Medical Nutrition Therapy: An Essential Component of COPD Care

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Abstract: COPD affects all organ systems by inducing chronic systemic inflammation as well as metabolic alterations. Various pharmacological, medical & surgical approaches are available for management of COPD. We can’t ignore the importance of nutrition to promote the sound state of health in all COPD patients. Intake of essential micronutrients in adequate amount as per recommended dietary allowance (RDA) & maintenance of normal body-mass index (BMI) is the fundamental requirement for achieving beneficial effects. Here, in this review, we will discuss all the facts related to the scientific role nutrition plays in the pathogenesis of COPD as well as clinical implications referring to the supplemental benefits of nutrients.

Keywords: Body-mass index, Chronic Obstructive Pulmonary Disease, medical nutrition therapy, metabolism, Pulmonary cachexia, recommended dietary allowance.

1. INTRODUCTION

According to GOLD guidelines, COPD as a clinical spectrum is defined as a limitation of conducting airway which is slowly progressive, occasionally reversible and pathologically associated with a chronic inflammation in the involved structures in response to various noxious stimuli [1]. Worldwide, the global prevalence of this disease is continually increasing, currently being 9%, and expected to rise up to 16% till 2025 [2, 3]. It will be the seventh leading cause of DALY’S lost as per projections, attributed to social & economic burden. The development of COPD is multifactorial. Proposed multifactorial pathogenesis include the theory of proteinase-antiproteinase pathway, immunological changes mechanisms, oxidant-antioxidant imbalance, systemic inflammation, apoptosis & ineffective repair.

Among various contributors to chronic disease progression & pathogenesis, the majority are modifiable and diet & nutrition play a significant role. BMI & fat-free mass, major objective parameters of nutrition assessment are found to be low in all patients of COPD. Various descriptive & analytical studies are currently being done to assess the impact of diet & nutrition on disease outcome. Hence, we can’t ignore the adjuvant role of diet & nutrition in disease progression as well as prevention in addition to conventional pharmacotherapy & physical rehabilitation. Pulmonary-cachexia syndrome, an entity characterized by loss of fat-free body mass causing muscle wasting is usually seen in COPD patients due to hypermetabolic & chronic inflammatory state. Generalized muscle wasting is a common scenario.

The muscle wasting leading to skeletal muscle hypofunctioning is a major predictor of functional decline and mortality [4]. We, in this review, will discuss evidence of various dietary components and their usage in the clinical management of COPD.

2. DOES FOOD INTAKE ALTER BREATHING?

Metabolism, the process of changing food to fuel in the body produces carbon dioxide and energy as end products. Breathing requires more energy for people with COPD on account of the laborious breathing & hence, increased resting energy expenditure [5]. Eating a diet with less calories from carbohydrates and more from fat helps faster breathing in patients of COPD.

3. COPD & NUTRITION

25-40% of all COPD patients have low body weight, majority among them also have extremely low fat-free mass (FFM) index [5]. Fig. (1) shows the descriptive analysis in a bar diagram. The risk of acute exacerbation is higher in patients with their BMI on the lower side as compared to normal individuals [6].

Pulmonary cachexia, a chronic hypo nutritive state, is usually seen in COPD patients, characterized by persistent weight loss as compared to ideal body weight. It is evident from various observational studies of COPD patients that around a quarter of patients will definitely develop pulmonary cachexia unless intervened.

Continuing tissue hypoxia, disuse atrophy, persistent catabolic state, chronic inflammatory state, aging & medicinal side effects all collectively contribute to a worsening nutritional state [7, 8]. These patients also have
decreased appetite because of decreased mobilizing capacity, persistent depressive state, or arduous eating [9].

COPD is a systemic inflammatory disorder associated with increased production of inflammatory cytokines such as interleukin (IL)-6, IL-8, tumor necrosis factor (TNF)-α, and chemokines [10, 11]. A correlation between the elevated serum TNF-α levels and weight loss in COPD patients is demonstrated by Görek et al. [11]. Koehler et al. [12] in 2007 demonstrated a significant correlation between increased levels of IL-6 and decreased appetite.

