COMPARISON OF ENTERAL AND PARENTERAL NUTRITION IN CANCER PATIENTS WITH DYSPNEA: EVIDENCE-BASED CASE REPORT

Ni Putu Menganti Harum Putrinata[1] Gurmeet Singh[2]

[1]Faculty of Medicine, Universitas Indonesia

[2]Pulmonology Division, Internal Medicine Department, Cipto Mangunkusumo National General Hospital, Faculty of Medicine, Universitas Indonesia

ABSTRACT

Background: The role of nutritional support for cancer patients in palliative care still become a controversial topic, because an ambiguity in choosing between enteral and parenteral treatment were still found in clinical practice, yet a comparison of effectiveness between enteral and parenteral nutrition in cancer patients with dyspnea still remain scarce.

Objective: The purpose of this evidence-based case report is to identify the effectiveness of enteral nutrition compared to parenteral nutrition in adult patients with cancer and dyspnea.

Methods: Literature searching were performed on Pubmed, Cochrane, and Google Scholar database to obtain RCT studies. Searches were made with keyword "enteral nutrition", "parenteral nutrition", "dyspnea" "cancer" and "dyspnea score". Selecting the studies were further based on exclusion and inclusion criteria by results, title, abstract, and full-text screening.

Result: Two studies were found to be relevant according to the criteria. These studies showed that enteral nutrition showed more effectiveness compared to parenteral nutrition in reducing dyspnea score. Study by Cotogni P et al showed enteral nutrition was more significant in giving lower Modified Borg Dyspnea Score [p =0.01], similarly to the results of study by Kao et al [p=0.05]. However, included study patients is different than patients in clinical practice settings. Therefore, there is a consideration regarding the applicability.

Conclusion: Based on two articles that have been reviewed, enteral nutrition has a positive effect on reducing Modified Borg Dyspnea Score in patients with cancer compared to parenteral nutrition.

Keywords: enteral nutrition, parenteral nutrition, dyspnea score, cancer

INTRODUCTION

Case Illustration

Mrs. S, a 46-year old woman, came to the ER due to complaints of shortness of breath since 1 week ago (BP 142/82 mmHg, RR 22x/min, HR 117x/min, SpO2 96, Temperature 36.6oC). Shortness of breath was felt both during rest and while performing daily activities. The patient felt a decrement in shortness of breath whenever she sits, and increases when in a lying position. An additional sound of wheezing was occasionally heard by the patient. The patient also felt chest pain, specifically in the middle area every time she inhales. Moreover, the patient had additional complaints of phlegm cough, in which she felt difficult to expel the phlegm since 5 months ago. The patient denied complaints of fever, sudden wake up at night, and swelling of the legs. She also denied any complaints of urination and defecation. The patient was found to have a lump in her left breast. The patient had the lump in her left breast since two years ago. Initially, the size of the lump was small, but soon it broke and pus oozed, so the patient was referred to the Oncology Surgery Department at Cipto Mangunkusumo Hospital 1 year ago. The patient underwent a biopsy, and came to a diagnosis of breast cancer. Further, the patient was then planned for a mastectomy. However, during the procedure preparation, the patient exacerbated shortness of

Address for correspondence :
Ni Putu Menganti Harum Putrinata
Faculty of Medicine, Universitas Indonesia
Email: ni.putu810@ui.ac.id
Number: +62 87731102000

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breath. The patient was consulted to the Pulmonology Department at Cipto Mangunkusumo Hospital and right pleural effusion was obtained during chest x-ray. Since then, the patient underwent pleural puncture, which was done twice. 950 mL of serous fluid was found during the first puncture, and the second with 1375 mL. The result of pleural effusion was suspected due to metastasis of the breast cancer. The patient's history of breast cancer and pleural effusion lead to the need of palliative treatment. Currently, the patient is subjected to conduct routine evaluation and palliative treatment, in which one of them involves enteral treatment for administering adequate nutrition and control in dyspnea. However, doctors question the comparison of using enteral and parenteral treatment to control dyspnea in breast cancer patients with pleural effusion.

