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Wholegrains: Emerging Concepts, Controversies and Alternatives

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ABSTRACT

Intake of wholegrain foods has been associated in large prospective cohort studies with decreased rates of diseases such as type 2 diabetes, ischaemic heart disease and hypertension. Multiple mechanisms for the protectiveness of wholegrain foods have been reported. Health authorities in western countries recommend wholegrains as one of the major food sources in a healthy diet, otherwise rich in vegetables, legumes and low-fat dairy. However, the existing evidence for the intake of wholegrains is highly subject to confounding. Many of the results seen in the prospective cohort studies have not been borne out in randomised controlled trials or good-quality meta-analyses. The recommended intake of wholegrains suggested in some countries is well above what there is evidence for. Products labelled wholegrain have variable quantities of the intact grain and differ widely in their effect on blood glucose. Excessive quantities may add to glycaemic load, and anti-nutrients in wholegrains may have adverse health consequences. With the rate of diabetes and obesity increasing, some researchers have questioned the role of grains as part of a healthy diet. Palaeolithic diets, those that are more in keeping with our evolutionary legacy, contain no grains or dairy, but are rich in vegetables, meat, fish and eggs, with the inclusion of some tubers. Smaller trials in animals and humans comparing a palaeolithic diet to a grain-based diet show improved metabolic profiles in the former.

Keywords: Diet; Palaeolithic; Disease Prevention; Whole-Grains; Glycaemic Index

1. Introduction

Wholegrain foods are defined by the American Association of Cereal Chemists as consisting of the intact ground, flaked or cracked grain, whose principal components, the starchy endosperm, germ and bran, are present in the same relative concentrations as they exist in the intact grain [1]. Cereal grains have only been a significant part of the diet of humans since the agricultural revolution (approximately 10,000 years), but they are now a staple part of the diet for most of the world [2]. In the latter part of the 20th century, processes to refine grains have improved such that they constitute the majority of grain consumption in the western world [3]. However, refinement of the grain removes the germ and bran which contain the fibre and phytonutrients that are thought to confer the nutritional benefits of the grain, hence wholegrains are nutritionally superior to refined grain foods [3].

Multiple prospective cohort studies such as the Nurses' Health Study and the Health Professionals Follow Up Study have examined the associations between dietary habits and incidences of illnesses like ischaemic heart disease, diabetes and cancer. They have particularly focused on the role of wholegrains in such a diet. Almost universally, they have found wholegrain intake is inversely associated with the incidence of these diseases. Such studies have been highly quoted. On the basis of these studies, public health authorities have, in recent decades, recommended the consumption of a low fat, high carbohydrate diet, rich in wholegrains as well as fruits, vegetables and legumes [4,5]; this advice is followed by millions in the western world. However, diseases such as diabetes and obesity continue to increase [6]. The role of wholegrains in a healthful diet has been questioned, and diets which are concordant with our evolutionary legacy (which lack grains) have been advocated in the popular media. These so-called "palaeolithic diets" have been compared in smaller trials with the recommended diet, and larger trials are underway.

This review will examine the mechanisms for the benefits of wholegrains, then review the evidence for wholegrains as it pertains to various diseases. It will then examine the possible negative nutritional consequences of high wholegrain intake, and review the evidence for

alternatives to a high wholegrain diet.

2. Mechanisms for the Benefit of Wholegrains

The protective effects of wholegrains on cardiovascular disease are mediated by fibre, magnesium, folate and vitamins B6 and E. Higher intake of soluble, viscous fibre (such as from oat bran) has been shown to decrease low density lipoprotein (LDL) and total cholesterol, and has been shown to lower blood pressure [7]. Nutrients such flavonoids, phenolates and zinc exert anti-inflamematory and antioxidant action [8]. Fibre in wholegrains has effects on enteric hormones such as cholecystokinin which increase satiety. This is thought to be the major mechanism for the association between increased wholegrain consumption and decreased body mass index [9]. Fibre aids in the prevention of colon cancer by diluting faecal carcinogens, modulating colonic transit time, altering bile acid metabolism and reducing colonic pH with the production of short chain fatty acids [10].

