Vitamin D to prevent exacerbations of COPD

systematic review and meta-analysis of individual participant data from randomised controlled trials

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Introduction

- COPD affects more than 170million people worldwide and caused an estimated 3.2million deaths in 2015.
- COPD mortality arises primarily during episodes of acute worsening of symptoms termed exacerbations: these may be classified as severe (ie, requiring emergency department attendance or hospitalisation) or moderate (ie, requiring treatment with systemic corticosteroids or antibiotics, or both, but not precipitating emergency department attendance or hospitalisation).

Introduction

- COPD exacerbations are commonly triggered by respiratory viruses and bacteria, which increase airway inflammation.
- Vitamin D metabolites support the induction of antiviral and antimicrobial effector mechanisms and attenuate inflammatory responses.
- Moreover, meta-analyses of individual participant data (IPD) from randomised controlled trials (RCTs) have shown that vitamin D supplementation reduces risk of acute respiratory infections and exacerbations of asthma.

Introduction

- Taken together, these lines of evidence suggest a potential role for vitaminD supplementation in prevention of COPD exacerbations.
- Vitamin D deficiency is common in patients with COPD, but consistent associations between circulating concentrations of 25-hydroxy vitaminD (25(OH)D, the major vitaminD metabolite) and risk of COPD exacerbation have not been demonstrated.

Introduction

- Four double-blind placebo-controlled RCTs have been published, investigating effects of vitamin D supplementation on the risk of COPD exacerbation: of these, three reported no effect overall and one reported a protective effect overall.
- These RCTs have not previously been meta-analysed. We therefore set out to meta-analyse IPD from these studies to determine whether vitamin D supplementation reduces COPD exacerbation rate overall and to explore whether the effects of this intervention vary according to potential effect modifiers, including baseline vitamin D status.

background

randomised controlled trials (rcts) of vitamin D to prevent COPD exacerbations have yielded conflicting results.

individual participant data meta-analysis could identify factors that explain this variation.

Methods

PubMed, embase, the cochrane central register of controlled trials and Web of Science were searched from inception up to and including 5 October 2017 to identify rcts of vitamin D supplementation in patients with cOPD that reported incidence of acute exacerbations.

individual participant data meta-analysis was performed using fixed effects models adjusting for age, sex, global initiative for chronic Obstructive lung Disease spirometric grade and trial

results

Four eligible rcts (total 560 participants) were identifed; individual participant data were obtained for 469/472 (99.4%) participants in three rcts.

Supplementation did not influence overall rate of moderate/severe COPD exacerbations (adjusted incidence rate ratio (airr) 0.94, 95% ci 0.78 to 1.13).

Pre specified subgroup analysis revealed that protective effects were seen in participants with baseline 25-hydroxyvitamin D levels <25 nmol/l (airr 0.55, 95% ci 0.36 to 0.84) but not in those with baseline 25-hydroxyvitamin D levels ≥25 nmol/l (airr 1.04, 95% ci 0.85 to 1.27; p for interaction=0.015).

Vitamin D did not influence the proportion of participants experiencing at least one serious adverse event (adjusted Or 1.16, 95% ci 0.76 to 1.75).

Conclusions

Vitamin D supplementation safely and substantially reduced the rate of moderate/ severe COPD exacerbations in patients with baseline 25-hydroxyvitamin D levels <25 nmol/l but not in those with higher levels