Insulin like growth factor-1 (IGF-1), a neurohormone needed in proteogenetic mechanisms decreases significantly in exacerbation as compared to a healthy state. Glucocorticoids, used as major therapy in exacerbations as well in maintenance, play an important role in creating sarcopenia as they inhibit protein synthesis and promote catabolism. Usually, these side effects are dose-dependent and occur at a dose of more than 60mg/day [13]. Older age, as most of the COPD patients belong to this group only, also plays a precipitating role in the loss of fat-free body mass leading to a persistent decline in muscle strength.

Various studies of dietary supplements have documented slowing of disease progression. This also helps in the pacification of detrimental consequences related to COPD, particularly muscle wasting and weight loss.

4. MANAGEMENT - NUTRITION THERAPY

Along with measures to increase functional ability of COPD patients, maintaining optimal nutritional status also plays a key role in decreasing mortality & morbidity by delaying the process of weight loss and muscle wasting. On the other hand, the intake of extra calories and being overweight also increases the work of breathing, making breathing more difficult. This suggests the need for careful balance in nutritional advice.

5. CHECK YOUR WEIGHT

A universal advice should be given to all patients to monitor their weight at least once or twice a week unless the patient is on diuretics or oral steroids. Those having a marked change in their weight in a short span should report to the treating doctor or registered dietitian nutritionist. COPD patients should be monitored for the presence of pulmonary cachexia or weight loss approximately every 6 to 12 months or at the time of routine visits. Optimizing lung function with aid of drugs, diet and compliance helps in reducing the work of breathing. Moreover, regular exercise also improves the effectiveness of nutrition therapy [14].

6. DIETARY PATTERNS

The “western” dietary pattern, prevailing in high-income countries, designated by huge consumption of refined cereals, processed & cured food items including high-fat dairy products [15]. The “western” diet is associated with an increased risk of COPD [15] occurrence as observed in various cross-sectional studies. Additionally, an acute intake of high fat, fast-food meal has been shown to worsen inflammation [16], increasing the risk of recurrent exacerbations. Differently, Mediterranean dietary pattern includes a high intake of plant foods, namely; fruit, vegetables, bread, cereals, beans, nuts and seeds, low intake of dairy products; minimal fish, poultry, wine and red meat (Table 1).

There is no clear-cut evidence of this diet pattern with a decrease in the occurrence of cases of COPD; however, an inverse correlation is seen with Mediterranean diet.
consumption and atopy-related wheezing or asthmatic symptoms in child-age groups [17].

Dietary supplementation with branched chain amino acids results in amplified protein synthesis. A meta-analysis [18] involving 13 studies indicated that different dietary patterns have variable odds-ratio in relation to the disease occurrence risk; some are beneficial while others are harmful. An increase in the “unhealthy/western-style” dietary patterns has the highest relative risk of chronic obstructive pulmonary disease [18] (Table 2).

### Table 1. A compilation of various studies relating to dietary pattern and COPD occurrence.

<table>
<thead>
<tr>
<th>Author</th>
<th>Pattern of Study</th>
<th>n</th>
<th>Study Objective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varraso et al.</td>
<td>Prospective cohort study</td>
<td>42,917</td>
<td>Dietary pattern &amp; COPD prevalence</td>
</tr>
<tr>
<td>Wood et al.</td>
<td>RCT</td>
<td>37</td>
<td>Dietary pattern &amp; airway inflammation</td>
</tr>
<tr>
<td>Arvanti et al.</td>
<td>Cross-sectional study</td>
<td>700</td>
<td>Mediterranean diet &amp; airway changes in COPD</td>
</tr>
<tr>
<td>Zhang et al.</td>
<td>Meta-analysis</td>
<td>13 studies (1990-2015) MEDLINE, EBSCO</td>
<td>Dietary pattern &amp; airway changes</td>
</tr>
</tbody>
</table>

