

Dairy products and Hypertension

INTRODUCTION

According to the World Health Organisation (WHO), hypertension contributes to a significant proportion of the global burden of disease and is strongly associated with cardiovascular and renal diseases.¹ It is estimated that this condition affects about a quarter of the world's adult population and its prevalence is predicted to increase by 60% by 2025, mainly due to the increase in hypertension in developing countries undergoing the nutrition transition.²

According to the 1998 SA Demographic and Health survey, age-adjusted prevalence of hypertension in the adult South African population was estimated to be 21% (systolic pressure 140mmHg or higher) and 25% (diastolic pressure 90mmHg or higher), amounting to 6 million South Africans.³ Hypertension was responsible for 9% of all deaths in South Africa during 2000, with 50% of stroke and 42% of ischaemic heart disease attributed to high blood pressure.⁴

In view of the high prevalence and major implications of hypertension, attempts to decrease blood pressure are justified.

Diet and hypertension

Blood pressure is determined by genetic and environmental factors. The latter includes obesity, cigarette smoking and alcohol consumption.⁵ As far as dietary factors are concerned, the intake and relative ratios of minerals such as sodium, potassium, magnesium and calcium are related to blood pressure regulation.⁶⁻⁸ However, since nutrients and foods are habitually eaten in combination, the impact of different dietary patterns, rather than individual nutrients, on blood pressure need to be assessed.⁶ The benefits of eating a diet high in fruit and vegetables on blood pressure have been widely reported^{5,9} and the further benefit of a diet rich in fruit, vegetables and low fat dairy together with reduced total and saturated fat intake has been demonstrated in the Dietary Approaches to Stop Hypertension (DASH) trial.⁵ About 50% of the reduction in blood pressure associated with the DASH diet has been attributed to dairy.¹⁰

The inverse association between dairy consumption and blood pressure is supported by a growing evidence-base. Various study designs have been applied in investigating this association, including observational studies (cross-sectional^{8,11,12} and longitudinal cohort studies^{9,13-18}), randomised controlled trials,^{5,19-25} and systematic reviews.^{6,7,26-30} The studies have included participants who

were normotensive, hypertensive or both; had a normal weight or were overweight; had a wide age range; and were from different ethnic backgrounds. Although differences in nutrient composition of dairy products may affect outcomes such as blood pressure differently, some studies evaluated the effect of total dairy product intake, while other studies have differentiated between low-fat dairy products, high-fat dairy products, yoghurt, cheese and liquid versus solid foods. Other factors that may impact on blood pressure and should ideally be adjusted for include smoking, alcohol consumption, physical activity and other dietary confounders (such as total energy intake). Despite these complexities, there is extensive evidence that three servings of dairy per day, as part of a balanced diet, are beneficial in preventing both pre-hypertension and stage I hypertension.

OVERVIEW OF STUDIES INVESTIGATING BLOOD PRESSURE AND DAIRY FOOD CONSUMPTION

Observational and epidemiological studies

A number of cross-sectional studies have indicated that dairy intake may be inversely associated with the risk and prevalence of hypertension.^{6,7,12} These studies have indicated that populations with a low dairy intake (a major source of dietary calcium, potassium, magnesium and protein) have a higher prevalence of hypertension. The inverse relationship between dairy intake and hypertension is stronger in populations at higher risk for hypertension, such as blacks and elderly persons that typically have a low intake of dairy.^{31,32} A study by Charlton *et al.*, conducted amongst 325 men and women from three different ethnic groups in Cape Town South Africa, found that calcium intake was low in all ethnic groups, but especially in black participants. In this study, calcium intake was found to be significantly lower in hypertensive compared to normotensive subjects and dietary calcium intake was inversely associated with both systolic and diastolic blood pressure.⁸ Other cross-sectional studies have, however, reported an inverse effect on only one measure of blood pressure, usually systolic blood pressure,¹² while others have found no association.¹¹ Cohort studies that have reported an inverse association between intake of dairy and hypertension are described below:

The Coronary Artery Risk Development in Young Adults (CARDIA) study included 3157 black and white adults from the US, aged 18-30 and followed up for ten years.¹⁸ Results from the CARDIA study showed that intake of low fat dairy products was significantly associated with lower incidence of high blood pressure. Similarly, the Women's Health Study of 28 886 women in the United States





who were followed up for ten years, reported that skim milk intake was associated with decreased risk of hypertension. This same association was, however, not found for other low-fat dairy products such as low fat yoghurt and cottage cheese.¹⁶ The Seguimiento Universidad de Navarra (SUN) study of 6686 adults in Spain that were followed up for two years reported a significant reduction in hypertension in participants with the highest low fat dairy consumption compared to those with the lowest consumption.¹⁷ The Prevention with Mediterranean diet or PRE-DIMED study of 2290 elderly subjects in Spain found an inverse association of low-fat dairy, but not high-fat dairy, with blood pressure change during one year of follow-up.¹⁵ In older adults included in the Rotterdam study of 2245 normotensive subjects (older than 55 years) in the Netherlands followed up for two years, intake of low-fat dairy was also found to be linked to lower risk of hypertension.¹³ This antihypertensive effect of dairy has also been noted in children.³³

According to the Atherosclerosis Risk in Communities (ARIC) study, a significantly lower increase in blood pressure was found in white Americans (n=6912) that consumed three or more daily servings of low-fat milk compared to those that consumed less than one serving per week after nine years of follow-up. Among African Americans in the same study (n=1296), however, intake of dairy was not associated with changes in blood pressure over time.³⁴ The authors warned that results of the black subgroup should be interpreted with caution due to the small sample size and the fact that they had a lower range of dairy intake due to a higher prevalence of lactose intolerance.

Cohort studies that have not confirmed an association between dairy intake and hypertension have also been reported. A study by Dauchet *et al.*, in a cohort of 2341 French subjects with a median follow-up of 5.4 years, showed little evidence of an association between dairy food consumption and blood pressure. In this study total dairy intake was assessed (milk, cheese, yoghurt and other dairy products) and the contribution of individual products was not assessed.⁹ Similarly, an association between total dairy consumption and blood pressure was not found in a young to middle-aged cohort of the Rotterdam study

that included 3454 participants, 20-65 years of age, followed for five years.¹⁴ The Hoorn study in 1124 elderly subjects (50-75 years) that were followed up for 6.4 years also found no association between total dairy consumption and changes in blood pressure.¹¹

Reasons for differences in results obtained for low-fat versus whole-fat dairy may be related to differences in the saturated fatty acid content of these foods, which, in turn, is associated with atherosclerotic plaque development, decreased vascular plasticity and increased vascular resistance.⁶ Secondly, the high sodium content of cheese may contribute to the lack of benefit of that dairy product on blood pressure. Thirdly, Soedamah-Muthu *et al.*, report that "people who consume low fat dairy may be more health conscious and have a healthier eating and lifestyle pattern" (e.g. consume less alcohol, have a healthier body weight, exercise more, do not smoke and drink fewer other beverages, such as sugar-sweetened beverages).²⁷

Randomised controlled trials

The most well-known randomised controlled trial related to diet and hypertension is the DASH trial, that showed that dietary interventions can effectively impact on blood pressure, to the same extent or more as single-drug therapy.⁵ A diet rich in fruit, vegetables and low fat dairy products combined with lower intakes of total and saturated fats over a period of eight weeks, resulted in a significant decrease in blood pressure compared with that of subjects on a typical American control diet (5.5 mmHg systolic blood pressure and 3.0 mmHg diastolic blood pressure). Participants on a diet high in fruit and vegetables (without dairy foods) had a decrease in blood pressure that was half that seen in participants on the DASH diet (2.8 mmHg systolic blood pressure and 1.1 mmHg diastolic blood pressure). The most significant decrease in blood pressure was seen in the hypertensive group and in African American participants.²⁵