Background

Dyspnea, also commonly known as breathlessness or air hunger, is a subjective experience of discomfort in breathing that consists of qualitatively distinct sensations and vary in intensity.[1,2] Dyspnea is one of the most frequent and distressing symptoms affecting patients with advanced cancer.[1-5] A meta-analysis study reported that more than 10,000 patients with advanced cancer, 10%-70% of patients developed dyspnea. Dyspnea typically increases in prevalence and intensity as patients approach the last weeks to days of life. In a longitudinal observational study of patients with cancer, dyspnea was consistently ranked as the most dreaded symptom.[1,2] Cancer patients may experience dyspnea or shortness of breath as a result of various factors such as metastasis to the lungs, chemotherapy, or radiation therapy. The burden effects of dyspnea in cancer patients are further compounded by other related symptoms such as malnutrition, fatigue, anxiety, and depression, resulting in functional limitation and compromised quality of life. The presence of dyspnea in late-stage cancer, particularly at rest, indicates a poor prognosis and has important clinical implications. Hence, a patient's prognosis could significantly affect recommendations regarding treatments and managements. It is required for clinicians to ensure prognostic understanding, discuss how dyspnea should be managed by providing cancer treatments and palliative options, and support advance care planning.[1-3] Dyspnea significantly affects the quality of life of cancer patients, and therefore, it is essential to manage this symptom adequately.[3,4] One of the possible treatment options for dyspnea is enteral or parenteral nutrition. Enteral nutrition involves administering medication or nutrients through the gastrointestinal tract, while parenteral nutrition involves delivery through an intravenous route. Enteral nutrition may be preferred as it is generally considered safer, less invasive, and less expensive compared to parenteral treatment. However, parenteral nutrition may be more effective in cases where the gastrointestinal tract is compromised due to cancer or treatment side effects.[1-7] The role of nutritional support for cancer patients in palliative care still become a controversial topic, because an ambiguity in choosing between enteral and parenteral nutrition were still found in clinical practice, yet a comparison of effectiveness between enteral and parenteral nutrition in cancer patients with dyspnea still remain scarce.[3-6,8] Moreover, tailoring the type of nutritional intervention to patients with advanced cancer may be beneficial. Hence, the purpose of this case report is to identify the effectiveness of enteral nutrition compared to parenteral nutrition in adult patients with cancer and dyspnea.[7]

Clinical Question

In adult patients with cancer and dyspnea, how effective is enteral nutrition compared to parenteral nutrition?

METHODS

Search Strategy

We conducted our search in three major databases: PubMed, Cochrane, and Embase. The key terms used included "enteral nutrition", "parenteral nutrition", "dyspnea", "breast cancer" up to 26th June 2023. **Table 2** shows the results of the search based on the key terms used. Suitable advanced search techniques, including MeSH Terms, were applied whenever appropriate. The literature search was limited by the English or Bahasa Indonesia language. Availability of full-text articles was also one of the limitations.

Table 2 Article Search Strategy

Database	Search Strategy	Hits	Selected Article
PubMed	("breast neoplasms"[MeSH Terms] OR ("breast"[All Fields] AND "neoplasms"[All Fields]) OR "breast neoplasms"[All Fields] OR ("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields]) AND ("enteral"[All Fields] OR "enterally"[All Fields]) AND ("parenteral nutrition"[MeSH Terms] OR ("parenteral"[All Fields] AND "nutrition"[All Fields]) OR "parenteral nutrition"[All Fields] OR "parenteral"[All Fields] OR "parenterally"[All Fields] OR "parenterals"[All Fields])	20	1
Cochrane	("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields] AND ("enteral"[All Fields]) AND ("parenteral nutrition"[MeSH Terms])	10	1
Google Scholar	("breast"[All Fields] AND "cancer"[All Fields]) OR "breast cancer"[All Fields] AND ("enteral"[All Fields]) AND ("parenteral nutrition"[All Fields])	17	0

