



The Important Role of Dietary Calories in Asthma Pathogenesis

Muyun W¹, Jieli C², Zhimin T³, Zhujun Y³, Hao L⁴ and Jing C^{5*}

¹Department of Medical Oncology, The Fifth People's Hospital of Wuhu, China

²Department of Stomatology, Guangdong Second Traditional Chinese Medicine Hospital, China

³The First Clinical Medical College, Shandong University of Traditional Chinese Medicine, China

⁴Guangdong Key Laboratory of Pharmaceutical Bioactive Substances, Guangdong Pharmaceutical University, China

⁵Department of Clinical, Guangdong Pharmacy University, China

Abstract

Objective: In our previous work, we proposed that dietary calories play an important role in the onset of asthma. To provide further evidence of the importance of calorie reduction in the onset of the disease, we conducted an in-depth analysis on this subject.

Data Sources: Our updated analysis was based on our previous research, namely dietary non-allergic factors and atopic diseases, and our 2005 systematic review on calorie-controlled diets for chronic asthma.

Study Selections: In our search for articles published between January 2005 and October 2022, we sought directly related Randomized Controlled Trials (RCTs), which assessed the effects of calorie reduction in people with asthma compared to those on conventional diets.

Results: A total of 12 articles, with 1,794 patients, were identified and included in our updated calorie control analysis. In addition, some of the articles contained data on the impact of exercise on patients with asthma. The studies involved adults or children with a diagnosis of asthma in general practice or in outpatient departments. In particular, they demonstrated approaches for varying degrees of improvement in asthma symptom control, lung function, and inflammatory markers. Due to heterogeneity and differences among data sets, only Forced Vital Capacity (FVC) ($p < 0.05$), the Asthma Quality of Life Questionnaire (AQLQ) ($p = 0.002$), and the Asthma Control Questionnaire (ACQ) ($p = 0.00001$) could undergo meta-analysis, and yielded significant findings.

Conclusion: Our updated analysis highlights the significant role of dietary calorie control in the onset of asthma.

Keywords: Dietary Nonallergic Factors (DNAF); Mediators; Leukotrienes; Gut-lung Axis; Asthma; Risk Factors

Introduction

In China, over the past 30 years, there has been a sharp upward trend in the incidence of asthma, possibly a fourfold increase. The National Epidemiological Survey of Asthma in children aged 0 to 14 years showed the prevalence of asthma in Chinese children (aged 0-14 years old) as having increased by more than 50% every 10 years, from 1.09% in 1990 to 3.02% in 2010, and 4.2% in 2019 for adults [1]. Such an elevated prevalence, as determined by the survey, is difficult to explain by factors such as environmental pollution and increased mites.

Diet and asthma

As early as 1997, we analyzed the extensive and profound relationship between diet and asthma [2] (Figure 1), and since then, many researchers have studied this issue [3-8]. At the time, we also suggested that diet might play the most important role in the development of asthma. We comprehensively and systematically summarized the possible contribution of dietary changes to the increase in asthma and atopic diseases, and discussed in detail the relationship between diet and the disease in terms of lipid metabolism, vitamins, trace elements and other aspects of diet [2]. Later, Julia et al. in 2015 [9], followed by the Diet and Immunomodulation Working Group

OPEN ACCESS

*Correspondence:

Cheng Jing, Department of Clinical, Guangdong Pharmacy University, Guangzhou, Guangdong, China

Received Date: 12 Oct 2023

Accepted Date: 28 Oct 2023

Published Date: 02 Nov 2023

Citation:

Muyun W, Jieli C, Zhimin T, Zhujun Y, Hao L, Jing C. The Important Role of Dietary Calories in Asthma Pathogenesis. *Clin Case Rep Int.* 2023; 7: 1622.

Copyright © 2023 Jing C. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.



Figure 1: The same theme continues over 24 years (1997 to 2021).

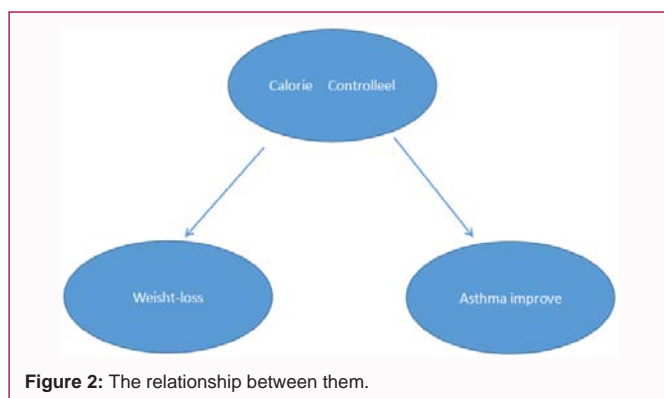


Figure 2: The relationship between them.

of the European Society for Allergy and Clinical Immunology [10] in 2019, and Frontela-Saseta et al. [11] in 2020 all reported on the continuing academic work on this topic. In 2005, we proposed a new concept of Dietary Non-Allergic Factors (DNAF) [12]. Later, in 2013, we supplemented our findings by describing all the dietary factors apart from the allergy caused by protein, including: Lipids, protein, carbohydrate, vitamins, trace elements, dietary probiotics, gastric esophageal reflux, etc. [13].

