



Review

Dietary intake and nutritional status of micronutrients in adults with cystic fibrosis in relation to current recommendations

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SUMMARY

An increased prevalence of cystic fibrosis (CF) related complications such as impaired bone health and diabetes has accompanied increased survival of patients with CF. This review was conducted to determine the extent to which adults with CF are meeting current nutrition recommendations for micronutrients in association with CF-related complications management. Although dietary intake and nutritional status in CF has improved significantly in recent decades, micronutrient status seems to have diverged. While vitamin A and E intakes appear adequate, frequent vitamin D and K deficiency/insufficiency and compromised bone health in CF, occurs despite supplementation. Although deficiency of water-soluble vitamins and minerals is uncommon, ongoing surveillance will enhance overall health outcomes, particularly in cases of CF-related liver disease and deteriorated lung function and bone health. Salt and fluid status in CF may also need attention due to diminished thirst sensation and voluntary rehydration. Further investigation in micronutrient status optimisation in CF will inform the development of more effective and targeted nutrition therapies to enable integration of more refined recommendations for micronutrient intakes in CF based on individual needs and disease progression.

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1. Introduction

It is now common for individuals with CF to survive well into adulthood thanks to improved diagnosis and treatment, including nutritional management [1]. Despite overall improved nutritional status, dietary intake and status of several micronutrients seem to be associated with CF related chronic conditions such as impaired bone health and CF related diabetes (CFRD), the prevalence of which has increased with the improved survival in CF [1,2]. This change of epidemiology has been accompanied by regular

monitoring of dietary intakes and nutritional status, and frequent updating of specific outdated dietary recommendations in CF. From this perspective, the aim of this review was to compare recent reports of actual dietary intake and nutritional status of micronutrients, with relevant dietary recommendations for CF to inform further refinement of dietary micronutrient recommendations for CF, in view of increased prevalence of CF related comorbidities in this population as life expectancy increases.

2. CF specific recommendations

Dietary micronutrient recommendations for CF in various countries [4–13] summarised in Tables 1 and 2 were developed based on best available evidence and expert consensus at the time. Given the substantial changes in CF treatment and consequent improvements in life expectancy, many of these may be outdated for current practice. These recommendations address challenges of micronutrient intake, particularly of fat-soluble vitamins, mainly due to dysfunctions of the digestive system including exocrine pancreatic insufficiency (PI) [14]. The recommendations for fat-soluble vitamins for different age groups are more variable between countries, and have been complicated by the various age

Abbreviations: CF, cystic fibrosis; CFRD, cystic fibrosis-related diabetes; CFRDL, cystic fibrosis-related liver disease; PI, exocrine pancreatic insufficiency; EAR, estimated average requirement; NNR, Nordic Nutrition Recommendations; PS, pancreatic sufficiency; RNI, Reference Nutrient Intake; PERT, pancreatic enzyme replacement therapy; CRP, C-reactive protein; BMD, bone mineral density; 25(OH) D, 25-hydroxyvitamin D; 1,25(OH)₂D, 1,25-dihydroxyvitamin D; UV, ultraviolet; PTH, parathyroid hormone; DBP, vitamin D binding protein; PIVKA-II, proteins induced by vitamin K absence-II; %ucOC, undercarboxylated osteocalcin; ENaC, epithelium Na⁺ channel.

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Table 1
International nutrition recommendations for adults with CF – vitamins (Refs. [4–13]).

