



Effect of carnitine on patients with heart failure: an evidence-based case report

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Abstract

Background: Heart disease is one of the leading causes of death in Indonesia. Nutritional management plays an important role in overcoming heart disease, both as prevention and treatment. Carnitine plays a role in fat metabolism and can reduce the formation of thrombosis, resulting in improved heart function and quality of life of patients.

Objectives: This study is aimed to identify the effect of carnitine in patients with heart failure.

Methods: Existing research findings and articles are selected based on inclusion and exclusion criteria in three databases, namely PubMed, Cochrane and Wiley. The outcome were functional capacity and heart function.

Results: One meta-analysis that address with the clinical questions was obtained, and based on that article, giving carnitine to patients with heart failure has effects on increasing functional capacity, heart function, BNP serum and NT-proBNP levels. However, no effects found on mortality. Furthermore, no significant side effects on carnitine was found.

Conclusions: Carnitine supplementation at a dose of 1 up to 6 g/day has a positive impact on functional capacity, heart function, BNP serum and NT-proBNP levels in patients with heart failure, alongside with minimal side effects.

Keywords carnitine, heart failure, outcome

Clinical scenario

Mr. S, age 50, was admitted to the emergency room with the chief complaint of shortness of breath for the last 3 days, which would arise suddenly and became worse when in a sleeping position. History of diabetes was denied, however he had a history of high blood pressure for the past one year and was not taking medications regularly. Physical examination

revealed cardiomegaly, normal heart sounds, no murmurs or gallops. Laboratory results: Hb 16 g/dL, leukocytes 6500/mm³, platelets 230,000/uL, LDL 243 mg/dL, triglycerides 267 mg/dL, uric acid 10 mg/dL, troponin I 0.29 ng/mL, BNP 312 pg/mL. Electrocardiography test showed an enlarged left ventricle. The patient's body weight was 65.7 kg, with a height of 160 cm, and a body mass index of 25.6 kg/m². The patient was hospitalized and received treatment from internists and clinical nutrition specialists. Patient was diagnosed with obesity grade 1,¹ heart failure class 4 according to the New York Heart Association (NYHA), dyslipidemia, and hyperuricemia. Patient was given oral carnitine supplementation when discharged from the hospital at a dose of 1.5 g/day for 3 months

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period, and showed an improvement in NYHA class. Patient did not show any side effects after carnitine supplementation.

Introduction

Heart failure is a global problem with 26 million people worldwide and with 670,000 new cases found in America. Heart failure is the most common cause for hospital admittance in the United States and Europe.² In Indonesia, heart failure prevalence is 5%, with mortality rate up to 20%.³

One of the nutrients that has been found having an essential role for patients with heart failure is carnitine, which is an amino acid derivative that plays a role in fat metabolism and mitochondrial defence. Several studies have shown that carnitine, especially in the form of propionyl-L-carnitine, can reduce the accumulation of coronary artery thrombosis and embolism. Some sources of carnitine are milk and milk products, and red meat.

The role of carnitine in fat metabolism is as the transporter of acyl co-A into the mitochondrial matrix, so that fat can undergo β -oxidation and become a source of energy, especially for heart muscle cells.⁴ Healthy adult usually consume carnitine at a dose of 2-5 mg/kgBW/day.⁵

Patients with heart failure often suffer from carnitine insufficiency due to reduced intake, malabsorption, and decreased muscle mass. Carnitine insufficiency results in reduced left ventricular diastolic function, reduced physical activity ability, and an increased risk of heart attack.⁷ However, carnitine has not yet been recommended as a routine therapy in patients with heart failure by the American College of Cardiology Foundation / American Heart Association (ACCF / AHA).⁸ Even so, giving carnitine can be a nutritional therapy for patients with heart failure that can help improve heart function and the quality of life of patients. Jing et al.⁹ carried out a research by administering carnitine intravenously twice a day for seven days, in the form of 1 g of L-carnitine dissolved in 100mL of normal saline in patients with heart failure. The assessment was carried out on the NYHA class of patients. The results showed a 60.9% improvement in the NYHA class of intervention group, compared to the 44.7% improvement in the NYHA class of placebo group. A meta-analysis study of the effects

of carnitine given orally in accordance with the needs of 3 g/day or more on mortality rate in patients with acute myocardial infarction did not show any significant impact.¹⁰

This evidence-based case report will discuss specifically about the effects of carnitine on patients with heart failure.

Clinical questions

P: Adult patients with heart failure

I: Carnitine

C: Without carnitine

O: Functional capacity and heart function

Clinical question: What is the effect of carnitine as a nutritional management on functional capacity and heart function in patients with heart failure?

Methods

Article Search Strategy

Existing research articles were generated from PubMed, Cochrane Library, and Wiley Online on December 12, 2019. Searching terminology is described in Table 1.

Article Selection Strategy

Eligibility Criteria

Screening is based on Mesh Term, an assessment of conformity with PICO, and with inclusion and exclusion criteria. The inclusion criteria were 1. Study subjects were adult patients (aged ≥ 18 years old), 2. Subjects diagnosed with heart failure with various stages 3. Clinical trials or meta-analysis with carnitine treatment 4. Journals published in the last 5 years 5. Tests clinically carried out in humans. Meanwhile, the exclusion criteria were 1. Journal is not written in English and 2. full text is not available.