Calorie control

There are two types of calorie control: Calorie restriction and exercise, which actually limit calorie intake and increase calorie consumption. We published an article in 2005 and noticed the effectiveness of calorie control in the treatment of asthma patients. However, there were too few articles on randomized controlled trials at that time. At the same time, in theory, there is still no emphasis on this issue, but rather on the effects caused by weight loss. More emphasis is now placed on the relationship between weight gain or obesity [14] and asthma, while neglecting calorie. The relationship between them is shown in Figure 2. Although there is a growing body of research about the role of diet in the treatment of asthma, we sought to expand this knowledge by looking more specifically at current work on the role of calorie control in the treatment of asthma, including epidemiology and pathophysiology.

In our search, we identified reports summarizing all the literature on dietary interventions for asthma, divided into five categories: Low-

calorie diets; dietary pattern; antioxidants; lipids; and miscellaneous elements (dairy, vitamin D, salt). Their conclusions: The evidence shows that, for obese adults with asthma, the best dietary intervention seems to be caloric restriction, regardless of specific dietary components [15].

Objectives

To explore the role of calorie reduction in the treatment of asthma, including its impact on the exercise.

Types of intervention

We included studies assessing the effects of dietary calorie reduction in people with asthma, compared with conventional diet. We also noticed the articles on exercise of asthma patients. We excluded studies of dietary allergen avoidance and supplementation (such as fish oil or selenium). Studies of any duration were considered.

Types of outcome measures

Asthma Control Questionnaire (ACQ) score, Indicators of lung function- FEV1, Forced Vital Capacity (FVC), Asthma Quality of Life Questionnaire (AQLQ) Morning Peak Expiratory Flow (PEF), Health-Related Quality of Life (HRQOL), Pulmonary Diffusing Capacity (DLco): Quantity (ml) of carbon monoxide is transferred under unit of time (1 min) and unit of pressure difference (1kPa) (ml/kPa*min). It can be expressed by the following formula: DLco = Vco

(Vco: Carbon Monoxide of Lung Intake Rate).

Search strategy

The MEDLINE (via PubMed), Embase, and Scopus databases were searched for articles published from January 2005 to October 2022. The following search terms were used: Diet* or calorie* or energy* or food or feed* or eat* or weight* or obese*.

Study selection

CJ and WMY scanned the titles and abstracts of all reports identified through the searches were scanned by two reviewers. Disagreement was resolved by consensus. Full reports were obtained for trials appearing to meet the inclusion criteria or for which there was insufficient information in the title and abstract to make a clear decision.

Quality assessment

Methodological quality of all the trials was scored independently by two authors using two sets of criteria: Jadad and the Cochrane criteria for concealment of allocation.

Data extraction

Data were extracted by two reviewers independently using specifically designed data extraction forms. The characteristics of the trial participants, interventions and outcomes for the included trials are presented in study tables.

Data synthesis

Studies were to be pooled where possible. For continuous outcome variables, a treatment effect for each trial was calculated using RevMan analyses. Pooled estimates were to be generated using a weighted mean difference or a standardized mean difference depending upon whether the scales used to measure effects were the same. For dichotomous outcomes a Relative Risk (RR) was calculated. Pooled treatment effects would be expressed with their 95% Confidence Intervals (95% CI). Heterogeneity of effect size across pooled studies would be calculated, with $p < 0.05$ used as the cut

Table 1: Existing randomized controlled trials of calorie control in obese and non-obese adults and children with asthma.