Other randomised trials of dairy intake and blood pressure have shown mixed results. In a 4-week crossover study in 38 normotensive and hypertensive subjects that assessed the impact of conventional skim milk; high calcium skim milk; and high calcium and potassium skim milk on blood pressure, significant changes in systolic blood pressure were observed for all products, while diastolic blood pressure was lowered significantly after consumption of only the high calcium and potassium skim milk product.²⁴ In another clinical trial the blood pressure of 35 healthy overweight subjects was measured during an 8 week period during which low-fat dairy products (500ml low-fat milk and 150g low-fat yogurt) were consumed or carbohydrate-rich control products (600ml fruit juice and three fruit biscuits) were consumed in random order. Systolic blood pressure was significantly reduced by 2.9mmHg during the period that low-fat dairy was consumed.²⁰ In another 12-week trial Stancliffe *et al.* compared the blood pressure of 40 overweight and obese participants on an adequate dairy diet (3.5 daily servings) and an inadequate dairy diet (less than 0.5 daily servings). Intake of the adequate dairy diet resulted in significant reductions in systolic blood pressure of overweight participants and in both systolic and diastolic blood pressure of obese participants¹⁹.

In a parallel study in 204 older white normotensive participants with a low dairy intake, consumption of a diet containing three cups per day of low-fat or fat-free milk for four weeks, decreased both systolic blood pressure and diastolic blood pressure, but not more than in the control group.²² A randomised crossover trial that included an 8 week low fat dairy intervention in 45

normotensive younger volunteers between 10–45 years was not associated with changes in blood pressure.²² In a four week cross-over study, the effect of a dairy-based and a soy-based smoothie on blood pressure of 20 overweight and obese participants was assessed. Neither smoothies reduced blood pressure during this short term trial.²¹

According to Soedamah-Muthu *et al.*, no long-term randomised trials (more than one year) of dairy intake and hypertension have been conducted, making it difficult to draw firm conclusions.²⁷

Systematic reviews and meta-analyses

Meta-analyses often improve statistical power to such a degree that significant results can be achieved when the power of the primary studies was too small to achieve significance. A number of reviews of observational studies and randomised controlled trials related to dairy consumption and hypertension have been reported.

A systematic review by McGrane *et al.* covered recent, randomised controlled trials and cohort studies.⁶ The authors found significant inverse associations with hypertension for high versus low intake of total dairy, low fat dairy, and fluid dairy foods. In contrast, no significant associations were found for high fat dairy and cheese. Ralston *et al.* undertook a meta-analysis of five cohort studies involving nearly 45 000 subjects of which 11 500 had elevated blood pressure.²⁶ Their analysis showed significant inverse associations of total dairy, low fat dairy and fluid dairy foods (milk and yogurt) with blood pressure.²⁶

Limitations of the two mentioned reviews included variation in the types of dairy intake and serving sizes among different populations. For this reason, Soedamah-Muthu *et al.*, performed a dose-response meta-analysis of prospective cohort studies evaluating dairy intake and risk of hypertension in 57 256 subjects (of which 15 367 were hypertensive) who were followed up for between two and 15 years.²⁷ In their analysis, total dairy, low fat dairy and milk were all linearly associated with a lower risk of hypertension. High-fat dairy, total fermented dairy, yogurt and cheese were not significantly associated with hypertension risk. They recommended that these results need to be confirmed in randomized controlled trials.²⁷

Despite the significant inverse association of blood pressure with dietary intake of calcium found in observational studies, dietary calcium supplements may not affect blood pressure to the same extent as dairy foods. A meta-analysis of 40 randomised controlled trials showed a small but significant effect of calcium supplementation (1000mg/day) on systolic blood pressure and diastolic blood pressure,²⁹ while a Cochrane review of calcium supplementation for the management of hypertension²⁸ found that “an association between calcium supplementation and blood pressure reduction was weak due to poor quality trials and heterogeneity among trials”. In contrast to the results obtained in the calcium supplementation trials, another meta-analysis of potassium supplementation (2000mg/day) in 27 trials showed significant reductions in blood pressure.³⁰ The blood pressure lowering effect of potassium is enhanced in participants with high sodium intake and in black participants.⁷

MECHANISMS

The association between dairy products and blood pressure is stronger than the association between calcium intake and blood pressure, suggesting that other components in dairy products also play a role in this association.^{6,28}

