

There is no Indication for L-Carnitine in Secondary Treatment-Emergent Myopathy in COPD Patients

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Keywords: myopathy, COPD, side effect, steroids, mitochondrial, muscle wasting.

LETTER TO THE EDITOR

We read with interest the review article by [Hoang, B. X. *et al.*, 2023] on the proposal to administer L-carnitine for muscle wasting in patients with chronic obstructive pulmonary disease (COPD) [Hoang, B. X. *et al.*, 2023]. It was concluded that skeletal muscle involvement in COPD patients contributes to their outcome and that administration of L-carnitine may have a beneficial effect on muscle symptoms in these patients [Hoang, B. X. *et al.*, 2023]. The review is excellent but has limitations that are cause of concerns and should be discussed.

We disagree with the notion that COPD per se leads to muscle wasting as outlined in the review [Hoang, B. X. *et al.*, 2023]. Muscle wasting in COPD patients is mainly due to medications given to these patients for their lung disease. Drugs commonly given to COPD patients include steroids, beta-adrenergic drugs, and purine alkaloids [Bollmeier, S. G. *et al.*, 2020]. Among these, steroids in particular are known to cause myopathy as a side effect, depending on the type of steroids and their dosage. The mechanism by which steroids cause myopathy is not fully understood, however, there is evidence that steroids reduce mitochondrial functions, including respiratory chain activity [Surmachevska, N. *et al.*, 2023]. Salbutamol is known to cause rhabdomyolysis or myoclonus [Montoya-Giraldo, M. A. *et al.*, 2018]. Salmeterol has been reported to induce muscle cramps [Bedi, R. S., 1995]. Formoterol has been reported to cause mitochondrial dysfunction [Kiernan, M. C. *et al.*, 2004].

We also disagree with the suggestion of administering L-carnitine to COPD patients without documented decreased serum carnitine levels [Hoang, B. X. *et al.*, 2023]. Substitution with L-carnitine is only justified in patients with demonstrably reduced serum carnitine. Since secondary carnitine deficiency can occur in several

primary myopathies [Uchiyama, S.I. *et al.*, 2023], such diseases must be thoroughly ruled out in COPD patients. According to the current state of knowledge, the general administration of L-carnitine to all patients with COPD and muscle wasting is not justified.

A limitation of the study is that most of the studies on muscle involvement in COPD patients cited in the review were conducted in patients regularly taking medication for COPD [Hoang, B. X. *et al.*, 2023]. There are hardly any studies on muscle functions in COPD patients who do not take medication regularly. Therefore, these results are not reliable and representative and it is desirable that studies in untreated COPD patients be conducted to assess whether muscle wasting is an inherent feature of COPD patients not taking medication regularly.

It should also be taken into account that physical capacity can be significantly reduced in COPD patients. Because oxygen consumption can quickly exceed the oxygen availability, physical activity in COPD patients can be generally limited. However, reduced exercise can lead to muscle wasting and eventually muscle weakness. Inactivity or at least reduced physical activity can be the result and contribute to muscle wasting.

Cardiac involvement in COPD patients may be due to right heart overload or side effects of the medications used. Therefore, it is important to know whether or not the lung disease resulted in right ventricular hypertrophy, right ventricular dysfunction, pulmonary hypertension, enlargement of the right atrium, or hepatic congestion. It is known that steroids can trigger cardiomyopathy [Sheikh, T. *et al.*, 2020].

Before considering treatment of muscle wasting in COPD patients, a comprehensive evaluation of the myopathy is indicated. When secondary myopathy due to drug treatment is ruled out, the search for primary myopathy is indicated. A causal

connection with the COPD can only be considered if a primary myopathy has also been finally ruled out.

We disagree that treatment of muscle dysfunction in COPD patients is limited to graded exercise therapy and appropriate nutrition [Hoang, B. X. *et al.*, 2023]. The most important pillar of myopathy treatment in COPD patients is the withdrawal of muscle-toxic medication.

Overall, the interesting study has limitations that put the results and their interpretation into perspective. Addressing these issues would strengthen the conclusions and could improve the status of the study. According to the current state of knowledge, there is no general indication for the administration of L-carnitine in COPD patients with muscle wasting. Only in COPD patients with a documented carnitine deficiency could the substitution of L-carnitine be beneficial. However, well-designed, double-blind and controlled studies are essential to confirm such a presumed beneficial effect.

ACKNOWLEDGEMENTS

Statement of Ethics: a) The study was approved by the institutional review board (responsible: Finsterer J.) at the 4th November 2022. b) Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Compliance with Ethics Guidelines: This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Source of support: Nil;

Conflict of interest: Nil.

Cite this article as:

Finsterer, J. "There is no Indication for L-Carnitine in Secondary Treatment-Emergent Myopathy in COPD Patients." *Sarcouncil Journal of Medical Series* 2.10 (2023): pp 5-6.

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