Section	Study	Methods	participants	Asthma Diagnosis	Intervention and Dose	Duration	N	Age
Dietary restriction	Dias-Junior et al. [16]	Parallel	Obese adults with severe asthma	Previous physician's diagnosis and GINA guidelines	Low-calorie intake, use of sibutramine (10 mg/day) and use of orlistat (max. 120 mg/day)	6 months	33	43
	Jensen et al. [17]	Parallel	Obese children with asthma	Previous pediatrician's diagnosis	Energy reduction (-500 kcal/day) and counselling sessions	10 weeks	28	8--17
	Luna-Pech et al. [18]	Parallel	Obese children with asthma	Previous pediatrician's diagnoses and GINA guidelines	Normocaloric diet based on normal requirements for height and meal planning	28 weeks	51	12--16
	Özbey et al. [19]	Parallel	Obese adults with asthma	Previous physician's diagnosis	A modest weight loss of 5%-10% is recommended for overweight. A diet was planned to consist of 10%-20% proteins, 45%-60% carbohydrates and 25%-30% fats	10 weeks	55	20--65
Diet+ Exercise	Freitas et al. [20]	Parallel	Obese adults with asthma	Previous physician's diagnosis	Caloric restriction+ aerobic and resistance muscle training	3 months	51	30--60
	El-Kader et al. [21]	Parallel	Obese children with asthma	Previous pediatrician's diagnosis	The prescribed low-calorie diet was balanced, with 15% as protein, 30 to 35% as fat and 50 to 55% as carbohydrate, on average, to provide approximately 250 kcal per day, as previous research calculated that an energy deficit of more than 250 kcal per day is needed to prevent further weight gain + warm-up, maintaining, and cool down.	2 months	80	12--18
	Ma et al. [22]	Parallel	Obese adults with asthma	Previous physician's diagnosis	Healthy eating with moderate calorie reductions (by 500-1,000 kcal/d, but daily total calories no less than 1,200 kcal)+ensured intervention fidelity through standard training.	12 months	289	18--70
	Scott et al. [23]	3 arms	Obese adults with asthma	Previous physician's diagnosis	Participants were prescribed an intake of 3700-4900 kilojoules (kJ)/day (885-1170 kcal/day)+ Participants received a 12-week gymnasium membership and a group personal training session for 1 h each week.	10 weeks	38	18--70
	Stenius-Aarniala et al. [24]	Parallel	Obese adults with asthma	Previous physician's diagnosis	The daily dose gave 1760kJ of energy and contained daily allowances of all essential nutrients. + The patients were encouraged to increase exercise corresponding to an extra 30-minute walk daily.	10 weeks	38	18--60
	Toennesen et al. [25]	4 arms	Nonobese adults with asthma	Previous physician's diagnosis	The study was a single-center randomized controlled parallel group study with 4 randomization groups: (1) exercise group, (2) diet group, (3) exercise + diet group, and (4) control group (usual care). Exercise group. The training intervention consisted of 8 weeks of high-intensity interval training using the "10-20-30" concept on indoor spinning bikes 3 times a week. +Diet group Patients bought and prepared their food based on principles of overall high protein content (25%-28% of energy) and a low GI (≤ 55).	8 weeks	125	18--65
	Willeboordse et al. [26]	Parallel	Obese children with asthma	Previous physician's diagnosis and GINA guidelines	Multifactorial weight intervention consisting of 18 lifestyle sessions (including dietary advice and cognitive behavioral therapy), 10 parental sessions, 8 individual sessions, and regular sports sessions	18 weeks	74	6--16
Exercise	Wu et al. [27]	Systematic review (22)	Adults and children with asthma	Previous physician's diagnosis and GINA guidelines	Moderate intensity, at least 20 minutes and two times a week, over a minimum period of four weeks. the training modes were treadmill walking, cycling, and swimming	6-16 weeks	932	6--50

off level for significance.

Results

Description of studies

Electronic and manual searches in October 2022 identified 2865 references. Of these, a total of 29 articles were identified for possible inclusion. Neither HowNet nor Wanfang database can be found. After reviewing the methods section of each of these studies, we excluded 17 from the review. Twelve trials met the inclusion criteria. For a full description see characteristics of included studies (Table 1).

Twelve studies were involved 1,794 patients included in our systematic review of calorie control, all of which focused on improving asthma symptoms and lung function to varying degrees. They also identified various inflammatory factors, such as cells, such as sputum and blood, and pro-inflammatory markers such as C-reactive protein, and a decrease in the neutrophilic airway.

Table 1 lists the included 12 RCT studies of obese and non-obese children and adults that focused on dietary restrictions (four articles); diet and exercise (seven articles); and exercise alone (one article). Table 2 summarizes the results of those RCTs.

Results of the meta-analysis

Due to heterogeneity and differences between data, only FVC, AQLQ and ACQ, three projects can undergo meta-analysis, respectively $P < 0.05$, $P = 0.002$ and $P = 0.00001$ (Figure 3). In meta-analysis, there are only two for each project. The data that can be added cannot be analyzed using funnel plots.

These studies indicated that calorie control is the best intervention method of non-drug treatment at present, and its mechanism is worthy of further exploration.

Discussion

A Key role of DNAF in the pathogenesis of asthma?

What are the most important risk factors for asthma? Is it from the respiratory tract or the digestive tract? This is the most critical issue in understanding and treating asthma. This article proposes DNAF. We further analyze the macro and micro factors related to dietary calories (Figure 4). The macro level is the long-term aspect, which can also be said to be a general direction such as epidemiology, while the micro level is the detailed aspect specific local pathophysiology. The Mediterranean diet is based upon the eating patterns of traditional cultures in the Mediterranean region. It is a style of eating based on vegetables, fruits, fish, grains, beans and olive oil. Fruit and Vegetable index are based upon the eating patterns of Fruit and Vegetable.

We discovered that the Dietary Inflammatory Index (DII) [28-30], Mediterranean diet index [31], and Fruit and Vegetable Index (FAVI) [32] had different impacts on the onset of asthma. Furthermore, the low-fat group showed significant improvements in asthma, lung function, and inflammatory factors as compared to the high-fat group [33,34].