### Table 2. Following individual studies were considered for meta-analysis [18] conducted.

<table>
<thead>
<tr>
<th>Author/Publication Year</th>
<th>Study Design</th>
<th>n</th>
<th>Diet Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yang et al. 2015</td>
<td>Case-control</td>
<td>2086</td>
<td>Questionnaire</td>
</tr>
<tr>
<td>Varraso et al. 2015</td>
<td>Cohort</td>
<td>73228 F: 47026 M</td>
<td>Food frequency questionnaire (FFQ)</td>
</tr>
<tr>
<td>Yin et al. 2011</td>
<td>Cohort</td>
<td>48974</td>
<td>FFQ</td>
</tr>
<tr>
<td>Varraso et al. 2010</td>
<td>Cohort</td>
<td>121700 F: 51529 M</td>
<td>FFQ</td>
</tr>
<tr>
<td>Mckeever et al. 2010</td>
<td>Cross-sectional</td>
<td>12648</td>
<td>FFQ</td>
</tr>
<tr>
<td>Shaheen et al. 2010</td>
<td>Cohort</td>
<td>1551 M:1329 F</td>
<td>FFQ</td>
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<tr>
<td>Hirayama et al. 2009</td>
<td>Case-control</td>
<td>618</td>
<td>FFQ</td>
</tr>
<tr>
<td>Varraso et al. 2007</td>
<td>Cohort</td>
<td>72043</td>
<td>FFQ</td>
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<td>Cohort</td>
<td>42917</td>
<td>FFQ</td>
</tr>
<tr>
<td>Jiang et al. 2007</td>
<td>Cross-sectional</td>
<td>7352</td>
<td>FFQ</td>
</tr>
<tr>
<td>Kan et al. 2007</td>
<td>Cross-sectional</td>
<td>15792</td>
<td>FFQ</td>
</tr>
<tr>
<td>Varraso et al. 2007</td>
<td>Cohort</td>
<td>51529</td>
<td>FFQ</td>
</tr>
<tr>
<td>Watson et al. 2002</td>
<td>Case-control</td>
<td>230</td>
<td>FFQ</td>
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</table>

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### 7. CARBOHYDRATES

Consumption of diet having high carbohydrate versus fat ratio causes increased relative metabolic production of CO2 (VCO2) and RQ. This increases the net respiratory metabolic demands.

A study conducted on COPD patients who were given nutritional supplementation drinks containing 61% carbohydrate (CHO), 19% fat, and 20% protein, up to three times a day for 8 weeks, showed a significant increase in body weight, FMM, handgrip strength, and respiratory function as compared to a historical placebo group [19]. Similarly, a study where COPD patients were given a high-CHO oral nutritional supplement consisting of 83% CHO given three times a day along with pulmonary rehabilitation through exercise, showed significantly increased body weight, body mass index, FFMI, and also mid-thigh cross-sectional area [20]. This shows that proper intake of carbohydrates with exercise advise is always beneficial for patients.

### 8. FATS

Fatty acids, the basic structural component of dietary fat, guide metabolic need as well underlying inflammatory state in all COPD patients. The interactive equilibrium of serum levels of omega 3 & 6 fatty acids determines the final pro or anti-inflammatory state. These nutrients also act as antioxidants.
In a study involving 250 clinically stable COPD patients using dietary data from a 122-item questionnaire, it was shown that high levels of anti-inflammatory omega-3 fatty acid, linolenic acid in the patients’ diet was associated with proportionately low levels of TNF, an inflammatory cytokine [21]. These results suggest that COPD patients should be encouraged to increase omega-3 fatty acids consumption to promote the anti-inflammatory benefits of this supplement while avoiding foods dense in omega-6 fatty acids.

9. AMINO ACIDS

All COPD patients land up in sarcopenic state, either due to age or the causative disease. Amino acids, the building blocks of all types of anabolic proteins help in improving FFM as well the required respiratory strength. It also helps in preventing exacerbations. In COPD patients, there is a direct linear correlation between plasma concentrations of BCAA and FFM body composition [22].

In a study of 32 severe COPD patients, oral supplementation with EAAs for 12 weeks increased FFM by 10% and had beneficial effects on muscle energy metabolism, cognitive function, and perception of health status [23]. Various studies conducted to find out the intake of protein supplementation & its benefit in COPD patients suggest that a diet rich in EAA is helpful for all.

10. FRUIT AND VEGETABLES

COPD disease progression may be delayed with an increased intake of fruit & vegetables. A prudent diet rich in natural fresh fruits & veggies plays a protective role against declining lung function [24]. A 3-year study on 120 COPD patients revealed an improved lung functioning in the high fruit and vegetable consumption group as compared to the control group [25], as opposed to the results obtained in a 12 week follow up study which showed no effect on FEV1, systemic inflammation [26]. This suggested that long-term intervention is the need of the hour to observe an appreciable therapeutic effect. This applies to all severity stages of COPD equally.