Salmon
Fortified cereal
Milk
Vitamin D
Cheese
Tuna
Eggs
Sunlight

Vitamin D Overview

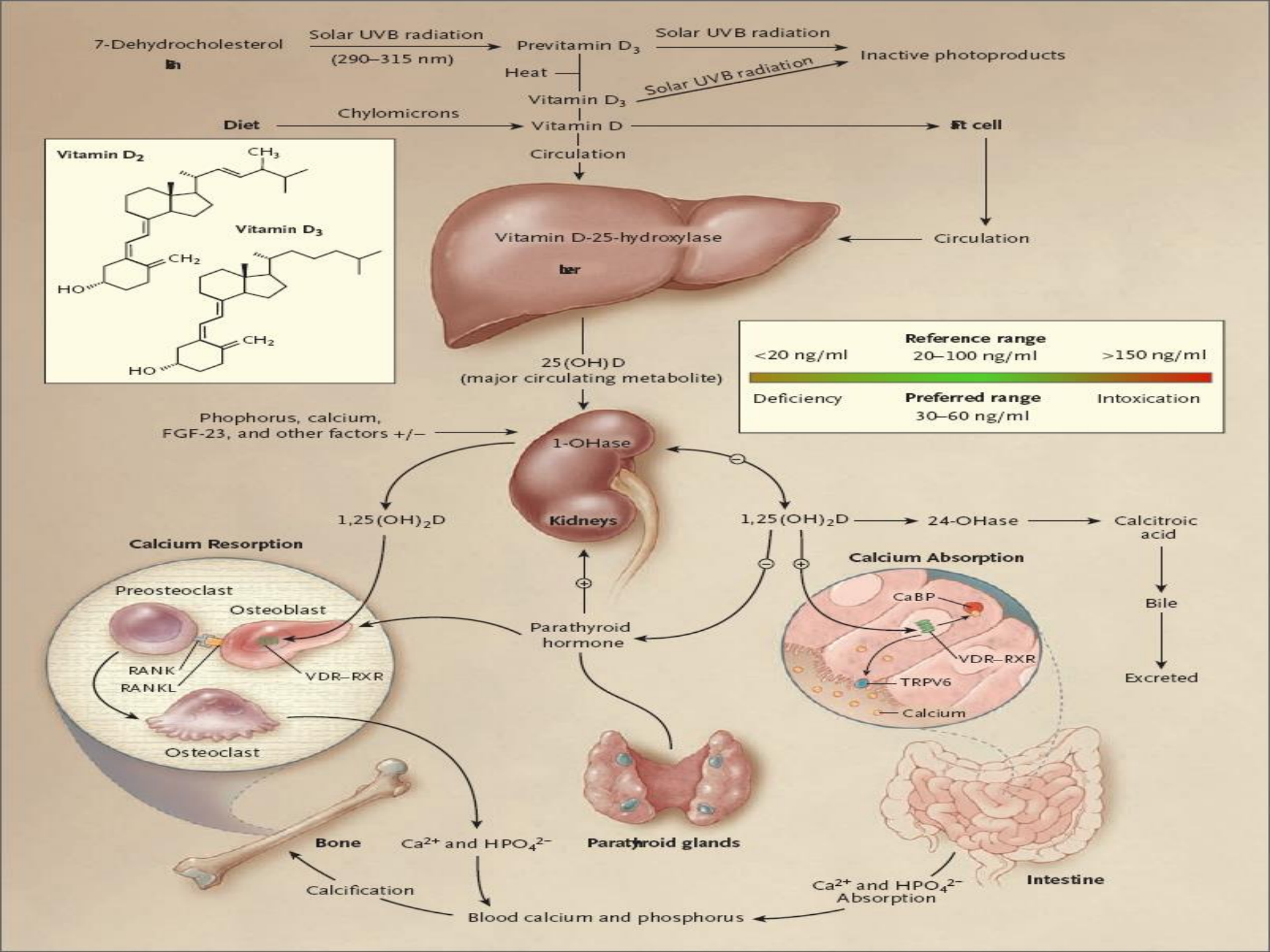
It is a fat soluble vitamin.

Not just a vitamin it is a prehormone

Found in some food and made in the body after exposure to UV rays

Major biological function is to maintain normal blood levels of Ca and $P0_4$

Other tissues like macrophages, prostrate tissue also have vit D receptor


7-Dehydrocholesterol
Solar UVB radiation
(290–315 nm)
Previtamin D3
Solar UVB radiation
Inactive photoproducts
Heat
Vitamin D3
Solar UVB radiation
Diet
Chylomicrons
Vitamin D
Fat cell
Circulation
Vitamin D2
Vitamin D3
Vitamin D-25-hydroxylase
Liver
Circulation
25(OH)D
(major circulating metabolite)
Reference range
<20 ng/ml
20–100 ng/ml
>150 ng/ml
Deficiency
Preferred range
30–60 ng/ml
Intoxication
Phosphorus, calcium,
FGF-23, and other factors +/–
1-OHase
Kidneys
1,25(OH)2D
1,25(OH)2D
24-OHase
Calcitroic acid
Bile
Excreted
Calcium Resorption
Preosteoclast
Osteoblast
RANK
RANKL
VDR–RXR
Osteoclast
Parathyroid hormone
Calcium Absorption
CaBP
VDR–RXR
TRPV6
Calcium
Bone
Ca2+ and HPO4 2–
Parathyroid glands
Intestine
Calcification
Ca2+ and HPO4 2–
Absorption
Blood calcium and phosphorus