3. Review of the Evidence Regarding Benefit of Wholegrains

There have been multiple large-scale epidemiological studies, most notably the Nurses Health Study and the Womens' Health Study (women) and the Health Professionals Follow Up Study (men), which have collected many patient-years of data to examine cardiovascular and metabolic health outcomes. These have been the main source of the recommendations regarding wholegrain intake, and have been reviewed below.

3.1. Studies in Women

De Munter *et al.* [11] analysed the data from the Nurses Health Study with respect to incidence of type 2 diabetes. They found an overall inverse association between wholegrain consumption and risk of type 2 diabetes. However, they found that higher intake of wholegrains was associated with other healthy behaviours, such as higher physical activity, lower body mass index, a lower likelihood of smoking and lower consumption of alcohol, processed meats and soft drinks. The inverse association was attenuated but still highly significant when adjusted for these factors, as well as quintiles of energy intake, family history of diabetes, and less important factors such as coffee intake and oestrogen use. While wholegrain intake was associated with decreased risk of diabetes, it was also associated with increased dietary glycaemic load, which would seem incongruous.

Liu *et al.* [12] examined wholegrain intake with respect to incidence of coronary heart disease in the Nurses Health Study. Even adjusting for known cardiovascular risk factors, the people with the highest wholegrain intake had the lowest relative risk for heart disease. The association was non-significant, however, when adjusted for intakes of protective nutrients such as folate, fat, fibre, vitamin B6 and vitamin E. There was also no adjustment for intake of other potentially protective foods, such as fruit and vegetables-indeed, the people who had the highest wholegrain intake had the highest intake of fruit and vegetables. The same team examined wholegrain intake with respect to incidence of stroke in this population [13]. It found that the incidence of stroke was inversely proportional to wholegrain intake, but this association became statistically non-significant ($p = 0.08$) when two other cardiovascular risk factors were adjusted for. In this study, there was no adjustment made for food or nutrient intake.

Wang *et al.* [14] examined the data from the Women's Health Study in terms of incidence of new onset hypertension. They found, again, that wholegrain intake was inversely proportional to the risk of developing hypertension, but no association was found between refined grain intake and hypertension. Similarly to other studies, the wholegrain data was adjusted and although the association was attenuated it still remained significant. Of note, the authors compared the intake of various food groups and nutrients for quintiles of both wholegrain and refined grain intake. Among the highest quintiles of intake of both groups, the pattern of food intake was similar; higher consumers of both groups ate more calories, fruit, vegetables, meat and dairy products. Refined grain intake was inversely proportional to folate, fibre, potassium and magnesium intake, however there was no greater risk of hypertension with increased refined grain intake. This would appear to be inconsistent with the authors' hypothesis that these nutrients, particularly fibre, are intermediary in the prevention of hypertension.

3.2. Studies in Men

Fung *et al.* [15] analysed the data of the HPFUS with respect to the incidence of type 2 diabetes. Again, wholegrain intake was inversely associated with diabetes risk. This association remained significant but attenuated when adjusted for other variables, such as body mass index, energy intake, physical activity, family history of diabetes, smoking and alcohol intake. Of note, however, higher wholegrain intakes were associated with increased energy intake, but similar body mass indices across the quintiles of wholegrain intake. This would suggest energy inefficiency or increased exercise in those who ate more wholegrains, or, more likely residual confounding. There was no adjustment for fibre, however the authors found that the positive trend was not significant when adjusted for fibre intake.

Flint *et al.* [16] analysed the data of the HPFUS as above. Risk of incident hypertension was inversely associated with wholegrain intake. This association was weakened but still significant when adjusted for multiple covariates as above (but also height and marital status). In this study on the same cohort of men as the diabetes study, energy intakes were *negatively* associated with wholegrain intake, but body mass indices were similar across the groups. As calorie intake and weight modulation are important factors in the beneficial effects of wholegrains and hypertension and type 2 diabetes, the inconsistencies between these two studies on the same cohort cast doubt on the accuracy of the findings.

