Blood type diets lack supporting evidence: a systematic review[1–3]

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ABSTRACT

Background: Diets that are based on the ABO blood group system have been promoted over the past decade and claim to improve health and decrease risk of disease. To our knowledge, the evidence to support the effectiveness of blood type diets has not previously been assessed in the scientific literature.

Objective: In this current systematic review, published studies that presented data related to blood type diets were identified and critically appraised by using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach.

Design: A systematic search was performed to answer the following question: In humans grouped according to blood type, does adherence to a specific diet improve health and/or decrease risk of disease compared with nonadherence to the diet? The Cochrane Library, MEDLINE, and Embase were systematically searched by using sensitive search strategies.

Results: Sixteen articles were identified from a total of 1415 screened references, with only one article that was considered eligible according to the selection criteria. The identified article studied the variation between LDL-cholesterol responses of different MNS blood types to a low-fat diet. However, the study did not directly answer the current question. No studies that showed the health effects of ABO blood type diets were identified.

Conclusions: No evidence currently exists to validate the purported health benefits of blood type diets. To validate these claims, studies are required that compare the health outcomes between participants adhering to a particular blood type diet (experimental group) and participants continuing a standard diet (control group) within a particular blood type population. *Am J Clin Nutr* 2013;98:99–104.

INTRODUCTION

The Blood Service of Belgian Red Cross–Flanders occasionally receives inquiries regarding the validity of diets that are based on blood group systems, which are often endorsed as a program to improve health. To our knowledge, evidence for these claims has not been substantiated in the scientific literature, and this current review is the first systematic review performed on the topic.

Blood can be classified according to the presence or absence of certain antigens on the surface of red blood cells, and these antigens are controlled at specific gene loci (1). Relevant to this study are the following 2 of ~30 recognized blood grouping systems: the ABO system (the most important antigens being A, B, and H) on chromosome 9 and the MNS system (the most important antigens being M, N, S, s, and U) on chromosome 4 (2). ABO blood typing is typically correlated with blood transfusions because ABO blood product incompatibility can potentially prove fatal. More recently, an extensive collection of epidemiologic studies have assessed the significance of ABO status in relation to physiologic variations and pathologic processes. From among the varied results (with some consistent and some inconsistent findings), the use of genome-wide association studies have supported a number of associations between ABO blood type and certain diseases, including pancreatic cancer, venous thromboembolism, and myocardial infarction in the presence of coronary atherosclerosis (3). Therefore, it appears possible that the ABO blood group system plays a role in determining an individual's susceptibility to certain diseases.

This established association between blood types and disease has been translated into the basis for a range of diets. Of the many authors of blood type diets (4–8), D'Adamo is arguably the most prolific (9–23). Within his initial ABO blood type diet book entitled *Eat Right 4 Your Type* (9), which was published in 1996, D'Adamo claims that each ABO blood type processes food differently, and adherence to a diet specific to an individual's ABO blood group could improve health, wellbeing, and energy levels and reduce risk of developing diseases such as cancer and cardiovascular disease. D'Adamo diets, one for each ABO blood type, are based on a theory that each blood type contains the genetic message of the diets and behaviors of our ancestors, and these traits still have an impact on us today. The validity of the scientific basis for any of the blood type diets is beyond the scope of this systematic review, which is solely focused on the related health outcomes of adherence to the prescribed diets.

Considering the substantial reach of the blood type diets [eg, there are >7 million copies (24) of D'Adamo's 1997 book in print in >60 languages (25)], it seemed pertinent to be able to substantiate the health claims of blood type diets so that inquiries to blood services, physicians, and dietitians can be adequately addressed.

METHODS

Search strategy

The population, intervention, comparison, and outcome (PICO) question was as follows: In humans grouped according to

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blood type (population), does adherence to a specific diet (intervention) improve health and/or decrease risk of disease (outcome) compared with nonadherence to the prescribed diet (comparison)?

All searches were performed on 3 October 2012 within the following databases: The Cochrane Library (via Wiley: http://onlinelibrary.wiley.com/cochranelibrary/search), MEDLINE (http://www.ncbi.nlm.nih.gov/pubmed), and Embase (http://www.embase.com/). All databases were searched from inception to ensure that all relevant articles would be retrieved.

