



Dietary Fat and Blood Pressure

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Abstract

Purpose of Review Do dietary fats lower blood pressure? This review covers total fats, individual fatty acids and foods that provide specific fats.

Recent Findings Evidence for blood pressure lowering is stronger for supplements providing individual marine fatty acids than for fish intake since data on fish consumption are scarce. Such effects are more readily apparent in hypertensive than normal subjects. Biological mechanisms to support linkage between dietary fish oils and blood pressure are plausible. Information on other dietary fatty acids (saturates, linoleic acid, alpha-linolenic acid) is mostly less robust and therefore inconclusive. However, findings with respect to consumption of dairy foods especially of the low-fat variety do suggest association with lower blood pressures.

Summary Apart from marine fatty acids which have mostly been significantly associated with clinically modest blood pressure-lowering, the effects of other dietary fatty acids are inconsistent or clinically minor. Consumption of dairy especially of yoghurt has been linked with lower blood pressure despite the relatively high saturated fat content but the mechanism is unclear.

Keywords Blood pressure · Dietary fatty acids · Marine oil and fatty acids · Dairy fat consumption · Fish consumption

Introduction

Unlike the well-established effects of dietary sodium, potassium, alcohol and obesity, the roles of dietary fat and of individual fatty acids are uncertain. The probable exception is that of marine long-chain polyunsaturated omega-3 fatty acids which is backed by a large body of research although this conclusion is by no means unchallenged. Additional support derives from epidemiological and observational studies of dietary patterns in which the possible effect of fat and fatty acids can be inferred. Further evidence can be derived from total fat consumption including primarily low-fat foods in categories of foods including dairy products and fish.

This review will focus on recent reports but will include earlier studies whenever such studies provide the clearest information.

Fat Consumption and Blood Pressure: Findings from Changes in Total Diets

These data were derived from studies of patterns of food consumption and changes within habitual diets that have included major reductions in fat intake. Inferring the potential contribution of the fat component to the magnitude of blood pressure reduction is at best semi-quantitative especially when other dietary components that affect blood pressure may also have changed.

Nevertheless, several major controlled intervention studies have plausibly evaluated the effects of “healthy” or “prudent diets” in which total fat and type of fat or oil have been interchanged or reduced in quantity. Parallel intervention studies have compared change in the amounts of fat that is consumed habitually versus low-fat intakes within a healthy pattern of eating. The DASH diet (Dietary Approaches to Stop Hypertension) first published in 1997 [1•] compared in 459 subjects a control diet (total fat 37%en, saturated fat 16%en) with a diet (total fat 27%en and saturated fat 6%en) over 8 week periods. Sodium intakes were similar. Systolic and diastolic pressures were 5.5 and 3.5 mmHg lower with the fat reduced diet. Subsequent DASH type diets have included other changes, notably sodium restriction. Other key components of the DASH diets have included increases in fruits and vegetables which were calculated

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to account for about half the benefit (assumed due to higher intake of potassium), and nut consumption and decreased meat intake, illustrating the complexity of interpretation even before taking into account potential interactions among nutrients and between whole foods. Finally, there is sparse evidence of the sustainability of the reduced blood pressure effect of low-fat diets. One of the largest and longest such trials was within the Women's Health Initiative (WHI) which tested in a randomised design a low-fat versus conventional-fat diet [2•]. Thirty-one thousand one hundred forty-six post-menopausal women were normotensive at baseline; blood pressures were measured annually although telephone inquiries regarding hypertension were made twice yearly. Hypertension developed in about half the cohort; at 1 year, the low-fat group showed significantly lower average blood pressure; however, the benefit gradually diminished and was no longer evident by year five despite good dietary compliance [2•].

The uncertainty surrounding extrapolating the effect of one component of a major dietary change from that of other components was suggested in a lengthy 15-year observational study of younger men (Coronary Risk Development in Young Adults; CARDIA) in which the plant foods (whole grains, fruits, vegetables, nuts or legumes) were inversely related to elevated blood pressure [3]. Furthermore, the possible role of the low-fat component of the DASH diet was evaluated in a small (36 subject) short-term 3-week-period trial comparing the standard low-fat DASH diet with a full-fat DASH variation [4]. Blood pressures were lowered similarly but the limitations of the study are obvious.