Jensen *et al.* [17] analysed the data from the HPFUS in terms of risk of onset of ischaemic heart disease. The findings with regards to wholegrains were similar to above. When adjusted for the intake of protective nutrients, diabetes, hypertension and hypercholesterolaemia, the association lost statistical significance. It is difficult, therefore, to make the conclusion that wholegrains intake is independently inversely associated with risk of ischaemic heart disease in men.

Koh Banerjee *et al.* [18] utilised the data from the health professionals follow up study to assess changes in weight over 8 years. Overall the study found that those who ate the most wholegrains gained 0.49 kg (gain of 0.75 vs 1.24 kg) less weight over the time than those who ate the least wholegrains, even when adjusted for multiple factors including caloric intake and exercise. Fibre intake was independently inversely associated with weight gain, but cereal and fruit fibre were equally powerful. Again, in this study, people with high wholegrain intake had high intakes of protective nutrients and had other healthy habits, so a degree of residual confounding is likely. The other issue is the clinical significance of this half-kilogram difference in weight gain; no attempt was made in this study to link this differential weight gain with any change in outcomes.

3.3. Wholegrains and Risk of Colorectal Cancer

The National Institutes of Health-AARP (Formerly American Association of Retired Persons) study [19] found that colorectal cancer incidence was 21% lower in the highest versus the lowest quintile of wholegrain intake, even adjusted for confounding factors such as smoking. There was no adjustment made for family history of colorectal cancer. Interestingly, despite the fibre being the main mediator of bowel cancer prevention, there was no relationship between overall fibre intake and risk of colon cancer in this study. There are no pooled analyses to examine the association between wholegrain consumption and colorectal cancer, instead, the studies examine fibre intake. In the analyses, fibre intake (cereal, fruit or vegetable) was not independently associated with the risk of colorectal cancer [20].

3.4. Prospective Studies

It is difficult to ascertain the effect of confounding factors in all of these studies. Those who eat wholegrains tend to be from a higher socio-economic group, weigh less, eat more fruit and vegetables, take more exercise and are less likely to smoke [21]. Most of the prospective cohort studies adjusted for these factors, and in most cases, the benefit was attenuated after adjustment. Therefore, in order to effectively address the question of the protective value of wholegrains in disease prevention, prospective studies have been carried out, and meta-analyses performed on the basis of these. There are multiple published systematic reviews on the benefits of wholegrains, however only two Cochrane reviews have been carried out. With regard to the prevention of type 2 diabetes mellitus, one analysis included one randomised controlled trial and eleven cohort studies. This review found that the evidence for wholegrains in diabetes prevention was too weak to make conclusions [22]. The second review, included 10 randomised controlled intervention trials mainly using oat cereal, examined coronary heart disease risk factors. It found slightly lower LDL and total cholesterol in the treatment arms [23]. The trials were of too short of duration to make any conclusion regarding cardiovascular mortality. The review also made comment regarding the funding sources of the trials (cereal companies). The WHOLEHeart study [24] was the first to investigate the effects of increasing wholegrain intake on cardiovascular risk factors. No difference in body mass index, endothelial function, insulin sensitivity, lipids or inflammatory markers was seen between the groups over a period of 4 months.

4. Glycaemic Index, Glycaemic Load and Nutrition

The glycaemic index (GI) is a measure of how quickly a food increases serum glucose, relative to a serve of pure glucose with the same amount of carbohydrate. The glycaemic load (GL) of a food, measured in grams, is the carbohydrate content of the food "adjusted" for its GI [25]. There is evidence that diets high in glycaemic index and load contribute to increased systemic inflammation, [26], oxidative stress [27] and blood lipids [28]. High GI and GL diets are associated with higher rates of cardiovascular disease in women [29] and colonic and endometrial cancers [30]. A food being labeled wholegrain gives little indication of its glycaemic index or load; for the purposes of the cohort studies, a wholegrain food was defined variably, anything between >25% and >50% wholegrain. Qualitatively a food labeled as wholegrain

can vary from a sugary, processed cereal with GI 75 and GL 18 per serve on one extreme, and a serve of unrefined oats on the other (GI 50, and GL approximately 10, depending on brand) [31].