The development of search strategies was performed independently by 2 reviewers (LC and EDB). Final search strategies were combined to ensure maximal search sensitivity before the commencement of study selection. The subsequent study selection was performed independently by the same 2 reviewers in 2 phases. Initially, the titles and abstracts identified by the search were scanned for relevance to the PICO question. Full texts of any relevant references were obtained to assess whether exclusion and inclusion criteria were met. Independent results from the selection phase were compared to ensure that all relevant studies had been identified. *See* the online Appendix under "Supplemental data" in the online issue for search strategies.

Finally, references from identified studies, along with other articles that cited the identified studies, were assessed for relevance. The first 20 relevant studies (as suggested by MEDLINE) were also assessed for pertinence to the current review.

Study selection: inclusion and exclusion criteria

Language

All languages were included.

Study type

All experimental and observational studies were included (ie, randomized controlled trials, controlled clinical trials, cohort studies, case-control studies, and case series). In vitro studies were excluded, along with narrative reviews, commentaries, letters, and opinions.

TABLE 1
Assessment of each identified reference according to inclusion and exclusion criteria[1]

Reference	Study type	Population	Intervention	Outcome	Meets criteria?
No author listed, 2000 (27)	Narrative review	NA	NA	NA	No
Baldwin, 2004 (28)	Narrative review	NA	NA	NA	No
Birley et al, 1997 (29)	Experimental	Humans grouped according to MNS blood group system	Low-fat diet	Quantitative measurements of reduction in LDL cholesterol	Yes
Cowley and King, 1997 (30)	Opinion piece	NA	NA	NA	No
Langman et al, 1966 (31)	Experimental	Humans grouped according to ABO blood group system	Fatty breakfast followed by a small bar of milk chocolate[2]	Serum concentrations of intestinal alkaline phosphatase[3]	No
Langman et al, 1967 (32)	Narrative review	NA	NA	NA	No
Larhammar, 2005 (33)	Opinion piece	NA	NA	NA	No
Mäkivuokko et al, 2012 (34)	Observational	Humans grouped according to ABO blood group system	No intervention	Determination of microbiota profiles	No
McGowan, 2001 (35)	Letter	NA	NA	NA	No
Meltzer et al, 2002 (36)	Narrative review	NA	NA	NA	No
Moen, 2001 (37)	Narrative review	NA	NA	NA	No
Mysterud, 2002 (38)	Letter	NA	NA	NA	No
Nylund et al, 2004 (39)	Narrative review	NA	NA	NA	No
Poleszynski, 2001 (40)	Narrative review	NA	NA	NA	No
Power, 2007 (41)	Experimental	Humans grouped according to ABO blood group system	Food-allergy tests (mRAST and ELISA/ACT LRA tests)	Quantitative measurements of IgG, IgE, and T cells	No
Schroder, 2005 (42)	Narrative review	NA	NA	NA	No

[1] Inclusion and exclusion criteria were as follows: study type included experimental and observational studies and excluded in vitro studies, narrative reviews, commentaries, letters, and opinions, population included humans grouped according to blood group system and excluded animal studies, intervention included adherence to a diet designed to improve health and excluded any other intervention or no intervention, and outcome included any quantified measure of health. ACT LRA, advanced cell test lymphocyte response assay; mRAST, modified ratio allergosorbent test; NA, not applicable (because there was no study performed, and therefore, the other criteria could not be met).

[2] This intervention was not designed to be adhered to for health improvements.

[3] Alkaline phosphatase is not usually considered a health outcome per se.

Population

Studies were included if they contained humans grouped according to a blood group system. Animal studies were excluded.

Intervention

Adherence to a prescribed diet that was designed to improve health was necessary for inclusion. Any studies with another intervention or no intervention were excluded.

Outcome

A decreased incidence of disease, improved BMI, and any other quantified measure of health were included.

Data collection

Relevant information, including the study design, study population, sample size, and details of the intervention and outcomes, was extracted from the identified study (by LC).