Possible mechanism of asthma: the pathological digestion and absorption of protein and fat

Our analysis features the continuing study of the impact of calorie control on the onset of asthma. To further understand the relationship between calorie intake and the onset of asthma, as described in the included articles, it is worth commenting on the bidirectional communication pathway between the gut and lung, i.e., the gut-lung axis [35,36]. At present, this academic perspective is limited to the probiotics between the intestinal tract and the respiratory tract, and has not yet expanded to other fields. The connection between the gut and the respiratory tract is much broader in terms of physiology and pathophysiology. The medium may cause an increase in airway

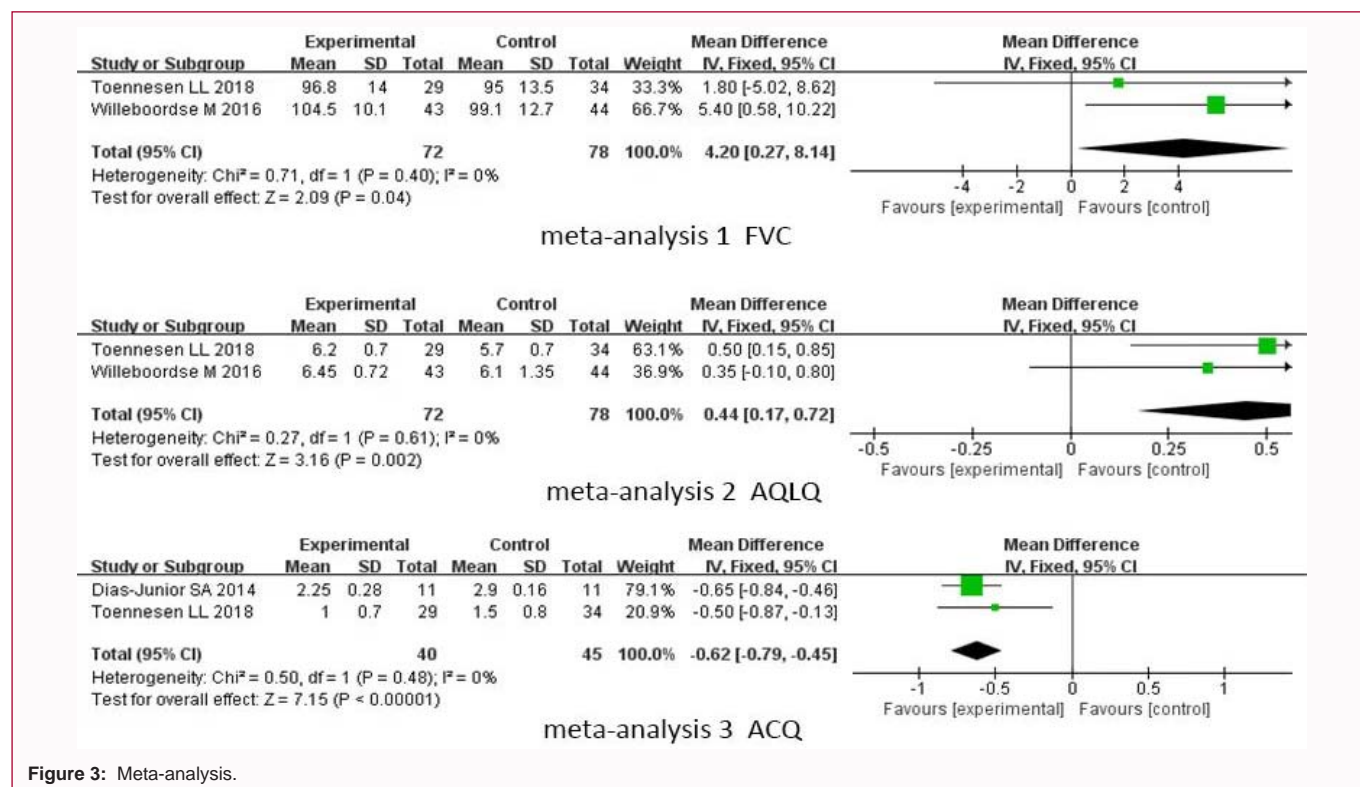


Figure 3: Meta-analysis.