The other important factor in glycaemic load is quantity of the food eaten. In the prospective cohort studies, the highest quintile of wholegrain intake consisted of around 3 serves per day. By contrast, American and Australian authorities recommend between 4 and 11 servings of grain based foods per day, in the case of the USA, more than 50% should be wholegrain [4,5]. The guidelines from these countries concede that there is little evidence for this dosage. Though not studied directly, it is conceivable that consuming these foods at the higher end of the guidelines given, may contribute to a high dietary glycaemic load and associated chronic diseases.

Wholegrains are a major source of so-called "anti-nutrients" such as lectins and phytates. Lectins are glycoproteins present ubiquitously in nature, but in higher quantities on legumes and cereal grains, and do not degrade with heating. In high quantities, they cause nausea, diarrhoea and bloating, and may cause increase in intestinal mucus which can impede nutrient absorption [32]. In animal models, lectins (and, indeed, other cereal proteins) may also be immunogenic, and have been implicated in the pathophysiology of auto-immune diseases like rheumatoid arthritis [33]. Phytates are present in the hulls of nuts, seeds and cereal grains. They have antioxidant activity but bind with calcium, iron, magnesium and zinc to form insoluble complexes, and therefore interfere with the intestinal absorption of these nutrients. This is of particular concern in people whose entire diet is grains, such as in third world populations [34].

5. Evidence for Alternatives

Many of the prospective cohort studies showing a benefit for wholegrains compare wholegrain intake with refined grain intake. Indeed, there is little doubt that dietary patterns associated with high wholegrain intake are generally considered to be healthier than those associated with higher refined grain intake. However, there is an emerging concept that diets that are more in concordance with our evolutionary legacy, so called "Palaeolithic Diets", may be less liable to cause diseases of affluence, such as obesity and the metabolic syndrome. Palaeolithic (2 million to 10,000 years BC) diets are based on vegetables, meats and fish, fruits, nuts and tubers, but lack dairy, wholegrains, legumes and refined oils [35]. The effects of these diets compared with so-called "prudent" diets, which contain wholegrains, legumes and dairy, have been studied in smaller trials. A study of palaeolithic compared with cereal-based diets was performed in piglets. At the end of the 15 month intervention period, compared with the cereal fed pigs, palaeolithic diet-fed pigs weighed 22% less and had 43% lower subcutaneous fat, improved insulin sensitivity and response, and lower diastolic blood pressure. There were increased numbers of leucocytes in the pancreases from the cereal fed pigs, but no immunohistochemical differences [36].

The findings in pigs have been borne out in human studies. A cross-over trial comparing a conventional diabetes diet and a palaeolithic diet showed reduced blood pressure, weight, waist circumference and body mass index, and improved lipid profile and HbA_1C [37]. In men with ischaemic heart disease, a palaeolithic diet improved glucose tolerance more than a mediterranean diet [38], despite similar glycaemic indices (50 and 55 respectively).

6. Conclusions

Wholegrains are more nutritious than refined grains. There are multiple putative benefits of wholegrain consumption, and multiple prospective cohort studies have shown that wholegrain intake is inversely associated with risk of multiple diseases. However, these results are not replicated in good-quality Meta-Analyses. There is only one prospective randomised controlled trial of increasing wholegrain intake (the WHOLEHeart study), and no benefit for increasing wholegrain intakes was shown. Most prominently, the prospective cohort studies are highly subject to confounding. Less obviously, there are inconsistencies within and between the studies in terms of confounding factors. Overall dietary and lifestyle patterns are more likely responsible for the results seen in the published cohort studies.

There seems to be little evidence for the suggested intake of wholegrains, and foods labelled wholegrain are qualitatively heterogeneous. Excessive intakes of poorly selected wholegrain foods may be high in glycaemic index and load. This may lead to a pro-inflammatory milieu and contribute to diseases of affluence. There are also anti-nutrients present in wholegrains; though the effects have not been well studied, they may be clinically relevant in individuals.

There is some evidence for alternatives to grain consumption in the context of a nutritious and complete palaeolithic diet. These require larger, longer-term studies to assess the safety and efficacy of these diets in terms of disease prevention. In the future, the findings of these trials may challenge the conventional wisdom of what constitutes a healthy diet, and the role of grains in such a diet.

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