ORIGINAL RESEARCH PAPER

Pulmonary Medicine

KEY WORDS: asthma, chronic obstructive pulmonary disease, chronic respiratory diseases, fatty acids, noncommunicable diseases (NCDs), obesity, population nutrient intake goals(PNG), World Health Organization (WHO),

A PERSPECTIVE ON DIET AND NUTRITION AND CHRONIC RESPIRATORY DISORDERS (CRD)

Dhastagir Sultan Sheriff* Department of Biochemistry Faculty of Medicine University of Benghazi Benghazi, Libya *Corresponding Author

Rageia Elfageih Department of Biochemistry Faculty of Medicine University of Benghazi Benghazi, Libya

ABSTRACT

Diet and nutrition are important factors in the prevention of major chronic noncommunicable diseases (NCDs).World Health Organization (WHO) Global Action Plan for the Prevention and Control of Noncommunicable Diseases has placed greater emphasis on diet and nutrition. It has formulated dietary recommendations to achieve Population nutrient intake goals (PNG) for a population. PNG have been set based on the evidence linking dietary factors as risk factors for developing obesity, type 2 diabetes, cardiovascular diseases, and cancer. Chronic respiratory diseases (CRD) which are one of the major causes of mortality require studies to elaborate the role of diet on CRD. In the present short review an attempt has been made to elicit the role of diet and nutrition in the prevention and control of CRD. Recommendations of diet for the prevention of CRD may be integrated with that of PNG for NCDs, so that an integrated approach for prevention and control of CRD could be worked out.

Introduction:

Diet and nutrition play an important role in the cause and prevention of non-communicable diseases including chronic respiratory diseases. Dietary constituents modulate host response to environmental pollutants. A balanced diet may help to inhibit, prevent or reverse the chain of adverse reactions leading to causation of a disease.

A diet deficient in certain nutritional components like anti-oxidants may make a person susceptible to environmental toxicants like tobacco smoke, allergens, infectious agents and air pollution. This is true of respiratory disorders. Deficiency of antioxidant vitamins, omega 3 (n-3)fatty acids, higher consumption of omega 6 (n-6)fatty acid rich oils, processed foods and salt may affect airway smooth muscle contraction, neuromuscular transmission and initiate adverse inflammatory reactions.

Lung is an organ that is bathed in oxygen-rich medium. It has an effective intra-cellular and extracellular antioxidant defense system. Maintenance of normal pulmonary cellular function depends upon the tight control of such a defense system. An increase in oxidant stress or a deficient antioxidant components may initiate a chain reaction that may precipitate cellular death and pulmonary dysfunction. [1,2]

Oxidant stress is defined as a shift towards proxidant stress due to an imbalance between antioxidants and oxidants.

Free radicals are unstable ions generated usually from molecules of reactive oxygen species and reactive nitrogen species generated inside the human body. These radicals tend to capture electrons to become stable. The electron dense regions the unsaturated double bonds of a molecule become susceptible to such attacks and in the process lose their structural integrity. The loss of structural integrity in a plasma membranes of organelles lead to structural damage of the organ leading to loss of function. Free radical induced damage can cause hemolysis to cardiac dysfunction.

Free radicals could be derived from oxygen or nitrogen. These could be called as Reactive oxygen species (ROS) and reactive nitrogen Species (RNS). Types of free radicals are shown below in the Table.

Table 1: Biologically significant free radicals.3

Reactive Oxygen Species	
O2?$^-$	Superoxide radical
?OH	Hydroxyl radical
ROO?	Peroxyl radical
H2O2	Hydrogen peroxide
1O2	Singlet oxygen
NO?	Nitric oxide
ONOO$^-$	Peroxynitrite
HOCl	Hypochlorous acid

What are antioxidant defense system in the lung? [2, 5, 6] The first line of defense against oxygen free radicals are free radical scavenging agents. These agents are present to varying degrees in the intracellular and extracellular spaces, and they function by either eliminating oxidants or preventing their conversion to more reactive species [4,7].

Antioxidants act either by scavenging free radicals or binding metal ions or by eliminating oxidatively modified biomolecules7.

Antioxidant defense system in the lung include endogenous enzyme systems and nonenzymatic antioxidant compounds.