A variation of the healthy diet from Scandinavia (Healthy Nordic diet) includes more fish and nuts and specific berries and is low in fat; much of the fat was derived from rapeseed oil and low-fat dairy (as in DASH). When such a diet was compared with a habitual Nordic pattern of eating in a 12-week study of only 37 subjects the ambulatory diastolic but not systolic pressures were lower in the healthier diet, sodium and potassium excretion being similar [5]. The largest randomised, controlled trial of a healthier pattern of eating, in which a key component was the addition of a substantial amount of olive oil is the PREDIMED trial (Prevencion con Dieta Mediterranea) [6]. The control diet was similar but low in fat (and oil) yet the olive oil supplemented diet reduced blood pressures more but only very modestly after 4 years; diastolic pressures declined by < 2 mmHg in the olive oil supplemented group compared with the control group. An earlier investigation at 1 year had determined 24 h ambulant blood pressures in a sub-group and confirmed the minor difference between the olive oil supplemented and control groups [7•]. This casts doubt on a clinically useful benefit of additional olive oil within a healthy diet. A Cochrane review of Mediterranean dietary patterns requiring at least two key components of which the first was a higher monounsaturated to saturated fat ratio (as in olive oil) found that blood pressures were reduced in only three of the five included studies [8].

A further randomised controlled trial of 137 adults extending over 6 months compared a Mediterranean style diet with an Australian habitual diet; the test diet included additional olive oil leading to a greater fat intake than that in the habitual diet (38.5%en versus 35.7%en). This led to higher intakes of mono- and polyunsaturated and reduced saturated fatty acids. Both systolic and diastolic pressures were reduced significantly during morning and afternoon but not evening measurements (pre-specified plan was to measure blood pressure over 5 days at home at 3 and 6 months). However, the reductions were of the order seen in the PREDIMED Study that is clinically very modest [9].

Fat Consumption and Blood Pressure: Changes Within Individual Food Groups

The two best examples have been carried out with dairy foods and with fish consumption. The changes with higher fish intakes are regarded as reflecting those of the individual fatty acids characterising fish but since interactions with other constituents of fish cannot be excluded, the evidence with fish consumption will be evaluated in this section and that of the individual fatty acids in a later section.

Two recently published randomised controlled trials investigated the effects of individual dairy foods [10] or of whey protein on blood pressure [11]. The first [10] comprised only 4 week periods in comparisons between either cheese or butter against a low-fat period and two other periods enriched in monounsaturated or polyunsaturated fat to match the saturated fat intake with the dairy foods. The outcomes were traditional cardiometabolic risk factors among which blood pressure did not differ significantly across the 5 streams of the study. By contrast in a study comparing 56 g whey protein with 56 g caseinate or 54 g maltodextrin in mildly hypertensive subjects, the primary focus was on blood pressure that was measured by 24-h ambulatory analysis [11]. Compared with the maltodextrin control period systolic and diastolic pressures declined by 3.9 and 2.5 mmHg respectively (both significant) after whey. Central systolic pressure also declined with whey by 5.4 mmHg. This latter study which was superior in design to the former study supports the conclusions drawn from the majority of observational studies but suggests that the beneficial effect of dairy foods on blood pressure may be mediated through its protein content.

There have been a good number of long-term well-conducted observational studies in which total or individual dairy foods were measured and evaluated against blood pressure outcomes as part of incident cardiovascular events. In two studies from the Netherlands, dairy consumption appeared to associate with lower blood pressures. The Hoom Study of 755 subjects followed for 5 years reported total dairy consumption was associated with lower diastolic blood pressure although individual dairy foods showed only marginally significant inverse associations with

blood pressure [12]. In the Rotterdam Study, the inverse association between total dairy consumption and blood pressure was due mainly to the influence of low-fat products and of specific foods only milk and milk products showed a significant trend [13]. In the Women's Health Study in the USA, among the largest and longest of recent observational studies of middle-aged and older women, the data on dairy consumption showed a similar inverse association between low-fat dairy intake and blood pressure [14]. Finally, a meta-analysis of nine prospective cohort studies numbering > 57,000 individuals followed for up to 15 years confirmed the apparently beneficial influence of eating low-fat dairy foods on the future development of hypertension. By contrast, full-fat dairy foods provided no such benefit [15]. Wang et al. [16] confirmed the beneficial effect on blood pressure of total dairy and total low-fat/fat-free dairy intakes especially through consumption of yoghurt in the Framingham Heart Study Offspring Cohort.

There have been relatively few observational studies that investigated specifically *fish* consumption in contrast to the substantive evidence on the effects of the major long-chain polyunsaturated fatty acids in fish oil [17]. A study in a Mediterranean population whose pattern of eating included regular consumption of fish suggested reduced probability of incident hypertension among those eating most fish [18]. Another intriguing observational study among villagers in Tanzania (618 fish eating villagers versus 645 plant eating vegetarian villagers) has shown that eating fish habitually significantly reduced incident hypertension over time [19]. Inhabitants with access to fish from their fishing culture showed lower age-related blood pressure than those who lived some distance from sources of fish and ate little or no fish. Neither in this study nor in other reports could the consumption of fish be clearly separated from differences across the whole diet. There are few randomised controlled trials of fish consumption although an interesting Australian study showed that the blood pressure lowering effect of weight loss could be augmented by a diet enriched with fish that contributed 3–4 g omega-3 fatty acids [20]. Daytime ambulatory blood pressure fell by as much as 13 mmHg compared with a control group. Importantly, the multinational INTERMAP Study that investigated the probable dietary intake of omega-3 long-chain polyunsaturated fatty acids derived predominantly from fish concluded that this contributed to reduced blood pressures although the levels of significance were not modest [21].

