 53-years-old male whose production of chylothorax was more than 1000 mL per day. The characteristics and diagnosis of the patient were similar to the population in the study. Enteral nutrition with high MCT can be given first, and if the volume production is not reduced, then total parenteral nutrition can be considered.

Conclusion

Low fat diet with LCT restriction takes quite a long time and has low adherence. Use of total parenteral nutrition or high MCT enteral nutrition in other hand are preferred in patients with chylothorax. Considering the risk of giving long-term TPN, high MCT enteral nutrition can be the first-line therapy in chylothorax patients. Close monitoring of chylothorax volume production is still needed.

Albeit the results shown from these studies are still inconsistent. There is still a lack of high-quality studies regarding the treatment of the chylothorax. The heterogeneity of the therapeutic regimens used and the variability of the treatment modalities make it more difficult to draw

conclusions regarding nutritional therapy for chylothorax. Since chylothorax is a rare case, future study can focus on using the Delphi approach to determine appropriate nutritional management in patients undergoing conservative therapy.

Conflict of interest

Authors declared no conflict of interest regarding this article.

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