11. ANTIOXIDANTS

All respiratory diseases are characterized by a persistent oxidative stress in airways leading to disease progression & functional decline [27]. Various reactive oxygen species (ROS) are generated in the airways due to interaction with air pollutants, irritants resulting in a persistent inflammatory cellular effect [28].

Vitamin C, vitamin E, flavonoids and carotenoids are avidly present in fruits and vegetables, as well as nuts, vegetable oils, cocoa, red wine and green tea. Diet rich in these is of great benefit. Lycopene, an antioxidant abundant in tomatoes is positively correlated with FEV1 improvement in COPD patients [29] as evident by the suppressed neutrophilic airway activity. Dietary antioxidants act as a primordial preventive measure against continually generating ROS. Similarly, sulforaphane, an organic compound found in various naturally grown food products including turmeric may have beneficial antioxidant properties.

12. VITAMIN C

Vitamin C also showed effect on blocking the production of IL-8 and inhibition of NF-κB activation pathway [30] in addition to its antioxidant properties. Chang et al. [31] found that high dose Vitamin C dietary intervention in mice resulted in decreased eosinophils in BALF and increased ratio of Th1/Th2 cytokine, thus supplementing the imperative role of the same in COPD pathogenesis and management.

A case-control study in Taiwan reported that subjects with COPD had lower serum levels of vitamin C than healthy controls [32]. An epidemiological study conducted in the United Kingdom including 7000 adults aged 45-74 years found that increased plasma vitamin C concentration was associated with a decreased risk of obstructive airways disease, suggestive of a protective effect [33]. However, available evidences are observational only & there is a dire need for interventional analytical studies in a prospective manner to avail the data applicable on a larger population.

13. VITAMIN E

The tocopherol family acts in a synergistic manner as vitamin C in reducing the deleterious consequences of ROS and associated airway inflammation [34, 35]. Some animal studies report that γ-tocopherol may attenuate the inflammatory effects of ozone, owing to its ability to oxidize reactive nitrogen species [36, 37].

Increased intake of vitamin E in COPD patients helps in reducing recurrent exacerbations, which are usually associated with reduced serum levels of the same [38].

In the Women’s Health Study (n = 38,597), the risk of developing chronic lung disease over a 10 year period was reduced by 10% in women using vitamin E supplements (600 IU on alternate days) [39]. However, enough data advocating universal supplementation is lacking.

14. VITAMIN D

Activated vitamin D, the most studied vitamin for its correlation on lung health signifies its importance in nutrition therapy. Besides sun exposure, dairy dietary supplementation is also a rich source. Recurrence of viral as well as respiratory infections also keeps on declining in vitamin D supplemented patients, indicative of the protective role it plays [40]. Activated vitamin D (1,25 (OH)2D) induced augmented production of cathelicidins and defensins helps bacterial decontamination and early wound repair [41].

Furthermore, various animal models also suggest that vitamin D can inhibit Th1 and Th2 cell cytokine production [42]. Serum vitamin D levels, when correlated with lung function in COPD patients & disease progression indicated increased disease incidence and morbidity associated with low levels [43-45]. The protective immunomodulatory effect of vitamin D abolishes with chronic smoke exposure induced altered cellular response [46].

In an observational study conducted on single nucleotide polymorphisms in the vitamin D binding protein (VDBP), lower vitamin D levels are correlated with increased risk for
the occurrence of COPD [47]. However, there is no definite evidence supporting the beneficial effect of vitamin D supplementation on exacerbations.

15. PHYTONUTRIENTS

Flavonoids, easily available in the form of fruit, vegetables, nuts, seeds, stems, flowers, roots, bark, dark chocolate, tea, wine and coffee are also considered to play a beneficial role in ameliorating the toxic consequences of ROS and its allergic-inflammatory associations [48]. No RCT done till date supports its supplementation role, however, the continually growing evidence in observational studies warrants further research. Minerals Essential micronutrients and various minerals are also supposed to have a protective respiratory role. Research studies on dietary mineral supplementation are sparse. A small observational study conducted in Sweden found that older patients with severe COPD have a lower intake as well as serum levels of folic acid and selenium [49]. It is advisable to accept a mineral enriched whole diet approach.

