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Hypothesis: Correction of low vitamin D status among Arab women will prevent heart failure and improve cardiac function in established heart failure

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Abstract

Vitamin D deficiency is common in Arab countries particularly among women. This is the result of a low dietary intake of the vitamin, limited exposure to sunlight (a paradox in view of the high sunshine figures), skin colour, obesity and high parity. Apart from its adverse effects on bone in women and their offspring, vitamin D deficiency has the potential to cause or exacerbate heart failure through a number of mechanisms including activation of the renin–angiotensin system and increased arterial pressure. Accordingly, we propose that ensuring adequate vitamin D levels in Arab women will have a much greater impact on health than just the prevention of bone disease. In particular, we suggest that prevention and correction of vitamin D deficiency will reduce the incidence of heart failure and, for Arab women with established heart failure and vitamin D deficiency, improve cardiac function.
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Keywords: Heart failure; Vitamin D; Renin–angiotensin system; Hypertension

1. Background

Women in Arab countries are commonly vitamin D deficient. This results from low exposure of the skin to sunlight associated with modest dress codes (including total body clothing) and skin melanin content, a sparse dietary intake of the vitamin, a high number of pregnancies [1–3], and presumably also from obesity [4] — a common problem among women in the United Arab Emirates [5]. That this deficiency has biological effects is clear from the frequency with which rickets is observed [6], and from the fact that circulating levels of bone resorption markers are higher [2,3] and bone density is lower in women in Arab countries than in the West [1,7–9].

Our hypotheses are first, that widespread vitamin D deficiency amongst Arab women is one contributor to the development and maintenance of hypertension, which is a major risk factor for heart failure [10,11], and second, lack of vitamin D exacerbates heart failure in Arab women with cardiac compromise from whatever cause (hypertension, coronary atherosclerotic disease etc) [12,13]. Since vitamin D deficiency is especially common in Arab women [1–3], we suggest that for them, the effects of avoiding or correcting the deficiency will prove particularly rewarding with regard to the prevention and treatment of heart failure.

2. Size of the problem

We are aware of only one systematic study of the prevalence of heart failure in an Arab country. This was carried out in the indigenous Arab population in Oman over the years 1992–1994 [14]. The prevalence of symptomatic heart failure (5.17/1000 population) is no less than in Western countries and may be higher given the high

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proportion of young people in the population studied [14]. The most frequent identified causes of heart failure in that study were ischaemic heart disease and hypertension [14] although the role of the latter may have been under-estimated [10]. Hypertension was considered to be the most common risk factor for heart failure in Qataris from a survey of hospitalised patients [11].

3. Vitamin D deficiency and hypertension

As noted above, hypertension is a, and perhaps the, most important identifiable risk factor for heart failure in Arab populations. The pathophysiology of primary hypertension is complex and involves both genetic and environmental factors. Amongst the latter, there is epidemiological evidence linking the lack of vitamin D with the prevalence of hypertension [15] although contrary evidence can also be quoted [16]. Exposure to ultraviolet B irradiation reduced arterial pressure in a cohort of patients with mild hypertension [17], and Pfeifer et al reported that vitamin D supplementation reduced systolic blood pressure in elderly women with low vitamin D status [18]. The linkage between vitamin D and blood pressure may relate, in part, to the fact that the vitamin is a negative regulator of renin release [19]. Indeed, vitamin D receptor-null mice exhibit increased renal renin mRNA expression, elevated plasma levels of angiotensin II, hypertension and cardiac hypertrophy [20].

4. Vitamin D deficiency and cardiac failure

Vitamin D has direct and indirect actions on various components of the cardiovascular system that are generally seen as protective [13]. A deficiency of the vitamin can have deleterious effects on both the heart and vasculature [13]. There are numerous case-reports of gross vitamin D deficiency causing heart failure which is reversible with vitamin D replacement. Furthermore, hypovitaminosis D is common in patients with established heart failure in the West [21,22], and was considered likely to be a contributor to cardiac dysfunction in a cohort of 54 Caucasian patients amongst whom there was an association between the severity of heart failure and vitamin D status [12]. We suggest that the contribution of vitamin D deficiency to the pathogenesis of heart failure in Arab countries, particularly among females, is likely to be greater than in the West, whatever the primary underlying aetiology. Thus, provision of vitamin D through dietary supplementation or exposure to ultraviolet B light should improve cardiac function in such patients. Salutary cardiac effects will be, we suggest, through direct and indirect actions of vitamin D on the heart [13], as well as the neurohormonal mechanisms noted above, together with amplification of type A natriuretic peptide receptor activity [23], through which the cardiac natriuretic peptides exert their various cardio-protective actions.

5. Testing the hypotheses

We present here a “broad brush” proposal for testing the hypotheses: space limitations preclude a more detailed exposition.

The vitamin D status of hypertensive versus matching normotensive Arab subjects can be assessed. Our supposition is that there will be a reciprocal relationship between vitamin D status (serum 25-OH vitamin D) and blood pressure in a cross-sectional study in Arab females. Since vitamin D status is but one factor affecting blood pressure, the cohort will need to be large and a formal power calculation will be necessary. A second study could document the effects of exposure to ultraviolet B irradiation on blood pressure in a cohort of hypertensive, vitamin D deficient Arab women — controlled as in the report by Krause et al [17].

In order to test the hypothesis that vitamin D deficiency exacerbates heart failure, a third study could involve female Arab patients with established heart failure and vitamin D deficiency (serum 25-OH vitamin D$<$50 nmol/L). Patients would be randomised to receive 50,000 units of vitamin D2 weekly or matching placebo for 6 months [24] in a double-blind, parallel group study. The study end-points (measured at baseline and after 6 months of treatment) would be plasma B-type natriuretic peptide levels (BNP, primary end-point), left ventricular function (echocardiography including tissue Doppler imaging), an objective measure of clinical well-being (visual analogue scale) and the 6-minute walk test. Again, a power calculation would be needed to determine patient numbers. If our hypothesis is correct, those receiving vitamin D will exhibit a fall in plasma BNP, improved left ventricular function, and increased well-being and walking distance.

6. Implications

Vitamin D deficiency is demonstrably common among women in Arab countries. Emphasis on the effects of this deficiency thus far has been on bone disease. By contrast, adverse effects involving the cardiovascular system have received scant attention. We contend that vitamin D deficiency is likely to be one contributor to the development of heart failure in Arab countries through protean effects on the cardiovascular and neuroendocrine systems and via the development of hypertension. Additional benefits from correcting vitamin D deficiency, not discussed here, might include protective effects against developing type 1 diabetes and some neoplasms, as well as correcting muscle aches and pains and weakness [24]. Should our hypothesis prove correct, the public health and financial implications for Arab countries will be considerable. A relatively simple program to prevent and treat vitamin D deficiency in Arab women (along with efforts to prevent obesity and diabetes) would repay the effort and costs many-fold.

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