Marine Fatty Acids and Blood Pressure

The major focus in this review will therefore be on the two major fatty acids in fish oil docosahexaenoic (DHA) and eicosapentaenic acid (EPA). The effects of supplemental fish oil or of the purified fatty acids in the oil remain controversial. Whereas several well-conducted controlled intervention trials have suggested beneficial influence of these omega-3 fatty acids

on blood pressure especially in hypertensive subjects, two major meta-analyses have differed in their conclusions. Although most interventions trialled relatively large doses of fish oil EPA and DHA, several studies utilised amounts that could be derived readily from consuming fish. Minihane et al. [22] reported a significant fall in systolic blood pressure of 5 mmHg in subjects with isolated systolic hypertension after 8 weeks on as little as 700 mg of EPA + DHA daily. Gelejnse et al. [23] concluded from a metaregression analysis of randomised controlled trials published until 2002 that more reasonable and acceptable doses of fish oil fatty acids (< 4 g daily) though in amounts greater than available from habitual fish consumption were useful in the treatment of hypertension. This was generally accepted as summarised by Mori in a 2010 review [24] which concluded that dosages in the range of 3–4 g daily were required to treat hypertension and that the benefit could be augmented by including a low-salt dietary component. This synergy was shown in a comparison of fish oil with sunflower oil with and without sodium restriction; only the combination of fish oil and reduced sodium lowered both systolic and diastolic blood pressures significantly [25].

Two recent reviews from authoritative sources, Agency of Healthcare Research and Quality Evidence in the USA [26] and Cochrane Reports from the United Kingdom [27], both online in 2018 have not accepted the evidence relating to the blood pressure lowering potential of fish oils and their fatty acids. The effects on blood pressure were reviewed within the wider framework of risk reduction for cardiovascular diseases. The Agency's review comprised 82 articles with a randomised control design although not all contained adequate blood pressure data. Nevertheless, with respect to marine oils, the conclusion states "There is strong evidence of no effect on BP (systolic and diastolic)." They conclude also that there is no significant effect of alpha-linolenate (ALA) intake on blood pressure. The Cochrane review included for the purpose of blood pressure effects 15 trials of at least 1 year's duration totalling > 34,000 participants: "meta-analysis suggested little or no effect of long-chain n-3 on systolic or diastolic blood pressure". The conclusion was also negative for interventions with ALA. It should be noted however that the primary focus of these reviews was on clinical cardiovascular outcomes and not on blood pressure. It is therefore uncertain how reliably precise the blood pressure measurements were made since these were opportunistic and of lower priority.

The blood pressure lowering that occurs with combined EPA + DHA at least in some controlled studies does not appear to extend to the plant derived omega-3 fatty acid, ALA. In a three-way study in normotensive subjects, conducted as 6 week cross-over interventions with EPA-enriched fish oil, linseed oil and safflower oil, only the fish oil lowered systolic blood pressure (–5 mmHg) whereas neither linseed oil (ALA) nor safflower oil (linoleic acid omega-6) influenced blood pressure [28].

Other Dietary Fatty Acids

There have been fewer comparisons of omega-6 fatty acids predominantly linoleic acid and of saturated fatty acids. Trans-fatty acids have been largely overlooked: in a review published in 2004 trans-monounsaturated fatty acids were compared with sources of saturated fat, oleic acid or linoleic acid in three studies [29]. Blood pressures were similar across the three studies. Information on dietary saturated and omega-6 polyunsaturated fatty acids is scarce and dates back to the 1990s. In the large United States Multiple Risk Factor Intervention Trial [30], the consumption of saturated fat was directly correlated with blood pressure in the 11,342 middle-aged men; some of whom had been treated for hypertension. This relationship remained significant following multivariate analyses adjusting for body mass, and consumption of sodium, potassium, caffeine and alcohol. In a Norwegian study of 4033 healthy men aged 40–42 years the cross-sectional relationship between blood pressure and dietary fat was evaluated from the phospholipid fatty acid profiles [31]. The inverse correlation between linoleic acid and blood pressure was a credible estimate of the effect of omega-6 linoleic acid consumption. However, the positive correlation between saturated fatty acids and blood pressure would have estimated both dietary and endogenously synthesised saturated fatty acid. A recent randomised trial in which three dietary interventions were tested in parallel design in a total of 195 subjects, the substitution of 0.5% of total energy from saturated fat with monounsaturated fat attenuated the increase in night systolic blood pressure by 4.9 mmHg [32].