16. OBESITY AND RESPIRATORY DISEASE

In over nourished individuals, augmented levels of free fatty acids seen with increased intake of dietary lipids, resulting in the increased inflammatory pattern. This is a type of active immune response involving the activation of TLR4 [50]. Leptin, a persistently elevated adipocytokine found in all obese and middle-aged females does have a role in Th1 proliferation resulting in the activation of neutrophils [51]. Also, bronchial and alveolar epithelial cells consist of leptin receptors which induce activation of alveolar macrophages [52]. Meta-analysis proven correlation of leptin levels, BMI & proportionate fat mass percent was observed in stable COPD patients [53]. Elevated leptin levels were associated with increased circulating TNF-α during exacerbation also [53]. Adiponectin, an anti-inflammatory adipokine also affects inflammation in COPD. Bianco et al. [54] describes the role of adiponectin and its effect on inflammation in COPD. Diverse isoformic nature of adiponectin acts via two different receptors (AdipoR1 and AdipoR2), located in the lungs that have opposite inflammatory effects [55]. There was a correlation between serum adiponectin levels in COPD patients with severity & functional status [56]. Expression of adiponectin receptors in the lungs of COPD patients is different to healthy individuals [57]. Persisting systemic inflammation and fluctuating levels of adipokines have significant negative effects on COPD patients with obesity.

17. CAREGIVER DIET HINTS

- Consider “eating” as active exercise, should be initiated after proper rest.
- More “eating” should be in morning hours, as patients are not tired.
- Eat more slowly. Breathe deeply in between small bites in a periodic manner to avoid precipitating discomfort.
- Easily chewable food items should be preferred.
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18. TIPS FOR GAINING WEIGHT

- Eat in a sitting posture to ease pressure on lungs.
- Foods that cause delayed gastric emptying or promote bloating should be avoided.
- Limit liquids with meals, as they make you too full and cause breathing difficulty.
- Eat multiple small quantity meals repeatedly after a span of 3-4 hours every day.
- Nutritional supplementation should always be added, based either on a deficit state or in a generalised fortification process.
- Always try to assimilate more fat in the form of PUFA, MUFA & low-cholesterol items, as more fatty diet is always beneficial in terms of efficacious energy output & reduced carbon waste production. Try to limit Trans and saturated fat.
- Plenty of water intake (6-8 glass per day) helps in maintaining hydration, also beneficial in easier removal of mucus from airways.
- All oral supplemental fluids should be caffeine-free as it only affects metabolism in a deleterious manner.
- Sodium intake should also be guided, as it may increase body fluids & blood pressure.
- Calcium supplementation with aided vitamin D should be considered.
- 20-30 grams of fibre per day in the form of bread, pasta, nuts, seeds and veggies should be taken.
- Complex carbohydrates are more preferable than simpler ones.
- Adequate protein supplementation according to RDA, at least once or twice a day.
- Alcoholic beverages don’t have nutritive value and can interact with medicines, so these should be avoided. Too much alcohol causes slower breathing and precipitous decline in mucus clearance.

CONCLUSION

This review demonstrates the valuable importance of nutrition therapy in the multidimensional management of COPD. Proper nutrition and supplementation help in improving functional status, in decelerating the rate of progressive decline and in preventing repeated exacerbations. It also aids in the overall survival as well as in decreasing morbidity. Well-nourished state also plays a
protective role in extrapulmonary mechanics including lowering of metabolic and cardiovascular risks [58]. Diets rich in naturally occurring organic food items excluding high-fat content are always beneficial for respiratory diseases.

A mixed-food supplemental approach has a dual beneficial impact in terms of increasing nutritive value and attenuating COPD risk. The detrimental effects of overnutrition, induced by immunometabolism besides affecting other organ systems, also have profound adverse effects on respiratory physiology. Further studies including RCTs are required in the future for generating guidelines about nutritional supplementation in disease management.

LIST OF ABBREVIATIONS

- 6MWT = Six-minute walk test
- BALF = Bronchoalveolar lavage fluid
- BMI = Body-mass index
- CHO = Carbohydrate
- COPD = Chronic Obstructive Pulmonary Disease
- DALY = Disability adjusted life years
- FFM = Fat-free mass
- FFQ = Food frequency questionnaire
- GOLD = Global initiative for COPD
- RDA = Recommended dietary allowance

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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Declared none.

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