Superoxide radical ($O2^-$) generated in the lungs are converted to hydrogen peroxide by the action of Cu-Zn Super oxide mutase (SOD).

$$O_2^- + O_2^- \longrightarrow H_2O_2$$

Super oxide radical SOD Hydrogen peroxide

Hydrogen peroxide so formed is further metabolized to water with the help of glutathione, a tripeptide (gamma glutamyl cysteinyl glycine) catalyzed by an enzyme known as glutathione peroxidase, a seleno cysteine enzyme.

$$H_2O_2 + 2\,G.SH \longrightarrow 2\,H_2O + G.S.S.G$$

Glutathione GSH peroxidase oxidized form of Glutathione (11)

$$H_2O_2 + H_2O_2 \longrightarrow 4\,H_2O$$

Hydrogen peroxide can also be converted into water with the help of another enzyme catalase mostly present in peroxisomes.[3]

Vitamin E otherwise known as alpha-tocopherol, ascorbic acid (vitamin C), Beta Carotene (a precursor of Vitamin A) ubiquinone, flavonoids, and selenium are nutrients present in the diet and are considered dietary antioxidants [7]

The lipid soluble Vitamin E protects against oxidant-induced membrane injury in human tissue, by inhibiting the lipid peroxidation chain reaction[8]

Vitamin C, a water-soluble vitamin, has a multiple role in acting as an antioxidant. Vitamin C scavenges super oxide radical. Vitamin C is present in abundance in the extra-cellular fluid lining of the lungs.[9] Vitamin C inhibits the generation of prostaglandin F2 formed from arachidonic acid and thereby inhibits broncho-

constriction induced by the prostaglandin 10 Vitamin C appears to help regeneration of membrane-bound oxidized form of vitamin E, promoting its chain-breaking function of lipid peroxidation of plasma membrane.[11].

B-Carotene a precursor to vitamin A is rich in tissue plasma membranes, scavenges superoxide anion, and reacts directly with peroxyl free radicals [7].

Therefore, dietary vitamins play a vital role in host defense against oxidative damage to the lungs. Flavonoids such as quercetin scavenge superoxide anion, lipid peroxyl radicals, show singlet oxygen-quenching properties, and can chelate iron ions [7].

Selenium has a prosthetic group function as selenocysteine in antioxidant enzyme glutathione peroxidase and supplements vitamin E function [12]

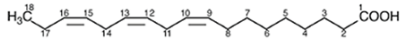
In patients with Asthma when exposed to infection or inhaled pollutants secrete more ROS when compared to normal subjects. ROS are known to cause smooth muscle contraction of the airways, stimulate histamine release from mast cells.[13]

An increase in lipid peroxidation products, higher exhalation of hydrogen peroxide and possibly DNA damage were observed in COPD. Cigarette smoke is the source of oxidants which is known cause of COPD. The oxidant stress present COPD therefore depends upon the presence of antioxidant defenses to normalize the state. The levels of Vitamin C, Vitamin E and beta-carotene are reported to be reduced in COPD. The deficiency is accompanied by inflammation of the airway and parenchymal cells in COPD patients.[13]

It is recommended that such patients take more fresh fruits and vegetables which contain considerable amounts of vitamin C (e.g., broccoli, spinach, tomatoes, and citrus fruits) and carotenoids (e.g., carrots, tomatoes beans, broccoli, and mangos)14 Vitamin E is present in oil products such as mayonnaise, vegetable and seed oils (corn, safflower, and soybean). Vitamin A is rich in carrots and fish oils. Fruits and vegetables (apples, lemons, oranges, potatoes, and cauliflower) and tea are rich sources of flavonoids [7]

Selenium is present in grain, meat, seafood, and certain vegetables. The current Recommended Dietary Allowance are 60 mg/day for vitamin C (100 mg/day for smokers), 800-1,000 retinol equivalents per day (1 retinol equivalent = 6 (ug of beta-carotene) for vitamin A, 8—10 mg/day for alpha-tocopherol, and 55-70 ug/day for selenium [15]

Omega (ω3-n3) and omega (ω6-n6-) Fatty acids:



The chemical structure of α-linolenic acid (ALA), 18:3n-3. ALA has 18 carbon atoms (C) and 3 double bonds, the first of which is located 3 carbon atoms from the terminal methyl group (omega [ω] end).

α– linolenic acid (ALA) is one of the essential poly unsaturated fatty acids (PUFA). It is otherwise known as omega 3 fatty acid (n-3)which has three double bonds, one of the bond being between 3 and 4th carbon atoms from the methyl end of the fatty acid (CH3 –omega carbon). The other omega 3 fatty acids are ALA, eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA), and docosahexaenoic acid (DHA). Dietary ALA is converted to EPA and then to DPA and finally to DHA. EPA and DHA are the two primary omega-3 PUFAs. Omega 3 fatty acids are stored in the plasma membranes and are anti-inflammatory in nature. The fatty acids are easily replaced by omega [6] fatty acid (n-6), particularly linoleic acid which is pro-inflammatory in action. Linoleic acid is converted into arachidonic which is a precursor for prostaglandin E2 and leukotriene B4 through cyclooxygenase and 5-lipoxygenase pathways, respectively. Both prostaglandin E2 and Leukotriene B4 possess biologically pro-inflammatory actions. [3]

The following Table summarizes the different poly unsaturated fatty acids present in our body.