Endocrine, paracrine and intracrine functions of Vitamin D

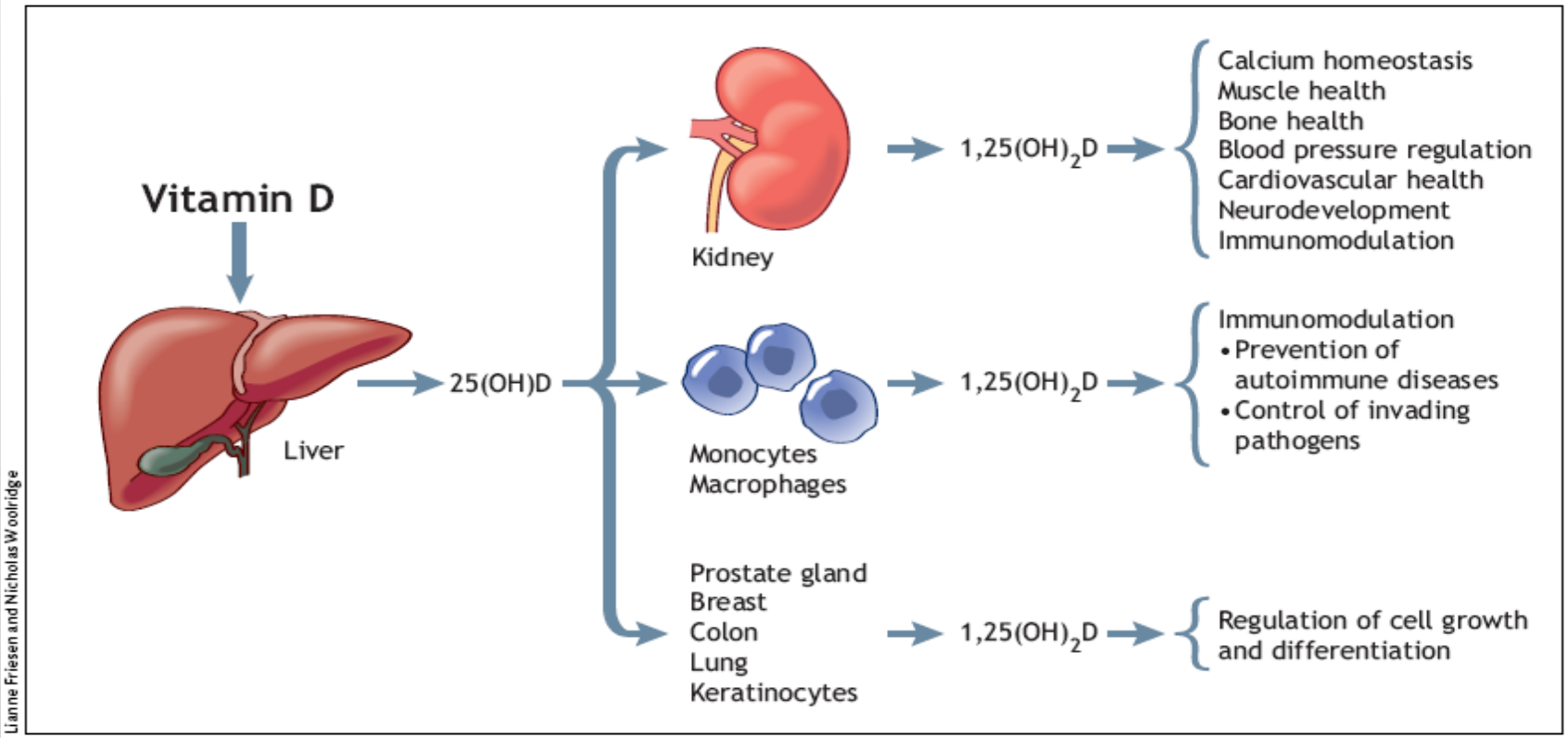


Fig. 2: The endocrine, paracrine and intracrine functions of vitamin D. Vitamin D is converted in the liver to 25(OH)D, which enters the systemic circulation and is converted to 1,25(OH)2D in a variety of end-organ tissues. As shown, 1,25(OH)2D is involved in the regulation of numerous systems.

Vitamin D Across the Lifespan

Factors influencing accumulation of bone minerals:

- Heredity
- Gender
- Diet
- Physical activity
- Endocrine status
- Maternal vitamin D status

Food Sources of Vitamin D

Cod liver oil – 1 TBS	1,360 IU
Salmon 3.5 oz.	360
Mackerel 3.5 oz.	345
Tuna, canned, in oil, 3 oz.	200
Sardines 3.5 oz.	250
Milk (fortified) 8 oz.	98
Ready to eat cereal (fortified) ¾ - 1 cup	40
Egg 1 whole	20
Liver, 3.5 oz.	15
Cheese, swiss 1 oz.	12

How much sun?

Depends on:

- Age
- Amount of vitamin D obtained from diet
- Skin darkness
- Sunshine intensity

How much sun?

- Significant skin exposure
  - Face, neck, arms, hands
  - Arms, legs
- Adequate sun strength
- Time
  - 25% of the time it would take to cause pinkness of the skin (Caucasians)
  - People with dark skin require significantly more sun exposure

25(OH)D concentration

To prevent deficiency disease –

> 25 nmol / L

To prevent complications of insufficiency –

≥ 50 nmol/L

For maximum bone health and prevention of chronic disease –

75 – 100 nmol/L

IRAN (vit D supplementation)

Age	dose
Pregnancy	1000 IU/ Daily
3-5 day- 2 yrs	400 IU/ Daily
6-17 yrs	50000 IU/ Monthly (9 PEARL)
18-29 yrs	50000 IU/ Monthly
30-59 Yrs	50000 IU/ Monthly
≥60	50000 IU/ Monthly


Thank you