Eligibility Criteria

Inclusion Criteria

- Adult patients (age > 18 years) having breast cancer with dyspnea
- Studies that compare enteral and parenteral nutrition
- Studies that used dyspnea score as the reference outcome

Exclusion Criteria

- Full text not available
- Unmatched PICO
- Studies using other language than English and Indonesian

Critical Appraisal Tool and Level of Evidence

Critical appraisal tool: Oxford CEBM Critical Appraisal on Randomised Controlled Trial (RCT)

Level of Evidence: Randomised Controlled Trial (Level 2)

Article Selection

A total of 47 articles were found after searching through the three databases. Among the articles found, 13 was screened based on the abstract after excluding 23 duplications and 11 title exclusions. We then conducted full-text assessments for 9 articles. Three articles were not retrieved due to the full-text unavailability. Furthermore, 4 records were excluded due to the unsuitable outcome analysis, leaving 2 final articles to be used in this case report. **Figure 1** further pictures the literature searching process.

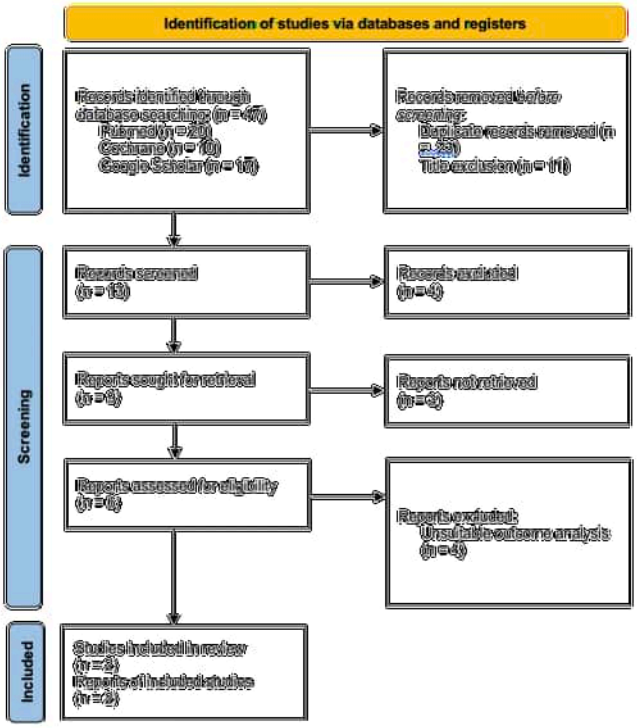

Figure 1. Search Strategy Flow

RESULTS

Study Characteristics

In general, this review included a total of 301 subjects. All studies were randomized controlled trials. Each study compared enteral and parenteral nutrition. The outcome of dyspnea improvement was assessed through a subjective self-report measurement that reported patient's difficulty in breathing, named Modified Borg Dyspnea Scale. Interventions were then assessed from a scoring of 0 to 10, where 0 represents no dyspnea and 10 represents maximal dyspnea.5 Further information of the characteristics can be found in **Table 3**.

Critical Appraisal

In this evidence-based case report, the author assesses selected studies using a critical appraisal tool named Oxford Center for Evidence-Based Medical on Randomised Controlled Trial (RCT).

Table 3. Study Characteristics

Author (Year)	Study Design	Population	Intervention	Comparison	Outcome
Cotogni P et al (2016)	Randomized, double-masked, randomized, placebo- controlled trial	50 adult palliative patients (60-80 years) with breast cancer and dyspnea recruited within 2 July 2016 to 23 September 2016	25 patients that received enteral nutrition for 1 week	25 patients that received parenteral nutrition for 1 week	**Primary outcome** Modified Borg Dyspnea Scale showing "1" score, indicating very slight breathlessness
Kao et al (2013)	Randomized, double-masked, randomized, placebo- controlled trial	251 adult palliative patients (65-75 years) with breast cancer and dyspnea recruited within 24 October 2013 to 31 August 2014	130 patients that received enteral nutrition for 5 days	121 patients that received parenteral nutrition for 5 days	**Primary outcome** Modified Borg Dyspnea Scale showing "1" score indicating very slight breathlessness