Table.2. Mono Unsaturated- and Poly Unsaturated Fatty Acids (PUFA) of importance

Name of Fatty Acid	Symbol	
Oleic acid	18:1[9]	An omega-9 monounsaturated fatty acid
Linolenic acid	18: [9,12,15]	An omega -3 PUFA in present in fish oils which can to converted to EPA and DHA.
Eicosapentaenoic acid (EPA)	20:5[5,8,11,14,17]	An omega-3 polyunsaturated fatty acid enriched in fish oils
Docosahexaenoic acid (DHA)	22:6[4,7,10,13,16,19]	An omega-3 polyunsaturated fatty acid enriched in fish oils
Linoleic acid	18:2[9,12]	An omega-6 polyunsaturated fatty acid
Arachidonic acid	20:4[5,8,11,14]	An omega-6 polyunsaturated fatty acid

Where omega 3 fatty acid (EPA) can inhibit formation of arachidonic acid metabolites competitively and therefore act as anti-inflammatory agent. EPA is converted to prostaglandin E3 and leukotriene B5 which show very little inflammatory actions. Therefore, omega 3 fatty acid supplementation will suppress the Linoleic action [16]

PG E2 inhibits formation interferon –λ in T-lymphocytes without suppressing the formation interleukin-4. Interleukin-4 production promotes synthesis of immunoglobin E and therefore allergic sensitization. Interferon- has the opposite action.[17]

Leukotriene B4 is known to increase vascular permeability, stimulates airway smooth muscle contraction and therefore, mediates pulmonary asthma by vasoconstriction and mucus secretion.

The competitive interactions between omega 6 and omega 3 fatty acids influence the cellular production or content of arachidonic acid and EPA. But in western diet 20 to 25 times higher concentration of omega 6 fatty acid linoleic acid compared to omega fatty acids may increase the prevalence of asthma [16]

n-3 PUFA are found in high quantities in fish oil whereas n-6 PUFA are found in soybean, corn, safflower, and sunflower oils [16] Due to the opposing effects of omega-3 and omega-6 fatty acids, a healthy diet should contain a balanced omega-6: omega-3 ratio. Human beings evolved eating a diet with an omega-6: omega-3 ratio of about 1:1. Modern Western diets instead have a ratio of 15:1 to 17.1 for omega-6: omega-3 fatty acids 15:1 to 17:1.12,13 Recent evidence suggests that fish intake may help alleviate childhood asthma and wheeze in children up to [4,5] years old, while fatty fish intake may be beneficial in older children up to 14 years of age [14-16] More studies are still needed to find the appropriate balance between n-6 and n-3 PUFAs to protect against CRD.

Intake of deep fried fast food and baked goods are the major sources of trans fatty acids in the diet.[17].In cross sectional studies higher prevalence of asthma is observed in those countries that have higher levels of trans-fatty acids intake [18] Higher levels of margarine consumption are also associated with the increased risk of asthma [19-20] An increased risk of development of COPD in men and women is reported to be associated with diet rich in desserts and French fries [21-22] Possible measures to limit intake of trans fatty acids in the diet are contemplated by WHO. [23]

There is little evidence on the effect of MUFAs on CRD. There are some data on the harmful effect of MUFAs which promote allergic sensitization [24-25] while SFA from dairy products are shown to reduce asthma risk [26-28] The only nutritionally important MUFA is oleic acid, which is abundant in olive and canola oils and also in nuts. It is recommended that adequate amounts of n-3 PUFA along with some amounts of SFA be included in the CRD patients' diet (It is calculated on the basis of = MUFAs by difference: total fat – (SFA+ PUFAs + Trans fatty acids).[26-28] However more studies in this area are needed taking into consideration the culture and habits of different population.