There have been a number of other direct comparisons between omega-6 (linoleic acid) or monounsaturated fat versus saturated fats; some were randomised controlled dietary trials, others were observational studies. The early OMNI Heart trial in hypertensive subjects observed an approximate 2 mmHg reduction at lower saturated fat and higher monounsaturated fat intakes [33]. Maki et al. [34] confirmed a greater (though small) fall with corn oil compared with olive oil, although the primary focus was on blood lipids. By contrast a Cochrane Report on primary cardiovascular prevention published in 2015 did not support the case for linoleic acid as a blood pressure-lowering approach [35].

Mechanisms

The control of blood pressure is complex, involving central mainly autonomic control and peripheral vascular functions including endothelial integrity, arterial compliance, smooth muscle cell contractility and multiple cytokines. Under abnormal cardiovascular conditions the state of myocardial function, heart rate and of structural changes in arteries such as loss of elasticity and collagen deposition will not be discussed except in the context of arterial stiffness.

Endothelial dysfunction that occurs with hypertension involves diminished nitric oxide production, adhesion molecules such as vascular cell adhesion molecule-1 and intercellular adhesion molecule-1, E-selectin, and possibly inflammation. Flow-mediated dilatation, a marker of endothelial function has been reported in a meta-analysis of 16 studies to have been improved with the consumption of supplemental long-chain omega-3 fatty acids [36], adhesion molecules are reduced [37], and acetylcholine mediated vasodilatation (a function of nitric oxide homeostasis) is improved [38]. Relatively large doses of EPA+DHA dose dependently suppressed the vasoconstrictive responses to norepinephrine and angiotensin II infused into the forearm artery, although studies by Mori et al. [39] showed superior response to DHA. Several studies including a recent comparison of EPA and DHA [40] have shown that compared to a control period (corn oil) both omega-3 fatty acids significantly reduced circulating concentrations of several inflammatory biomarkers including IL-6, CRP and TNF- α . Arterial stiffness is both a result of hypertension (through reduced smooth muscle cell relaxation and increased deposition of collagen) and a contributor to the rise in blood pressure with ageing. Arterial stiffness or its inverse measure, arterial compliance, have been found to improve significantly with fish oil or with individual EPA or DHA [41]. Whether DHA is superior to EPA is uncertain but both are effective in lowering arterial stiffness [42, 43]. Elasticity which diminishes with arterial stiffness was found to be significantly improved when elasticity was measured in small and large arteries by contour analysis of the radial artery in subjects consuming 4 g supplements of concentrated fish oil [44]. Heart rate is mediated through autonomic function and is both a determinant of blood pressure and a consequence of changing pressure. Higher heart rate is generally considered prognostically adverse but can be modestly suppressed to a desirable rate through the consumption of fish oils, reviewed in a meta-analysis of 30 randomised controlled trials [45].

Autonomic inputs thus influence several markers associated with or contributing to hypertension that are favourably modifiable with fish oil fatty acids: vascular reactivity, heart rate and arterial compliance.

Conclusions

1. The best evidence from randomised controlled trials or case-control studies for an inverse association between a group of fatty acids or of individual fatty acids and raised blood pressure or existing hypertension is with fish oil fatty acids, specifically DHA and EPA. Increasing consumption of these fatty acids as the oil or as supplements leads to lower blood pressure and amelioration of hypertension. The evidence is certainly not unequivocal but is reasonably persuasive at least in hypertensive subjects and is supported by plausible mechanisms. However,

two large recent meta-analyses related to clinical cardiovascular outcomes have failed to confirm such a conclusion albeit relying on blood pressure values that were not the primary focus of the trials.

2. Reduced fat diets, in observational studies and in several randomised controlled trials show beneficial lowering of blood pressure that may, however, not be sustainable.
3. There is an insufficient evidence to determine whether any of the following fatty acids influence blood pressure: the group of saturated fatty acids, the omega-6 fatty acid linoleic acid, the plant omega-3 fatty acid alpha-linolenic acid or the most commonly consumed trans-fatty acid elaidic acid (trans-oleic).
4. Whereas evidence from observational studies or intervention studies with total diets or with groups of foods are more difficult to evaluate than randomised controlled trials information derived from some such studies indicates a probable association with blood pressure. The most informative of these relates to dairy consumption especially of the low-fat varieties that has shown inverse associations with blood pressure in several large observational studies. Similar claims have been made for so-called Mediterranean patterns of food consumption in which olive oil is the predominant source of fatty acids. Evidence on fish consumption rests largely on a large multinational observational study that appeared to show association with reduced blood pressure albeit at a low level of significance.
5. The uncertainty around the importance of dietary fatty acids contrasts with the robust evidence pertaining to other dietary measures such as reducing sodium intake.

Compliance with Ethical Standards

Conflict of Interest The author declares no conflicts of interest relevant to this manuscript.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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