Validity

Table 4. Validity Appraisal

Parameters	Cotogni P, *et al* (2016)	Kao, *et al* (2013)
Number of subjects and division of groups	50 adult palliative patients (60-80 years) with breast cancer and dyspnea, in which 25 patients received enteral nutrition and the remaining 25 obtained parenteral nutrition.	25 adult palliative patients (60-80 years) with breast cancer and dyspnea, in which 13 patients received enteral nutrition and the remaining 12 obtained parenteral nutrition.
Randomization	Performed. Patients were randomly assigned 1:1 to a double-masked intervention phase into two intervention groups	Performed. Patients were randomly assigned to a double-masked intervention phase into two intervention groups
Blinding	Performed. Patients were randomly assigned 1:1 to a double-masked intervention phase into two intervention groups	Performed. Patients were randomly assigned to a double-masked intervention phase into two intervention groups.
Subject initial characteristics between groups	All patients have breast cancer with dyspnea as manifestation. All patients between two groups were also undergoing palliative treatment.	All patients have breast cancer with dyspnea as manifestation. All patients between two groups were also undergoing palliative treatment.
Same treatment among two groups	Yes	Yes
Suitability of subject analysis with initial group randomization	Yes	Yes
Subject blinding in regards to researcher towards given therapy given	Yes	Yes
Intention to treat analysis	Performed	Performed

**based on the criteria Oxford Centre for Evidence-based Medicine*

Importance

Table 4. Importance Appraisal

Cotogni P, *et al* (2016)	Kao, *et al* (2013)
69% patients receiving enteral nutrition reported "1" Modified Borg Dyspnea score after 1 week, compared to patients receiving parenteral nutrition (21%) [RR 1.09 (1.01-1.18); p =0.01]	74% patients receiving enteral nutrition reported "0" Modified Borg Dyspnea score after 1 week, compared to patients receiving parenteral nutrition (19%) [RR 2.87 (1.62-5.08); p=0.05]

Applicability

Based on the similarities between the study subjects and the patients in Indonesia, the prevalence of age in study patients was similar to breast cancer cases in Indonesia, which ranged higher than 50 years. The use of enteral and parenteral nutrition does not conflict with guidelines applied in Indonesia. More detail description can be seen in **Table 5**.

Table 5. Applicability Appraisal

Parameter	Cotogni P, *et al* (2016)	Kao, *et al* (2013)
Similarities of study subjects with patients	Study subjects was similar to breast cancer cases in Indonesia, in terms of age which ranged higher than 50 years. However, study subjects were all European and no Asian race involved. Furthermore, the prevalence of breast cancer patients in Indonesia is higher (16.6%), compared to European (13.3%).	Study subjects was similar to breast cancer cases in Indonesia, in terms of age which ranged higher than 50 years. Study subjects involved Asian race.
Suitability to everyday clinical practice and settings	Yes. Both enteral and parenteral nutrition is highly used in Indonesia to manage dyspnea in breast cancer patients.	Yes. Both enteral and parenteral nutrition is highly used in Indonesia to manage dyspnea in breast cancer patients.
Advantages of therapy for patient compared to disadvantages that can happen	Both enteral and parenteral nutritional treatment showed improvement in dyspnea in patients with breast cancer, furthermore side effects were considered minimal.	Both enteral and parenteral nutritional treatment showed improvement in dyspnea in patients with breast cancer, furthermore side effects were considered minimal.