Role of electrolytes

Sodium is important in different aspects of smooth muscle tone. Influx of sodium followed by stimulation of sodium-potassium ATPase (Na+-K+ ATPase) results in sustained hyperpolarization of airway smooth muscle cells. In other words the contractile response of airway smooth muscles cells by a specific antigen from the environmental pollution is supposed to be dependent on the level of hyperpolarization [29]

A diet rich sodium or salt content may predispose a person to development of airway hyper-reactivity. Dietary sodium intake may also influence such an activity by changing the levels of endogenous steroid hormones or catecholamine release [30]

Magnesium is one of the minerals involved in maintaining electrical potential across plasma membranes.[29-31] It may play a role in relaxing smooth muscle, bronchodilation in asthmatic patients, to inhibit neuromuscular transmission, stabilize mast cells and T-.lymphocytes and help generate nitric oxide and prostacyclin. [32] A diet low in magnesium could therefore be a risk factor for airway diseases. Magnesium in the diet is obtained principally from cereals, nuts, green vegetables, and dairy products [29-33.]

In a global context diet and nutrition have assumed prime importance to promote health and well-being. World Health Organization (WHO) global action plan for the Prevention and Control of Non-communicable Diseases (NCD) has laid great importance therefore, on diet and nutrition. WHO has recommended to achieve Population nutrient intake goals (PNG) based on the population's average intake that helps to maintain health in a population. PNG expressed in numbers have been calculated based on the available literature linking dietary factors to risk of developing obesity, type 2 diabetes, cardiovascular diseases and cancer.[34-36]

The recommended diet needs to have 55-75% carbohydrates, 10-15 % protein and 15-30 % lipids.

The composition of fat must include 6-10% polyunsaturated fatty acids (PUFA) with n-6 PUFA forming 5-8% and n-3 PUFA 1-2 % of the total fatty acid present in the diet. Monosaturated fatty acid is calculated as: total fat - (saturated fatty acids + polyunsaturated fatty acids + trans fatty acids) where trans fatty acids form <1%.

Conclusion:

Pulmonologists face challenges unique to a particular region and culture. The prevalence of obesity and sleep apnea, different types of smoking, environmental and occupational hazards, chest infections, inherited disorders like cystic fibrosis along with dynamic flow of immigrant population carrying drug-resistant tuberculosis make Respiratory Disorders of great public health concern. These health issues need an orchestrated approach involving public health department, respiratory medicine and possibly a specialist pulmonology unit along with Dietitian for effective management and compliance to medical care. People who ate a pre-industrial diet had an omega-6 to omega-3 ratio of about 4:1 to 1:4, most falling somewhere in between. The ratio today is 16:1, much higher than what people are genetically adapted to. n-3 PUFA control inflammation and excess n-6 PUFA promote inflammation.[34-36]

Therefore, chronic respiratory diseases (CRD) is one of the major public health problems and economic concern for most of the nations. Studies related to studying the dietary patterns of a specific population along with its cultural background may help devise population nutrient intake goals(PNG). CRD could be included along with NCDs for global action plan to set nutrient goals to prevent and control respiratory problems. Such an approach will form the basis for an integrated approach to combat CRD along with NCD_s.

References:

1. Rahman I, MacNee W. Role of oxidants/antioxidants in smoking-induced lung diseases. Free Radic Biol Med 1996;21:669-81.
2. Heffner JE, Repine JE. Pulmonary strategies of antioxidant defense. Am Rev Respir Dis 1989;140:531-54.
3. Sheriff Ds. Medical Biochemistry, Jaypee Medical Publishers, New Delhi, 2004
4. McGowan SE, Hunninghake GW. Neutrophils and emphysema. N Engl J Med 1989;321:968-70.
5. Sibille Y, Reynolds HY. Macrophages and polymorphonuclear neutrophils in lung defense and injury. Am Rev Respir Dis 1990;141:471-501.
6. Cantin A, Crystal RG. Oxidants, antioxidants and the pathogenesis of emphysema. Eur J Respir Dis 1985;66:7-17.
7. Sies H. Oxidative stress: introduction. In: Sies H, ed. Oxidative stress: oxidants and antioxidants. San Diego, CA:Academic Press, Inc, 1991:xv-xxii
8. Burton GW, Ingold KU. Autooxidation of biological molecules. 1. The antioxidant activity of vitamin E and related chain-breaking phenolic antioxidants in vitro. J Am Chem Soc 1981;103:6472-7.
9. Hatch GE. Asthma, inhaled oxidants and dietary antioxidants. Am J Clin Nutr 1995;61(suppl):625-30S.
10. Monteleone CA, Sherman AR. Nutrition and asthma. Arch Intern Med 1997;157:23-34.
11. McCay PB. Vitamin E: interaction with free radicals and ascorbate. Annu Rev Nutr 1985;5:323-40.
12. Oddy WH, de Klerk NH, Kendall GE, Mihrshahi S, Peat JK. Ratio of omega-6 to omega-3 fatty acids and childhood asthma. J Asthma 2004; 41 (3): 319-26.
13. Simopoulos AP. Omega-6/omega-3 essential fatty acids: biological effects. World Rev Nutr Diet 2009; 99: 1-16.
14. Almquist C, Garden F, Xuan W, et al. for the CAPS Team. Omega-3 and omega-6 fatty acid exposure from early life does not affect atopy and asthma at age five years. The Journal of Allergy and Clinical Immunology 2007; 119 (6): 1438-44.
15. Marks GB, Mihshahi S, Kemp AS, et al. CAPS Team. Prevention of asthma during the first 5 years of life: a randomized controlled trial. Journal of Allergy and Clinical Immunology 2006; 118 (1): 53-61.
16. Paramichael MM, Shrestha SK, Itsiopoulos C, Erbas B. The role of fish intake on asthma in children : A meta-analysis of observational studies. Pediatric Allergy Immunol. 2018 Mar 9.doi:10.1111/pai.12889 (E pub ahead of print)
17. M B Katan Trans fatty acids and plasma lipoproteins. Nutrition Reviews 2000; 58: 188-91
18. Weiland S K, Vonmutius E, Husing A, Asher M I. Intake of trans fatty acids and prevalence of childhood asthma and allergies in Europe. Lancet 1999; 353 (9169): 2040-2041.
19. Wijga AH, Houwelingen AC, Smit HA, et al. Fatty acids in breast milk of allergic and non-allergic mothers: The PIAMA birth cohort study. Pediatr. Allergy Immunol. 2003; 14 (3): 156 – 62.
20. Wijga AH, Smit HA, Kerkhof M, et al. Association of consumption of products containing milk fat with reduced asthma risk in pre – school children: in PIAMA birth cohort study. Thorax 2003; 58 (7): 567-72.
21. Varraso R, Fung TT, Barr RG, Hu FB, Willet W, Camargo CA Jr. Prospective study of dietary patterns and chronic obstructive pulmonary disease among US women. Am Clin Nutr 2007; 86(2): 488-95
22. Varraso R, Fung TT, Hu FB, Willett W, Camargo CA. Prospective study of dietary patterns and chronic obstructive pulmonary disease among US men. Thorax 2007; 62 (9): 786-91.
23. Uauy R, Aro A, Clarke R, Chafoorunissa E, L'Abbé M, Mozaffarian D, Skeaff M, Stender S. and Takella M, WHO Scientific update on trans fatty acids (TFA). European Journal of Clinical Nutrition, 2009, 63, S68-S75; doi;10,1038/ejcn.2009.15
24. Noncomminicable Diseases Progress Monitor 2017. World Health Organization Geneva, 2017,230.
25. Trak-Fellermeier MA, Brasche S, Winkler G, Koletzko B, Heinrich J. Food and fatty acid intake and atopic disease in adults. Eur Respir J 2004, 23:575-82.
26. Riedler J, Braun-Fahrlander C, Eder W; et al Exposure to farming in early life and development of asthma and allergy: a cross-sectional survey. Lancet 2001; 358:1129-1133.
27. Nagel G, Nieters A, Becker N, Linseisen J. The influence of the dietary intake of fatty acids and antioxidants on hay fever in adults. Allergy 2003; 58; 1277-1284.
28. Woods RK, Walters EH, Raven JM, et al. Food and Nutrition intakes and asthma risk in young adults. Am J Clin Nutr 2003; 78:414-21
29. Monteleone CA, Sherman AR. Nutrition and asthma. Arch Intern Med 1997;157:23-34
30. Britton J, Pavord I, Richards R, et al. Dietary sodium intake and the risk of airway hyperreactivity in a random adult population. Thorax 1994;49:875-80.
31. Knox AJ. Salt and asthma. (Editorial). BMJ 1993,307: 1159-60.
32. Britton J, Pavord I, Richards K, et al. Dietary magnesium, lung function, wheezing, and airway hyper-reactivity in a random adult population sample. Lancet 1994;344:357-62.
33. Linder MC. Nutrition and metabolism of trace elements. In: Linder MC, ed. Nutrition biochemistry and metabolism with clinical application. Norwalk, CT: Appleton and Lange, 1991:213-76.
34. Diet, Nutrition and the Prevention of Chronic Diseases. Report of a Joint WHO/FAO Expert Consultation. WHO Technical Report Series 916, Geneva, 2003 (31 May 2010 http://www.who.int/nutrition/topics/5_population_nutrient/en/index.html)
35. Global Strategy on Diet, Physical Activity and Health: a framework to monitor and evaluate implementation. Geneva, World Health Organization, 2008
35. Global Action Plan for the Prevention and Control of Noncommunicable Diseases 2013-2020.Geneva, World Health Organization, 2013:103.