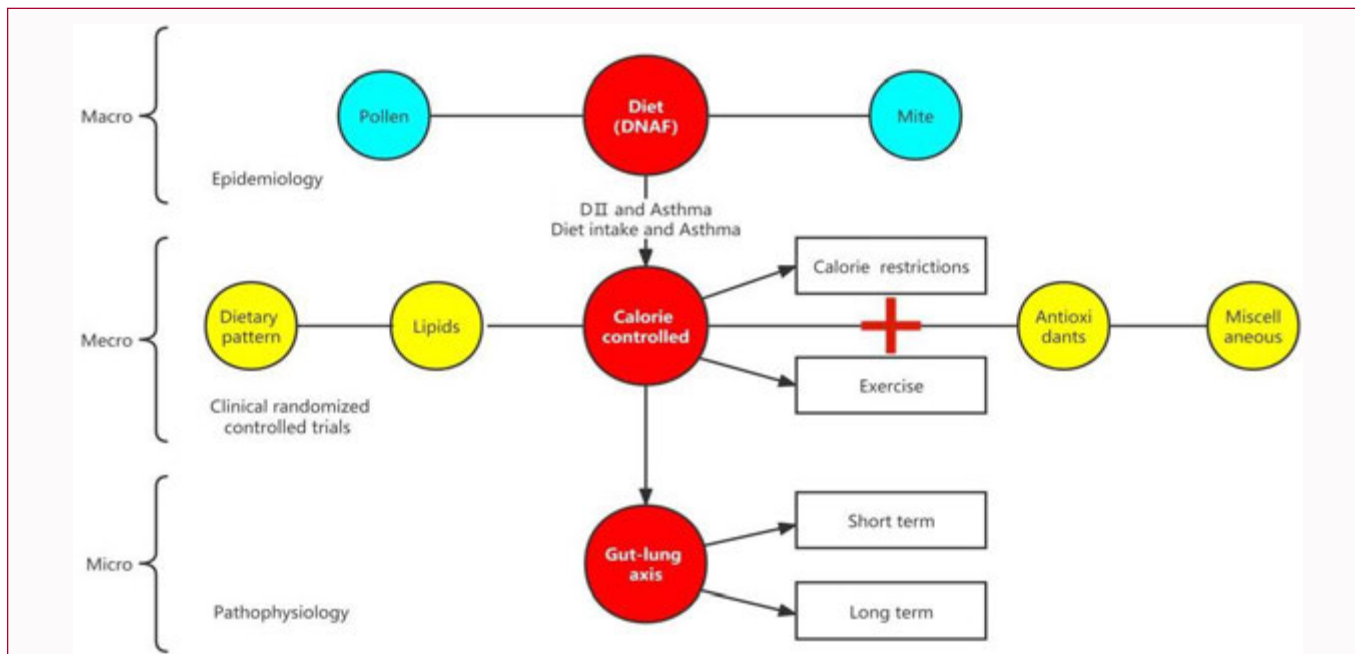


Figure 4: A Key Role of Dietary nonallergic factors in the pathogenesis of asthma.

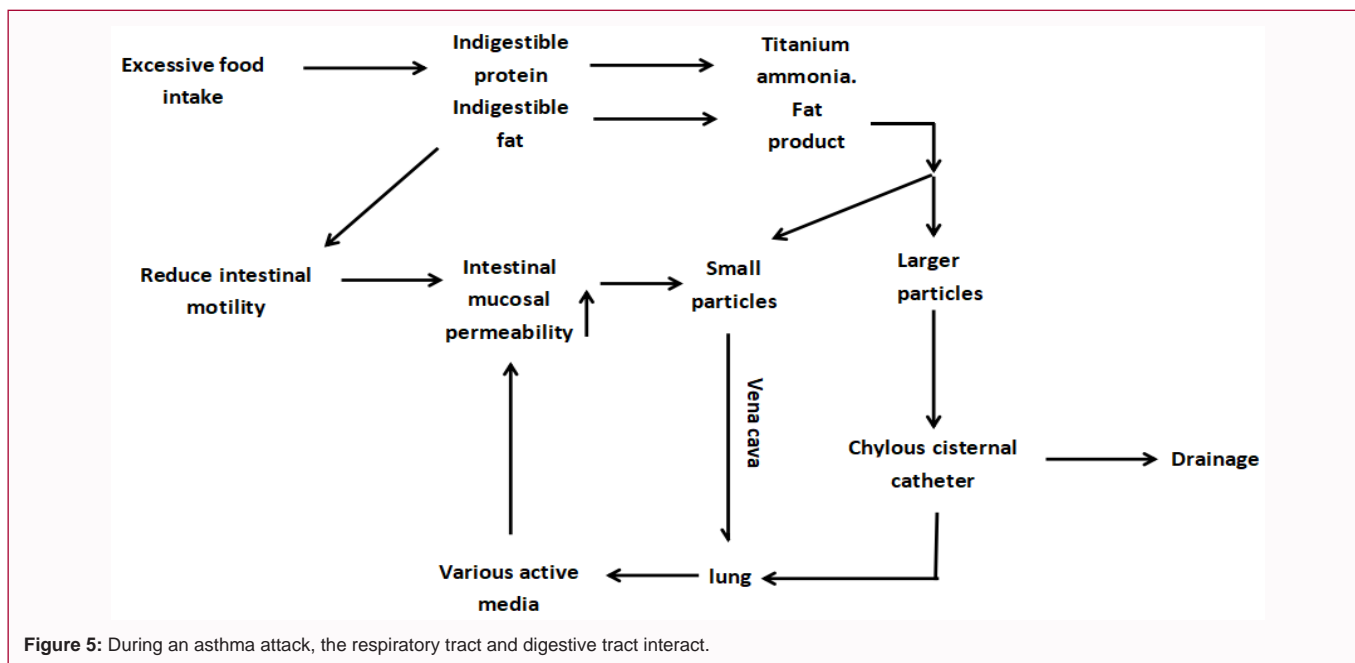


Figure 5: During an asthma attack, the respiratory tract and digestive tract interact.

inflammatory cells in the short term, and in the long term, there may be a formation of an allergic constitution through lipid metabolism disorder and a reduction in probiotics. When gastrointestinal dysfunction occurs, numerous events happen. First, food cannot be completely digested, protein turns into ammonia and peptide, fat turns into a variety of fat products, and incomplete digestion of food will weaken the gastrointestinal movement. Next, gastrointestinal mucosa permeability increases, and protein, as well as incomplete digestion products from fat, namely ammonia, peptide, and lipid products are absorbed through the blood circulation, serving as the active medium of an asthma attack. These mediators can be divided into large particles; large particles trans chylous pool chest ducts, and small particles through the vena cava. Both pathways can eventually

reach the lungs, and stimulate the respiratory tract, resulting in asthma.