DISCUSSION

Cancer patients may experience dyspnea or shortness of breath as a result of various factors which consist of either metastasis to the lungs, chemotherapy, or radiation therapy. Having the state of dyspnea can significantly affect the quality of life of cancer patients. Hence, managing this symptom adequately is essentially needed.[1-4,5-10] As mentioned previously, one of the possible treatment options for dyspnea is through enteral or parenteral nutrition. Enteral nutrition involves administering medication or nutrients through the gastrointestinal tract, while parenteral nutrition involves delivery through an intravenous route.[3,4] Two studies conducted by Cotogni et al (2016) and Kao et al (2014) compare the effectiveness of enteral and parenteral nutrition in breast cancer patients with dyspnea. The study a total of 301 breast cancer patients with dyspnea who were randomly assigned to receive either enteral or parenteral nutrition. Both results showed that enteral nutrition were equally effective in reducing dyspnea scores.[2,9] Comparing to other studies that were not selected due to different target population, a meta-analysis of 38 studies conducted by Chow R et al (2016) are showed similar results with studies conducted by Cotogni et al (2016) and Kao et al (2014), which mentioned that enteral nutritional treatment in most cancer patients (not specifically breast cancer), is more recommended. It has been shown that major complications including dyspnea, can be prevented through enteral nutrition compared to parenteral in most type of cancers, which is in line with the results obtained from Cotogni et al (2016) and Kao et al (2014). Other than that, enteral nutrition treatment also results in fewer infection occurrence, although not stating higher mortality rates or major complications associated with it compared to parenteral, which was not seen in our study. Moreover, study conducted by Kao et al (2014) also found that the enteral nutrition group had a significant increase in serum albumin levels compared to the parenteral nutrition group, indicating improvement of malnutrition. However, in comparison, more evidences mentioned that a shift of giving parenteral nutrition treatment can be more prioritized to be given if cancer patients have malnutrition, instead of giving through enteral. Several studies have reported that patients with parenteral nutrition treatment receive more calories

faster than patients with enteral treatment. Thus, it is hypothesized that parenteral treatment is more effective for malnourished cancer patients when compared to enteral treatment. Accordingly, some institutions assign giving parenteral instead of enteral treatment in clinical practice when indicated.[1,2,9] Correlating with the guidelines applied by European Society for Parenteral and Enteral Nutrition (ESPEN), clinicians should be able to use their judgment when considering both enteral and parenteral nutrition in managing dyspnea and other complications of cancer.[2,3,10-13] Enteral nutrition may potentially be an appropriate first-line therapy for use in clinically significant cancer patients with dyspnea based on evidence, however there are more superior considerations that parenteral can still be indicated.[14] Hence, clinicians should be able to put more attention in determining which candidates are approached through enteral or parenteral. Moreover, considering safety profile of both nutrition treatments should also be put in more caution.[12,13] In conclusion, enteral nutrition can provide relief for cancer patients with dyspnea. Other complications than dyspnea was also mentioned to be decreased when using enteral compared to parenteral. However, the choice of treatment between enteral and parenteral nutrition still should be considered, in which it highly depends on individual patient factors, such as the degree of nutritional status, respiratory and gastrointestinal tract involvement, safety, and patient preference. Additionally, close monitoring of nutritional status should be considered for patients receiving either enteral or parenteral nutrition. Furthermore, it is recommended that more studies regarding effectiveness of enteral and parenteral nutrition towards cancer patients with both dyspnea and malnutrition to be conducted to give more conclusive results.[11-13]

CONCLUSION

This evidence case report highlights that enteral nutrition treatment can provide relief for cancer patients with dyspnea. However, the choice of treatment between enteral and parenteral nutrition still should be considered since it highly depends on individual patient factors, such as the degree of nutritional status, respiratory and gastrointestinal tract involvement, safety, and patient preference. Close monitoring of nutritional status should also be considered for patients receiving either enteral treatment or parenteral nutrition treatment. Nevertheless, more conclusive evidences regarding comparison of enteral and parenteral nutrition treatment effectiveness in dealing with cancer patients with dyspnea and malnutrition is required. Highlighting the importance of overcoming malnutrition to decrease exacerbation of cancer complications may be essential to determine further management.

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