Method of critical appraisal

All authors did the critical appraisal by using the method according to the Center of Evidence Based Medicine (www.cebm.net) for intervention studies that has been modified in Indonesian language.

Findings

Based on the results of the search from the database, and by assessing the inclusion and exclusion criteria, an article that is eligible to be included as a reference for critical review is used (Figure 1).

Selected articles are meta-analysis of clinical trials, with a total number of 1625 patients. The length of follow-up of the subject in the articles is from 7 days to 3 years. Carnitine given to patients with a dose of 1 to 6 g/day.

The articles obtained have a level of evidence 1, which is a meta-analysis of 17 clinical trials. Findings from articles used in this work illustrate that carnitine administration has a positive impact on functional capacity and heart function. The validity of the criteria can be seen in table 3. The relevance of the criteria can be seen in table 4.

There were no differences of mortality rate in patients with heart failure ($p=0.08$) and carnitine side effects ($p=0.83$), there was an increase in functional capacity marked by a decrease in NYHA class ($p<0.01$), decrease in BNP serum markers ($p=0.01$) and NT-proBNP ($p<0.01$), as well as increased cardiac function ($p<0.01$).

Discussion

Song X et al. conducted a meta-analysis study for the effects of carnitine supplementation on patients with heart failure with a search time limit until September 30, 2016. The study looked for randomized controlled literature from various databases, abstracts of scientific meetings, as well as manually from unpublished articles and studies. Based on the search, 17 appropriate journals were found, with a total of 1625 research subjects. Patients' age ranged between 43 and 78 years. Carnitine dosage given ranged from 1 to 6 g/day, and administered from 7 days to 3 years. Patients receiving carnitine were classified as NYHA class II-IV, with a LVEF of 27% to 52% before the intervention.

Outcomes from this study showed that carnitine had a positive impact on the functional capacity, which is characterized by a decrease in NYHA class.¹¹ The literature that has the greatest weight in the meta-analysis was the research conducted by Jing ZC et al. The study gave carnitine of 1 g intravenously, twice a day for seven days. The effectiveness of carnitine reached 60.7% compared

to the control group of 44.7% ($P=0.012$). The 6-minute walk test did not show significant difference between control and intervention ($P=0.14$).⁹ The study from Song X et al. also showed that carnitine had positive effect on serum-BNP ($P=0.01$) and NT-proBNP ($P=0.0003$). Both BNP and NT-proBNP can act as prognostic factors in patients with heart failure or in patients with asymptomatic left ventricular dysfunction.¹¹

The heart function also showed significant improvement. The heart functions assessed were LVEF ($P<0.00001$), SV ($P<0.00001$), CO ($P<0.00001$), E / A ratio ($P=0.0003$), LVESD ($P=0.002$), LVEDD ($P<0.0001$), and LVESV ($P=0.01$).¹¹ The antioxidant effect of carnitine can prevent the formation of superoxide in heart muscle and excessive inflammation, which results in changes in heart structure.⁴

There was no impact on the mortality of patients with heart failure, both in intention to treat analysis and per protocol. From a total of ten literature, six literatures showed no side effects of carnitine administration in patients with heart failure, while four studies report side effects such as dry mouth and gastrointestinal disorders. One literature reported that there was skin rash as a side effect, but it did occur in both treatments, both the control group and the intervention group.¹¹

Based on the article in this evidence-based case report, it can be concluded that administration of carnitine can improve the quality of life of patients with heart failure, improve heart function and serum levels of BNP and NT-proBNP, with minimal side effects. Carnitine can be given orally by using carnitine supplements, and using food sources. Examples of food sources of carnitine are beef, with carnitine of 2320 mg/kg dry weight, duck meat with carnitine 732 mg/kg dry weight, skim milk with carnitine 400 mg/kg dry weight, condensed milk 396 mg/kg dry weight, and yogurt 142-139 mg/kg dry weight.

Recommendation:

Patients with heart failure can be given carnitine at least 1 g/day to 6 g/day. In administration of carnitine at a dose of 1 g, it can be given for 1 year, a dose of 1.5 g carnitine with a duration of 3 months, while a dose of 3 g and 6 g can be given for 7 days

Conclusion

Patients included in defined clinical scenario can be given carnitine up to 6 g/day, in the form of supplementation or derived from food sources such as milk, milk products, or meat. Giving carnitine can improve the quality of life of patients, heart function, reduce BNP serum and NT-proBNP levels, with minimal side effects. Giving carnitine has no impact on the mortality of patients with heart failure.

