Nutritional modulation of inflammation in airways disease

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Outline

• Asthma, Inflammation & Air Pollution
• Asthma and:
  ➢ Antioxidants
  ➢ Omega-3 fatty acids
  ➢ Vitamin D
• Summary and Conclusions
Global Burden of Asthma

Host Factors:
- genes
- gender

Environmental:
- allergens
- infections (early childhood)
- occupational exposure
- smoking
- air pollution
- diet:
  - low AO intake
  - low omega-3:omega-6
  - saturated/ trans fat

- Affects 300m people worldwide
- Prevalence: increased over time, higher in westernised countries
- Migration to western countries can lead to asthma
Asthma is a chronic inflammatory disorder of the airways. Inflammation occurs in asthma because asthmatics exhibit an exaggerated immune response to stimuli (e.g. air pollution, allergens, viruses). Chronically inflamed airways become hyperresponsive and have limited airflow, leading to recurrent episodes of wheezing, breathlessness, chest tightness and coughing.
What is Asthma?

Air enters respiratory tract via mouth and nose and enters bronchial tubes

Smooth muscle thickens, contracts and becomes hyperresponsive

Damage to airway epithelium

Excess mucus

ASTHMA: Inflamed bronchial tube

NORMAL bronchial tube

Key goal of asthma management is...

to prevent asthma exacerbations – acute episodes involving deterioration of inflammation, lung function and symptoms.
Asthma and Inflammation

ALLERGENS  VIRUSES  AIR POLLUTION

Activated macrophages and epithelial cells

Activated Th2 cells

IL-4, IL-5, IL-13 ↓ Eosinophils

IL-8, IL-6 ↓ Neutrophils

ROS

Airway Inflammation & Oxidative Stress

Systemic Inflammation & Oxidative Stress

Comorbidities

Asthma and Inflammation

% Subjects with High IL-6

Healthy Controls  Asthma (Non-neutrophilic)  Asthma (Neutrophilic)

P<0.001

*†

% FEV1  %FVC  FEV1/FVC  ACQ

p<0.001  p<0.001  p=0.016  p=0.008

Healthy Controls  Asthma (Non-neutrophilic)  Asthma (Neutrophilic)

Rhinitis  Cardiovascular  Hypercholesterolemia  GORD  Skin disorders  Mental health  Arthritis  Osteoporosis  Bowel disease  OSAS  Other

* (Wood Chest 2011)
Asthma and Antioxidants

Systemic oxidative stress in asthma
(Wood, Lipids, 2000)

Airway oxidative stress in asthma

Activated inflammatory cells in asthma
- host AO defences overwhelmed
  – antioxidant therapy?
Asthma and Antioxidants

Many observational studies link reduced levels of dietary AO to asthma:
- Vitamin C, E
- Carotenoids
- Selenium


*BUT*....

AO supplementation studies limited or no efficacy:
Vitamin C and E, Se
(Kaur, 2009; Shaheen, 2007; Pearson, 2004)
Asthma and Antioxidants

Whole food intervention effective (Wood, Am J Clin Nutr, 2011)

n=136 asthmatics

RCT: High vs Low AO diet for 14 wk

High vs Low AO diet:
- ↑ B grp vit, vit C, β-carotene intake
- ↑ plasma vitamin E levels

Low AO diet:
- ↑ exacerbation risk
- ↑ inflammation

→ AO combinations important
Asthma and Antioxidants

Summary

Observational studies:
• Dietary AO deficiencies occur in asthma (vit C, E, Se, carotenoids)

Supplementation studies:
• To date have focused on single nutrients (vitamin C, E and Se) and results are disappointing
• Whole food antioxidant intervention was effective in:
  • increasing levels of micronutrients (vit C, E, B grp, β-carotene)
  • protecting against inflammation
  • reducing asthma exacerbation risk
  → Multiple antioxidants likely to be important in combination
• Dietary pattern adopted during intervention routinely consumed by only 5% population
  → Role for supplementation?
Asthma and Omega-3 FA

Summary

Preclinical studies:
• Omega-3 FA suppress inflammatory response to asthma triggers: allergens (Wood et al, 2010, Clin Exp Allergy); viruses (Saedisomeolia, Wood et al, Brit J Nutr, 2009)

Observational studies:
• Omega-3 fatty acid or fish intake is associated with improved lung function, decreased asthma risk, AHR, wheeze in many (not all) studies (eg Schwartz, 94, 2000; Yu, 1996)

Clinical supplementation studies:
• Few available and data inconclusive, however .... no studies have examined the effect of omega-3s on exacerbation risk (Cochrane, 2011)
• Omega-3 to reduce asthma exacerbation risk ??
Asthma and Vitamin D

Summary

Observational studies:
- Some studies show an association between asthma risk or reduced lung function and low vitamin D levels
  
  (Black 2005; Brehm 2009)

Supplementation studies:
- Only one study to date:
  rate of first exacerbation reduced in vitamin D3 responders only (25-hydroxyvitamin D >30ng/mL)
  
  (Castro, 2014)
Summary & Conclusions

- Nutritional deficiencies linked to asthma include: vitamin C, vitamin E, Se, carotenoids, omega-3 FA, vitamin D
- Supplementation studies using individual nutrients show limited or no efficacy, while whole food intervention (leading to increased vitamin C and E, β-carotene and B group vitamin levels) reduced asthma exacerbation risk → nutrient combinations important
- Key outcomes for future nutritional interventions in asthma: reduction in inflammatory biomarkers (airway and systemic) and reduction in exacerbation risk
Acknowledgments

INVESTIGATORS
- Peter Gibson
- Katie Baines
- Paul Foster
- Phil Hansbro
- Peter Wark
- Leia Hazlewood
- Joanne Smart
- Hayley Scott
- Manohar Garg
- Ahmad Saedisomeolia
- Jodie Simpson
- HMRI Respiratory Research Laboratory Team

DSM
- Manfred Eggersdorfer
- Celine Zuber

FUNDING:
- NHMRC
- HMRI
- Asthma Foundation

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