Under normal circumstances, there are five barriers between the intestinal tract and blood vessels and lymphatic vessels: Biological; chemical; physical; immune; and vascular, preventing the abnormal exchange of substances between the intestine and blood vessels. However, under pathological conditions, this permeability is greatly increased, leading to a greater possibility of intestinal contents entering blood vessels and lymphatic vessels.

Thoracic catheter drainage was used for asthma

Thoracic catheter drainage in the treatment of asthma has achieved good results, which is also important evidence [37]. The

Table 2: Results of randomized controlled trials.

Study	Jadad	Lung Function						Inflammatory Markers		
		ACQ	LTA	AQLQ	FEV	FVC	ERV	FeNO	Cells (Sputum,Blood)	Pro-Inflammatory Markers
Dias-Junior et al. [16]	3	↑				↑				=
Jensen et al. [17]	3	↑					↑	↓		C-Reactive protein ↓
Luna-Pech et al. [18]	3	↑								
Özbey et al. [19]	2			↑	↑	↑				
Freitas et al. [20]	4									
El-Kader et al. [21]	2								↓ tumor necrosis factor-alpha (TNF-alpha), interleukin-6 (IL-6), interleukin-8 (IL-8)	
Ma et al. [22]	4	↓ weight loss of 10%	↑							
Scot et al. [23]	4	↑								↓ Neutrophilic airway
Stenius-Aarniala et al. [24]	3	↑			↑	↑				
Toennesenet al. [25]	4	↑		↑	=			=	=	
Willeboordse et al. [26]	3	↑		↑		↑				
Wu et al. [27]	Mean 2.9			↑	↑	↑				

Abbreviations: AQLQ: Asthma Quality of Life Questionnaire; LTA: Leisure-Time Activity; ERV: Expiratory Reserve Volume; FEV1: Forced Expiratory Flow in one second; FVC: Forced Vital Capacity; ACT: Asthma Control Test; ACQ: Asthma Control Questionnaire; (P)AQLQ: (Pediatric) Asthma Quality of Life Questionnaire; FeNO: Fractional exhaled Nitric Oxide; Th: T Helper Cell; IgE: Immunoglobulin E; QoL: Quality of Life; ↑: Significant Increase as Compared to the Control Group; ↓: Significant Decrease as Compared to the Control Group; =: no change as Compared to the Control Group; *: Jadad Score was Calculated to Assess the Methodological Quality of the RCTs

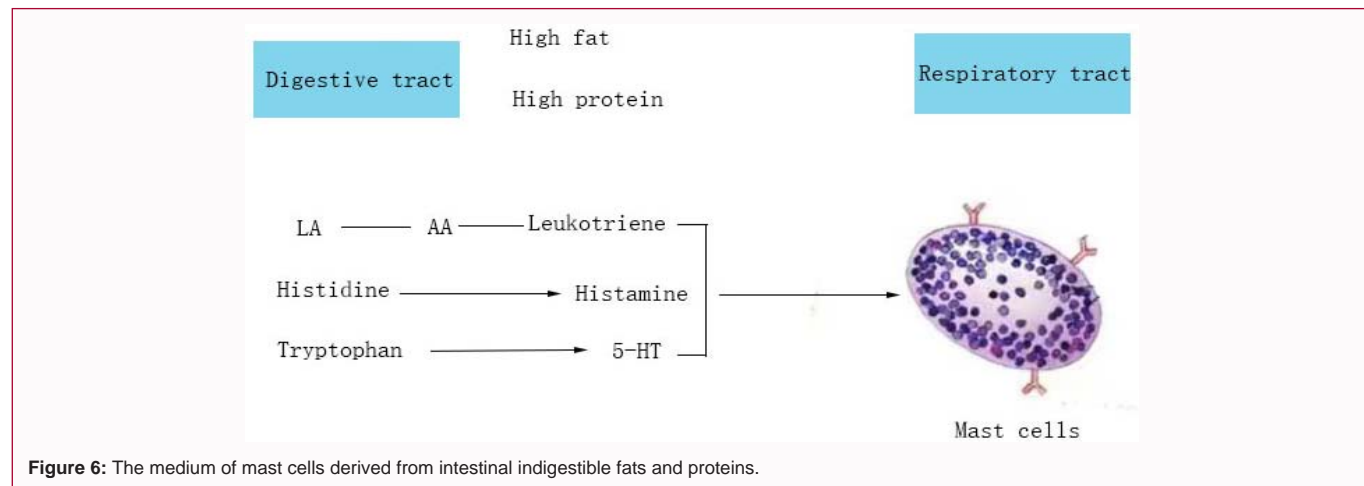


Figure 6: The medium of mast cells derived from intestinal indigestible fats and proteins.

thoracic duct is the largest lymphatic vessel throughout the body and transports about 70% of the lymphatic and chylous fluid throughout the body into the bloodstream (Figure 5).