	Scope	Vitamin A (IU) (1 IU = 0.33 µg)	Vitamin E (IU) (1 IU = 0.67 mg)	Vitamin D (IU) (1 IU = 0.025 µg)	Vitamin K (µg)	Water-soluble vitamins
US CFF 1992 [4]	All ages	– 1–2 standard adult vitamin/day	– 200–400/day	NI ^a	– 5000 × 2 weekly if on antibiotics or with cholestatic liver disease	NI ^a
European CFS 2002 [5]	All ages	– 4000–10,000 fat-soluble preparation/day for PI; – Always ≤20,000 – 0.5–1 mg/kg β-carotene for PI and very low plasma and lipoprotein levels	– ≤400/day	– 400–2000/day for PI, esp. northern countries; – 25(OH)D preferred	– 1000/day–10,000/week for PI and cholestasis; – 10,000/day for demonstrated or suspected deficiency	– Parenteral 100 µg vitamin B ₁₂ /month for extensive terminal ileum resection; – ≥100 mg vitamin C/day for deficiency
UK CFT 2002 [6]	All ages	– 4000–10,000/day	– 150–300/day	– 800–2000/day	– 10,000/day; – Suggestion not recommendation	– Supplement if documented poor dietary intake; – Parenteral vitamin B ₁₂ possible for extensive surgery for MI ^c
UK CFT 2004 [7]	CFRD at all ages	– 4000–10,000/day	– 150–300/day	– 800–2000/day	– 10,000/day; – Suggestion not recommendation	– Supplement if documented poor dietary intake; – Parenteral vitamin B ₁₂ possible for extensive surgery for MI ^c
US CFF 2004 [8]	Adults	– 10,000/day	– 200–400/day	– 400–800/day	– 2500–5000/week; – Additional 2500–5000/wk if frequent antibiotic courses or haemoptysis history	NI ^a
US CFF 2005 [9]	All ages	NI ^a	NI ^a	– 50,000–2 × 50,000/wk	– 300–500/day	NI ^a
Australasian Guidelines 2006 [10]	All ages	– 2500–5000/day	– 150–500/day	– 400–1000/day	– 300–500/day	– Supplement if inadequate dietary intake and/or evidence of deficiency; – Parenteral vitamin B ₁₂ if terminal ileum resected
US CFF 2010 [11]	CFRD at all ages	– CF specific multivitamins	– CF specific multivitamins; – Or a multivitamin and additional vitamin E	– CF specific multivitamins; – Or a multivitamin and additional vitamin D	– CF specific multivitamins; – Or a multivitamin and additional vitamin K	– CF specific multivitamins
European CFS 2011 [12]	All ages	NI ^a	NI ^a	– 1000–5000/day; – Adjusted based on 25(OH)D > 20 ng/mL (50 nM); – Preferably D ₃	– 1000–10,000/day	NI ^a
US CFF 2012 [13]	Vitamin D for all ages	NI ^a	NI ^a	– ≥800–2000 D ₃ /day ^b	NI ^a	NI ^a

^a NI = no information.

^b 1600–6000 D₃/day if 25(OH)D within 20–30 ng/ml (50–75 nM); 10,000 D₃/day if 25(OH)D persists within 20–30 ng/ml (50–75 nM) or <20 ng/ml.

^c MI = meconium ileus.

categories used in each set of guidelines. They have also been more frequently revised than recommendations for dietary energy and fat, reflecting the research dynamics in the field. Consequently, recommendations for fat-soluble vitamins for adults with CF have inherited substantial variations between countries and year of release.

3. Dietary studies and micronutrient status in CF

Dietary intakes and biochemical status of micronutrients have been reported both cross-sectionally and longitudinally in adults and adolescents with CF over the past decade (Tables 3 and 4), reflecting the change of epidemiology with increased life expectancy in CF. Micronutrient intake, particularly fat-soluble vitamins, add to the complexity of nutritional issues in CF. Further adding to the complexity, the extent of contribution of supplementation to overall intakes of micronutrients in these studies was not reported.

3.1. Fat-soluble vitamins

Supplementation of fat-soluble vitamins in a large proportion of the CF population raises intake and/or nutrient status, when compared with the relevant reference values for the general population [15–19]. When compared with the relevant CF recommendations at the time of study (Table 1), 2/4 studies that measured vitamin A, D and E intakes showed average dietary levels within or slightly exceeding CF recommendations [18,19].

Overall, vitamin A and E intakes seemed at least adequate and in some cases excessive (Tables 3 and 4). The mean intakes of vitamins A and E in a Scandinavian study [19] were within the range recommended by the European CF Society [5]. However, the actual intakes were possibly higher, as the intakes reported were from diet and energy supplements, not including micronutrient supplementation [19]. The mean vitamin A intake in a US study [18] slightly exceeded the recommendation by the US Cystic Fibrosis Foundation (CFF) [8]. A Polish study [16] did not report

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