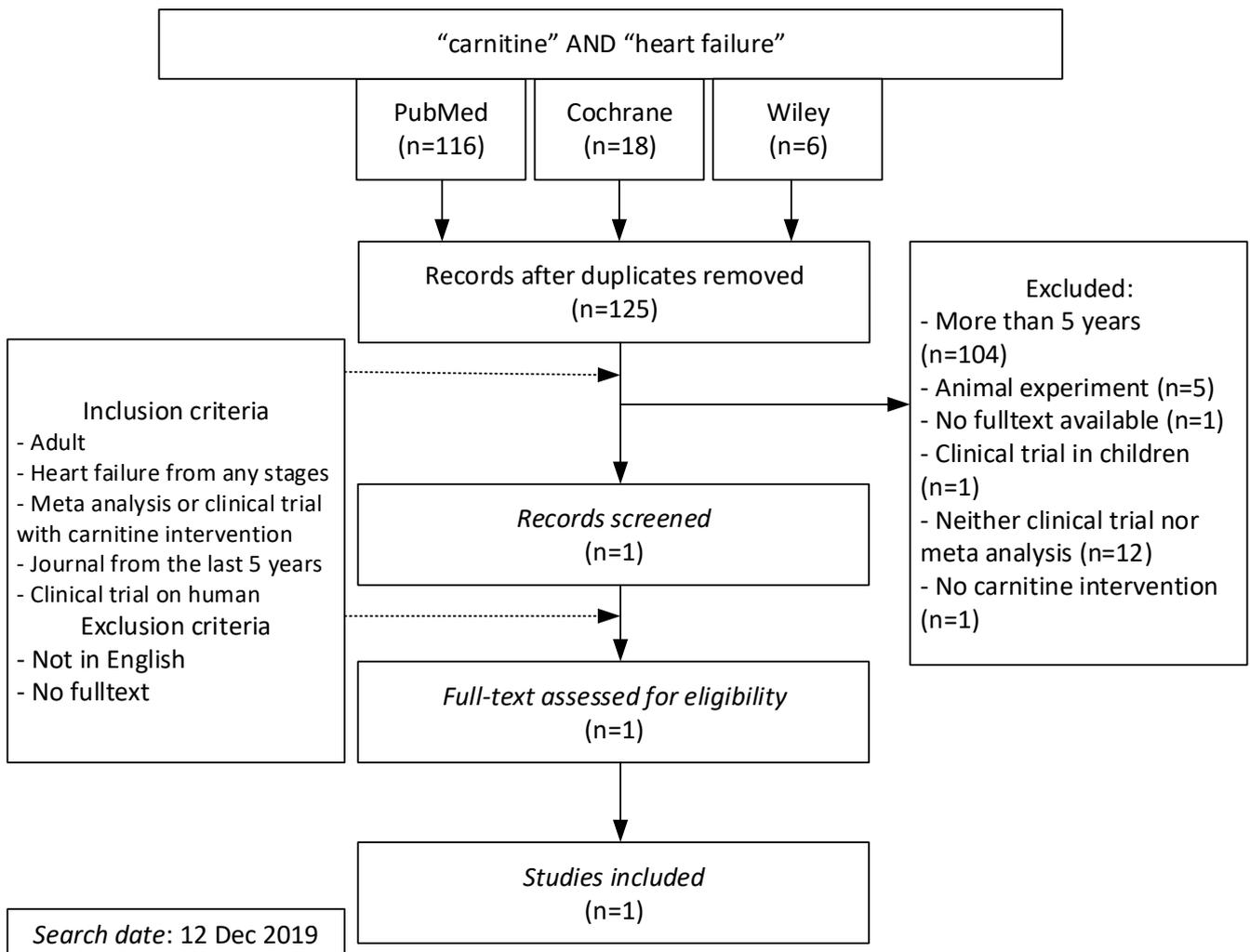


Figure 1. PRISMA flow chart

Table 1. Terminology

Database	Terminology	Hits	Eligible
PubMed	((carnitine[MeSH Terms] OR carnitine[Title]) AND ((heart failure[MeSH Terms] OR heart failure[Title]))	116	1
	ID Search	Hits	
	#1 "heart failure"	28578	
	#2 carnitine	1705	
Cochrane Library	#3 MeSH descriptor: [Carnitine] explode all trees	606	18
	#4 MeSH descriptor: [Heart Failure] explode all trees	8482	0
	#5 #2 OR #3	1719	
	#6 #4 AND #6	18	
Wiley Online Library	"carnitine" AND "heart failure" in Keywords	6	0

Table 2. Study characteristics

Article	Study design	Characteristics of the population	Number of subjects	Age group (years)	Intervention	Control	Outcome	Follow up Period
Song X, et al (2017) ¹¹	Meta analysis	Patients with heart failure	1625	43-78	Carnitine 1-6 grams	Without carnitine	Functional capacity, heart function, BNP and NT-proBNP level, side effects	7 days up to 3 years

Table 3. Validity criteria

Validity	Relevance									Result	Level of Evidence
Artikel	Common point	Follow up	Blind fashion	Sub-group analysis	Outcome	Precise	Apply	Important			
Song X, et al (2017) ¹¹	+	+	-*	+	+	+	+	+		A	1

* Only 3 journals stated that there was blinding in patients and study members

Table 4. Relevance criteria

Article	Similarity Population	Similarity determinant/ intervention/ indicators	Similarity Outcome
Song X, et al (2017) ¹¹	+	+	+

Conflict of interest

The authors declare no conflict of interest regarding this study.

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