There are new sources of mediators for mast cells

As determined by our systematic analysis, the medium of mast cells may be directly derived from intestinal indigestible fats and proteins. Linoleic acid is converted into arachidonic acid and then into leukotriene, which enters mast cells. Leukotriene is currently considered the most important mediator within mast cells. Similarly, histidine forms into histamine. The metabolism of mast cells and their intracellular media are closely related to lipids. Recent studies have revealed that in addition to the phospholipids in mast cell membranes, triglycerides in mast cell lipid droplets are also substrate sources for eicosanoid formation [38] (Figure 6).

Conclusion

Reducing the overall calorie intake of the diet is recommended for limiting the onset of asthma. Special attention should be paid to the proportion of basic nutrients intake, such as fat, protein, and sugar, while grains and vegetables should constitute the main part of a healthy diet.

Acknowledgment

We would like to express our gratitude for the support from the Layered Cultivation of Health High-level Talents of the "Huatuo Plan" of Wuhu City (WWZ [2021] No.42). We would like to thank Wu MY and Cheng JL who contributed equally to the writing of the manuscript and collected data. We would like to thank Tan ZM and Yu ZJ who revised and supplemented parts of the manuscript. We would like to thank Liu H who made the pictures. We would like to

thank Cheng J who reviewed and approved the final version of this article.

Funding

This study is partially supported by the Layered Cultivation of Health High-level Talents of the "Huatuo Plan" of Wuhu City (WWZ [2021] No.42).

