Is Vitamin K2 Supplementation Effective in Reducing Incidence of Fracture in Adults? An FPIN Evidence-Based Review

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INTRODUCTION

Osteoporosis is a chronic metabolic bone disease that affects more than 200 million people around the world. Characterized by bone fragility, it can increase a person's risk for bone fractures. These fractures can not only decreased quality of life but can also significantly increase a patient's morbidity/mortality, nursing home placement, and total health care costs. Although this disease process is most common in older females, it can also be diagnosed in men. The US Preventative Task Force recommends screening women 65 years and over with a DEXA scan no more than every 2 years or sooner, if indicated. Scan results determine what if any treatment is necessary. Several FDA-approved drugs are available to improve bone marrow density and reduce fractures including parathyroid hormone, bisphosphonates, raloxifene, and estrogen. Dietary supplements such as Vitamin D and calcium are also prescribed.

Objective:

Review current evidence for vitamin K2 supplementation and the impact in reducing the incidence of fractures in adults.

METHODS

OVID Medline and PubMed were searched for studies published from 2010-2019 using terms *vitamin K2*, *osteoporosis*, *fractures*, and *outcome*, using FPIN© HelpDesk Answer© evidence-based review methodology. Per FPIN©, 2-5 references were selected based on level of evidence.

EVIDENCE-BASED SUMMARIES

Summary 1

A 2019 systematic review and meta-analysis of 18 randomized controlled trials (N=8,882; 2 weeks to 4 years duration) evaluated menatetrenone (vitamin K2) in the management of osteoporosis.[1] Fourteen trials compared menatetrenone versus placebo on fracture incidence in adults with osteoporosis (N=7,944; 99% female) and four studies compared menatetrenone to alfacalcidone (0.5-1.0ug/day; N=1,350; 98% female). Two studies reported data on menatetrenone versus sodium etidronate (200mg/day; N=443) while three studies evaluated menatetrenone versus calcium (calcium lactate 2g/day or calcium aspartate 1,200mg/day; N=248). Intervention patients received either 45 mg/day or 90mg/day menatetrenone. No statistically significant decrease in fractures was observed with menatetrenone treatment versus placebo or other non-osteoporosis drug treatments (Table).

EVIDENCE-BASED SUMMARIES

Table: Menatetrenone versus placebo or other non-osteoporotic drugs in efficacy against fractures[1]

	Type of Fracture			
Comparison Drug	**Vertebral**	**Non- Vertebral**	**Hip**	**Non-Specific**
Placebo				
# of studies	**5**	**3**	**2**	**3**
# of patients	**5,508**	**2,196**	**322**	**6,079**
RR (95% CI)	**0.87 (0.64–1.2)**	**0.67 (0.39–1.2)**	**0.26 (0.03–2.3)**	**0.78 (0.48–1.3)**
I^2 (%)	**62**	**26**	**0**	**78**
Alfacalcidol				
# of studies	**2**	**1**	**1**	**2**
# of patients	**345**	**132**	**213**	**502**
RR (95% CI)	**0.65 (0.30–1.4)**	**0.33 (0.01–8.0)**	**2.9 (0.12– 71)**	**1.0 (0.65– 1.56)**
I^2 (%)	**26**	**NA**	**NA**	**0**
Sodium Etidronate				
# of studies	**2**	**1**	**--**	**--**
# of patients	**180**	**132**	**--**	**--**
RR (95% CI)	**1.1 (0.50– 2.5)**	**0.33 (0.01–8.0)**	**--**	**--**
I^2 (%)	**0**	**NA**	**--**	**--**
Calcium				
# of studies	**1**		**--**	**--**
# of patients	**47**		**--**	**--**
RR (95% CI)	**0.35 (0.08–1.6)**		**--**	**--**
I^2 (%)	**NA**		**--**	**--**

RR: Relative Risk; I^2 (%): % variation between studies based on heterogeneity

Summary 2

A 2017 randomized controlled trial compared the efficacy of concurrent treatment with risedronate and vitamin K2 with risedronate alone for incident fractures.[2] Participants were women with osteoporosis (aged 65 years or older) randomly assigned to either the risedronate (2.5 mg/day or 17.5 mg/week) and vitamin K2 (45 mg/day) group (N=931) or the risedronate alone (2.5 mg/day or 17.5 mg/week) group (N=943). Exclusion criteria included warfarin treatment, contraindication for vitamin K2 or risedronate administration, and prevalent vertebral fracture. The follow-up period was 2 years. No significant difference in incidence rate of any fracture was observed between the risedronate/vitamin K2 group and the risedronate only group (rate ratio [RR] 1.1; 95% CI, 0.81–1.4).

Source: https://th.bing.com/th/id/OIP.FhtEpl0siDxf2GPpyJ3n7AHaE8?w=300&h=200&c=7&o=5&dpr=1.5&pid=1.7

EVIDENCE-BASED SUMMARIES

Summary 3

A 2011 community-based longitudinal study assessed the association between dietary intake of vitamins K1 and K2 and risk of hip fracture.[3] Participants (N=2,807, 71-75 years old, 55% female) who previously participated in the 1992-93 Hordaland Homocysteine study completed the Food Frequency Questionnaire to assess the amount of vitamin K2 consumed through diet over one year. Intake of vitamin K2 was calculated using a food database developed at the University of Oslo and ranged from <7.2ug/day to >16.2ug/day. Follow-up was from enrollment (April 1998 to June 1999) until first hip fracture, death or 31 December 2009. For analysis, the daily intake range was divided into quartiles (Q1=lowest intake, Q4=highest intake), with Q4 as the reference. After adjusting for sex, energy intake, smoking, BMI, and vitamin D and calcium intake, vitamin K2 intake was not associated with hip fracture for any quartile compared to the highest quartile of intake (Q1: hazard ratio [HR] 1.0; 95% CI, 0.64–1.7; Q2: HR 1.1; 95% CI, 0.71–1.7; Q3 HR 1.2; 95% CI, 0.80–1.8).

EVIDENCE-BASED ANSWER

Vitamin K2 supplementation does not reduce the incidence of fractures in adults with osteoporosis compared to placebo or other non-osteoporotic drugs (SOR: **A**, a meta-analysis of 18 randomized controlled trials). Concurrent treatment with vitamin K2 and risedronate does not decrease the occurrence of fractures compared to risedronate alone (SOR: **B**, single randomized controlled trial). Dietary vitamin K2 intake was not associated with risk of hip fracture (SOR: **B**, a longitudinal cohort study).

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