Dairy products are usually low in sodium (cheese excluded) and rich in protein, minerals (calcium, magnesium, potassium and

phosphorus), vitamins (vitamin D in fortified milk and riboflavin), and trace elements (iodine, selenium and zinc), which may reduce blood pressure individually or in combination.^{6,7} The blood pressure-lowering effects of single nutrients may be too small to detect in primary clinical trials, but when consumed together (as in some trials such as DASH and in observational studies), their combined effect may be sufficient to be detected and provide protective effects. It is also possible that there may also be some unrecognised ingredients in dairy products that may affect blood pressure.³²

Although sodium is the mineral with the most significant impact on blood pressure,⁷ calcium and potassium also play a role. Low dietary calcium intake increases levels of intracellular calcium, which, in turn, increases 1,25-dihydroxyvitamin D3 and parathyroid hormone, resulting in an increased movement of calcium into vascular smooth muscle cells and increased vascular resistance.^{7,31} In addition, high intake of sodium increases urinary calcium losses.^{7,8} In susceptible individuals, low dietary calcium intake may predispose them to the pressor effects of sodium.^{8,31} Low dietary potassium intake increases renal sodium and chloride retention. Adequate potassium intake can, however, reduce the increase in blood pressure associated with sodium sensitivity.^{7,35}

The bioactive milk peptides in dairy, such as lactotripeptides, may also contribute to the protective effect of dairy on blood pressure. These bioactive peptides are released from dairy products after fermentation during food processing or digestion in the small intestine.^{7,26,31,36} and are hypothesised to inhibit the action of angiotensin 1-converting enzyme (ACE), and in so doing prevent blood vessel constriction. ACE is a key participant in the renin-angiotensin system, which is a primary regulator of blood pressure and fluid and electrolyte balance in the body. ACE converts inactive angiotensin I to angiotensin II, which increases blood pressure by constricting vascular smooth muscle.^{36,37} ACE inhibition lowers the production of angiotensin II, which inhibits the release of aldosterone (which conserves sodium, increases potassium loss and increases water retention) and so decreases blood pressure.

Food proteins are important sources of essential amino acids. In addition, many proteins contain peptide sequences with specific physiological functions.³⁶ Milk proteins (casein and whey) are rich sources of bioactive peptides that have been shown to inhibit the activity of ACE.^{7,37} Products derived from dairy protein that has been hydrolysed for optimal ACE activity have also been developed for commercial purposes. A study by De Leeuw *et al.*, showed that dairy products that contain the lactotripeptides, isoleucyl-propyl-propyl and valine-propyl-propyl (added as powdered hydrolysed casein to pasteurised yoghurt drinks) modestly lower blood pressure in mildly-hypertensive participants in a dose-dependent way.³⁸ Despite the positive results reported by some studies, McGrane *et al.* conclude that the recently published randomised controlled trials on lactotripeptides (or fermented milk) “show variable effects on blood pressure and related vascular outcomes in both hypertensive and prehypertensive individuals” and encourage further research in this area.⁶

CONCLUSIONS AND RECOMMENDATIONS

According to Norman *et al.* “there is considerable potential for health gain from implementing blood pressure-lowering interventions that are known to be highly cost effective.”⁴ Although pharmacological treatment of hypertension is effective in many patients, it might be inconvenient, expensive and accompanied with adverse effects in others.³⁹

A large number of observational studies and some randomised controlled trials have demonstrated an association between consumption of dairy products and reductions in blood pressure. The beneficial effect of dairy consumption on blood pressure appears to be derived not solely from calcium, but from the complete nutritional profile of dairy products. The synergy of minerals, vitamins, proteins and essential fatty acids, as well as the specific peptide sequences of dairy contribute to this effect.³⁷ Fat-free and low-fat dairy products, especially milk, appear to have an even more significant lowering effect on blood pressure than other dairy products.^{6,26}

Based on the evidence provided in this review, dietary recommendation to increase consumption of low-fat dairy foods and fruit and vegetables and decrease consumption of total fat and saturated fat seem to be justified.^{6,16,17}

The potential benefits of low fat dairy consumption on blood pressure justify recommendations to increase consumption of these foods.

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Author: Prof. CM Walsh Edited author: Dr FAM Wenhold

AN INITIATIVE BY THE CONSUMER EDUCATION PROJECT OF MILK SA

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Tel: 012 991 4164 • Fax: 012 991 0878

www.rediscoverdairy.co.za • info@dairy.co.za

