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SYSTEMATIC REVIEW

A systematic review of vascular and endothelial function: Effects of fruit, vegetable and potassium intake

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Abstract *Aim:* To review the relationships between: 1) Potassium and endothelial function; 2) Fruits and vegetables and endothelial function; 3) Potassium and other measures of vascular function; 4) Fruits and vegetables and other measures of vascular function.
Data synthesis: An electronic search for intervention trials investigating the effect of potassium, fruits and vegetables on vascular function was performed in MEDLINE, EMBASE and the Cochrane Library. Potassium appears to improve endothelial function with a dose of >40 mmol/d, however the mechanisms for this effect remain unclear. Potassium may improve measures of vascular function however this effect may be dependent on the effect of potassium on blood pressure. The effect of fruit and vegetables on endothelial function independent of confounding variables is less clear. Increased fruit and vegetable intake may improve vascular function only in high risk populations.
Conclusion: Increasing dietary potassium appears to improve vascular function but the effect of increasing fruit and vegetable intake *per se* on vascular function is less clear.

Introduction

Vascular function measures are utilised as surrogate, non-invasive measures of the risk of heart disease and stroke. Multiple methodologies used to assess vascular function and can be categorised as measures of arterial stiffness and measures of endothelial function. Arterial stiffness measures include pulse wave velocity (PWV), augmentation index (AI) and pulse pressure (PP). Endothelial function measures include flow mediated dilatation (FMD), peripheral artery tonometry (PAT) and laser Doppler imaging (LDI); and are outlined below.

PWV is considered as the gold standard method for assessing aortic stiffness, and is a strong predictor of future cardiovascular (CV) events and all-cause mortality [1]. It is assessed by measuring the difference in arrival time of the upstroke of the pressure wave at the femoral artery and at the common carotid artery combined with the distance between these two points and fully automated measurement is now available. Faster velocities indicate stiffer arteries. AI is also an index of arterial stiffness [2] strongly correlated with PWV and is an independent predictor of CV events [3]. It is measured by examining the radial (or femoral or carotid) artery profile and examining the time of arrival of the reflected wave and its contribution to systolic pressures. Higher values indicate stiffer arteries. Ambulatory Arterial Stiffness Indexes (AASI) is the linear regression slope of SBP vs DBP obtained through 24-h noninvasive ambulatory BP monitoring and s-AASI

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(symmetric ambulatory arterial stiffness index) has been shown to provide a clinically relevant evaluation of arterial stiffness [4].

Systemic arterial compliance (SAC) is a measure of large artery stiffness determined from carotid pressure and aortic volume flow measures and has been shown to contribute to higher brachial and carotid systolic and pulse pressure [5].

Endothelial dysfunction is strongly associated with traditional cardiovascular risk factors and precedes the development of clinical disease [6]. One of the major functions of the endothelium is to produce vasoactive molecules including nitric oxide (NO), a potent vasodilator. The assessment of endothelial function by measurement of ischaemia-induced FMD, an NO mediated response in the conduit arteries of the peripheral circulation allows the non-invasive study of vascular physiology in human subjects using ultrasound or MRI [7]. FMD is correlated with the extent and severity of coronary artery disease [8] and predicts events, although whether this is independent of traditional risk factors is not clear. PAT measures endothelial function by assessing finger pulse wave amplitude (PWA) at rest and during shear stress [9]. Reactive Hyperaemic-PAT (RH-PAT) is a ratio calculated using the post-occlusion (shear stress) PWA to the baseline (rest) PWA, expressed as reactive hyperaemic index (RHI) [9]. The lnPAT (log Endo-PAT) ratio is the natural logarithm of the ratio of the pulse amplitude recorded 90–120 s after cuff release to the baseline amplitude divided by the hyperaemic to baseline ratio in the contralateral control finger [9]. PAT is an independent predictor of CV events and all-cause mortality in populations with established CVD [10]. Endothelial function is commonly measured using forearm blood flow (FBF) assessed by strain gauge venous plethysmography during intra-arterial infusion of agonist (e.g. acetylcholine which releases NO) and antagonists (e.g. NG-monomethyl L-arginine [L-NMMA] which blocks NO production) or after ischaemia [11]. Reduced FBF measurements in response to intra-arterial infusion of acetylcholine are associated with increased risk of CV events [12]. LDI with iontophoresis of acetylcholine measures the microvascular perfusion across a selected region of the peripheral circulation [13]. Acetylcholine acts on muscarinic receptors of the endothelium producing endothelium-dependent vasodilation [14]. Impaired endothelium dependent vasodilation as assessed by LDI with iontophoresis of acetylcholine is associated with increased CHD [15]. The measurement of arterial compliance (e.g. AI) following administration of salbutamol (a β2-adrenergic receptor agonist that reduces arterial stiffness in an NO-dependent manner) can be used as a measure of endothelial function [16]. A reduced response to salbutamol administration has been demonstrated in hypercholesterolemic populations and is related to FBF responses to acetylcholine [17].

The association of high potassium diets with reduced stroke risk is now generally accepted within the literature independent of various confounding variables including sodium intake [18]. The mechanisms for this are unclear but may be via an effect on blood pressure [19].

Diets high in fruit and vegetables are associated with reduced cardiovascular disease.

Fruit and vegetables are a source of nutrients including potassium and non-nutrients such as polyphenols, and the high content of potassium in fruits and vegetables is a plausible mechanism to explain the apparent CV protection of fruits in vegetables in epidemiological reports [20].

The purpose of this review is to summarise the effects of fruits, vegetables and potassium on endothelial and vascular function in intervention studies.

Method

A systematic search was performed in MEDLINE, EMBASE and the Cochrane Library for original research articles investigating the relationship between potassium, fruits and vegetables and vascular function published before 01 June 2014. Reference lists of retrieved articles were also searched for relevant articles. No restrictions were placed on publication date. Studies were limited to those published in English, studies in humans and clinical trials. Key search terms were “potassium” OR “fruit” OR “vegetable” AND “endothelial function” OR “vascular function”. Individual fruits or vegetables were not included in the search strategy but were identified if “fruit” or “vegetable” was listed as a keyword, or from reference lists of retrieved articles.

Eligibility criteria

To be included in this review a published study had to meet the following criteria: 1) original research; 2) controlled intervention studies aiming to determine the effect of potassium, fruits or vegetables on endothelial and vascular function. Studies including vitamin, mineral supplementation (other than potassium), dietary changes (other than fruits and vegetables), mixed interventions (e.g. Low fat combined with increased fruit/vegetables), lifestyle modification (e.g. exercise or stress management) or pharmacological treatment were excluded. Dietary studies specifically increasing nitrate intake were excluded as this area has been reviewed recently [21].Vascular function was defined as measures of arterial compliance (PWV, AI, PP) and endothelial function. Blood pressure was excluded as this has been recently reviewed [19,22]. Biochemical markers of endothelial dysfunction included in this review were nitrate/nitrite as indices of NO production, adhesion molecules, Von Willebrand’s factor (vWF) which can increase the risk of clotting, and endothelin-1 (ET-1) which is a pro-inflammatory, pro-proliferative vasoconstrictor peptide [11]. Inflammatory molecules and cytokines were not included in this review and have been published elsewhere [23,24]. Cross-sectional, cohort, animal and cellular studies were not the focus of this review but were included to help explain the rationale and mechanisms behind the observed effect. Searches identified 4063 potential articles of which all but 44 were excluded on the basis of title and abstract (Fig. 1).