References

- Huang K, Yang T, Xu J, Yang L, Zhao J, Zhang X, et al. Prevalence, risk factors, and management of asthma in China: A national cross-sectional study. *Lancet*. 2019;394(10196):407-18.
- Cheng J. The nonspecific role of diet in the pathogenesis of asthma. *J Guangdong Pharm Univ*. 1997;13:170-3.
- Reyes-Angel J, Han Y-Y, Litonjua AA, Celedón JC. Diet and asthma: Is the sum more important than the parts? *J Allergy Clin Immunol*. 2021;148(3):706-7.
- Ellwood P, Asher MI, Björkstén B, Burr M, Pearce N, Robertson CF. Diet and asthma, allergic rhinoconjunctivitis and atopic eczema symptom prevalence: An ecological analysis of the International Study of Asthma and Allergies in Childhood (ISAAC) data. *Eur Respir J*. 2001;17(3):436-43.
- Spector SL, Surette ME. Diet and asthma: has the role of dietary lipids been overlooked in the management of asthma? *Ann Allergy Asthma Immunol*. 2003;90(4):371-7; quiz 377-8, 421.
- Tabak C, Wijga AH, de Meer G. Diet and asthma in Dutch school children (ISAAC-2). *Thorax*. 2006;61(12):1048-53.
- Han Y-Y, Blatter J, Brehm JM, Forno E, Litonjua AA, Celedón JC. Diet and asthma: Vitamins and methyl donors. *Lancet Respir Med*. 2013;1(10):813-22.
- Guilleminault L, Williams EJ, Scott HA, Berthon BS, Jensen M, Wood LG. Diet and asthma: is it time to adapt our message? *Nutrients*. 2017;9(11):1227.
- Julia V, Macia L, Dombrowicz D. The impact of diet on asthma and allergic diseases. *Nat Rev Immunol*. 2015;15(5):308-22.
- Venter C, Greenhawt M, Meyer RW, Agostoni C, Reese I, du Toit G, et al. EAACI position paper on diet diversity in pregnancy, infancy and childhood: Novel concepts and implications for studies in allergy and asthma. *Allergy*. 2020;75(3):497-523.
- Frontela-Saseta C, González-Bermúdez CA, García-Marcos L. Diet: A specific part of the Western lifestyle pack in the asthma epidemic. *J Clin Med*. 2020;9(7):2063.
- Cheng J, Pan T, Ye GH, Liu Q. Calorie controlled diet for chronic asthma. *Cochrane Database Syst Rev*. 2005;20(3):CD004674.
- Cheng J, Wu XH. Dietary non-allergic factors and atopic diseases. *J Clin Pulm Med*. 2013;114-7.
- Wood LG. Diet, Obesity, and Asthma. *Ann Am Thorac Soc*. 2017;14(Suppl 5):S332-8.
- Forte GC, da Silva DTR, Hennemann ML, Sarmento RA, Almeida JC, Dalcin PDTR. Diet effects in the asthma treatment: A systematic review. *Crit Rev Food Sci Nutr*. 2017;58(11):1878-87.
- Dias-Junior SA, Reis M, de Carvalho-Pinto RM, Stelmach R, Halpern A, Cukier A. Effects of weight loss on asthma control in obese patients with severe asthma. *Eur Respir J*. 2014;43(5):1368-77.
- Jensen ME, Gibson PG, Collins CE, Hilton JM, Wood LG. Diet-induced weight loss in obese children with asthma: A randomized controlled trial. *Clin Exp Allergy*. 2013;43(7):775-84.
- Luna-Pech JA, Torres-Mendoza BM, Luna-Pech JA, Garcia-Cobas CY, Navarrete-Navarro S, Elizalde-Lozano AM. Normocaloric diet improves asthma-related quality of life in obese pubertal adolescents. *Int Arch Allergy Immunol*. 2014;163(4):252-8.
- Özbey Ü, Balaban S, Sözüer ZÇ, Uçar A, Mungan D, Mısırlıgil Z. The effects of diet-induced weight loss on asthma control and quality of life in obese adults with asthma: A randomized controlled trial. *J Asthma*. 2019;57(6):618-26.
- Freitas PD, Ferreira PG, Silva AG, Stelmach R, Carvalho-Pinto RM, A Fernandes FLA, et al. The role of exercise in a weight-loss program on clinical control in obese adults with asthma. A randomized controlled trial. *Am J Respir Crit Care Med*. 2017;195(1):32-42.
- El-Kader MSSA, Al-Jiffri O, Ashmawy EM. Impact of weight loss on markers of systemic inflammation in obese Saudi children with asthma. *Afr Health Sci*. 2013;13(3):682-8.
- Ma J, Strub P, Xiao L, Lavori PW, Camargo CA Jr, Wilson SR, et al. Behavioral weight loss and physical activity intervention in obese adults with asthma. A randomized trial. *Ann Am Thorac Soc*. 2015;12(1):1-11.
- Scott HA, Gibson PG, Garg ML, Pretto JJ, Morgan PJ, Callister R. Dietary restriction and exercise improve airway inflammation and clinical outcomes in overweight and obese asthma: A randomized trial. *Clin Exp Allergy*. 2013;43(1):36-49.
- Stenius-Aarniala B, Poussa T, Kvarnström J, Grönlund EL, Ylikahri M, Mustajoki P. Immediate and long-term effects of weight reduction in obese people with asthma: Randomised controlled study. *BMJ*. 2000;320(7238):827-32.
- Toennesen LL, Meteran H, Hostrup M, Geiker NRW, Jensen CB, Porsbjerg C, et al. Effects of exercise and diet in nonobese asthma patients- A randomized controlled trial. *J Allergy Clin Immunol Pract*. 2018;6:803-11.
- Willeboordse M, van de Kant KDG, Tan FES, Mulken S, Schellings J, Crijs Y, et al. A multifactorial weight reduction program for children with overweight and asthma: A randomized controlled trial. *PLoS One*. 2016;11(6):e0157158.
- Wu X, Gao S, Lian Y. Effects of continuous aerobic exercise on lung function and quality of life with asthma: A systematic review and meta-analysis. *J Thorac Dis*. 2020;12(9):4781-95.
- Han Y-Y, Forno E, Shivappa N, Wirth MD, Hébert JR, Celedón JC. The dietary inflammatory index and current wheeze among children and adults in the United States. *J Allergy Clin Immunol Pract*. 2018;6(3):834-41.e2.
- Han Y-Y, Jerschow E, Forno E, Hua S, Mossavar-Rahmani Y, Perreira KM, et al. Dietary patterns, asthma, and lung function in the Hispanic community health study/study of Latinos. *Ann Am Thorac Soc*. 2020;17(3):293-301.
- Wood LG, Shivappa N, Berthon BS, Gibson PG, Hébert JR. Dietary inflammatory index is related to asthma risk, lung function and systemic inflammation in asthma. *Clin Exp Allergy*. 2015;45(1):177-83.
- Berthon BS, Macdonald-Wicks LK, Gibson PG, Wood LG. Investigation of the association between dietary intake, disease severity and airway inflammation in asthma. *Respirology*. 2013;18(3):447-54.
- Romieu I, Barraza-Villarreal A, Escamilla-Núñez C, Texcalac-Sangrador JL, Hernandez-Cadena L, Díaz-Sánchez D, et al. Dietary intake, lung function and airway inflammation in Mexico City school children exposed to air pollutants. *Respir Res*. 2009;10(1):122.
- Wood LG, Garg ML, Gibson PG. A high-fat challenge increases airway inflammation and impairs bronchodilator recovery in asthma. *J Allergy Clin Immunol*. 2011;127(5):1133-40.
- Li Q, Baines KJ, Gibson PG, Wood LG. Changes in expression of genes regulating airway inflammation following a high-fat mixed meal in asthmatics. *Nutrients*. 2016;8(1):30.
- Fрати F, Salvatori C, Incorvaia C, Bellucci A, Cara GD, Marcucci F, et al. The role of the microbiome in asthma: the gut-lung axis. *Int J Mol Sci*. 2018;20(1):123.

36. Hufnagl K, Pali-Schöll I, Roth-Walter F, Jensen-Jarolim E. Dysbiosis of the gut and lung microbiome has a role in asthma. *Semin Immunopathol.* 2020;42(1):75-93.
37. Xiaozhi Q, Jizong H, Yue C. Long term efficacy follow-up of thoracic catheter drainage treatment for refractory bronchial asthma. *Zhejiang Clin Med.* 2005;7(5):511-2.
38. Dichlberger A, Schlager S, Kovanen PT, Schneider WJ. Lipid droplets in activated mast cells – A significant source of triglyceride-derived arachidonic acid for eicosanoid production. *Eur J Pharmacol.* 2016;785:59-69.