Quality of evidence

The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach was used to grade the overall quality of evidence identified in this systematic review. The GRADE approach took into consideration any limitations of included studies that may have had an effect on the quality of the evidence including the study design (lack of allocation concealment and blinding, incomplete accounting of patients and outcome events, selective outcome reporting, and other limitations), inconsistency between different studies (because of differences in populations, interventions, or outcomes), indirectness (of the population, intervention, or outcome), imprecision of outcomes and publication bias (which can be difficult to determine when limited evidence is available). After the appropriate downgrading for each of the previously mentioned criteria (or upgrading in certain circumstances), the quality of the evidence was established as either high (A: further research is very unlikely to change our confidence in the estimate of effect), moderate (B: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate), low (C: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate), or very low (D: any estimate of effect is very uncertain) (26).

RESULTS

The following 1415 articles were identified: 6 articles from The Cochrane Library, 639 articles from MEDLINE, and 770 articles from Embase. Once duplicates were removed, a total of 1003 articles were screened by title and abstract for relevance to the PICO question. The remaining 16 articles were reviewed to assess inclusion and exclusion criteria. Reasons for inclusion or exclusion of each identified article are shown in **Table 1**.

From within the 16 articles, 4 articles met the inclusion criteria of both study design and population; 2 of these articles fulfilled the outcome inclusion criteria, and only one of the articles met the inclusion criteria for the intervention (ie, adherence to a diet that was designed to improve health). A flowchart of the study selection process is shown in **Figure 1**.

Ultimately, only one of the 16 identified papers fulfilled all of the inclusion criteria; Birley et al (29) studied the effects of a low-fat diet on LDL-cholesterol concentrations of study participants grouped according to MNS blood type. None of the studies showed an association between ABO blood type diets and health-related outcomes

The identified study analyzed a total of 254 participants [127 subjects within experimental groups (*MN* genotype: $n = 67$; *MM* genotype: $n = 38$; *NN* genotype: $n = 22$) and 127 subjects within control groups (*MN* genotype: $n = 61$; *MM* genotype: $n = 40$; *NN* genotype: $n = 26$)]. Intervention groups were given the objective of a 25% reduction in dietary fat intake, and their diet was supplemented with 25 g unprocessed wheat bran/d. Control groups did not change their diets. LDL cholesterol values of both control and experimental groups within each MNS blood type were measured at baseline and 6, 12, and 18 mo. These values are shown within the evidence summary presented in **Table 2**. A difference in responses to the low-fat diet was shown between the MN blood group and the combined MM and NN blood groups. In the ANOVA, this difference was statistically significant at both 6 and 18 mo ($P = 0.0031$ and $P = 0.0002$, respectively) but not at 12 mo ($P = 0.0936$). It was concluded that an association exists between MNS blood groups and the variability of responses to a low-fat diet, with MN individuals responding the least. Of interest, LDL-cholesterol concentrations within the MN control group (ie, without adherence to a low-fat diet) had decreased by the end of the 18-mo study from 4.6217 to 4.3847 mmol/L (a change of −0.237 mmol/L) compared with LDL-cholesterol concentrations within the MN intervention group, which had slightly increased from 4.2469 to 4.2516 mmol/L (a change of 0.0047 mmol/L).

The study was a controlled interrupted time series, with participants drawn from another study (43). The process of random

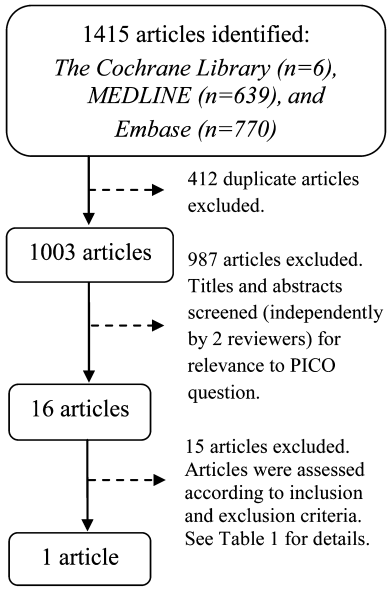

FIGURE 1. Flow diagram showing results of the search strategy. The Cochrane Library (via Wiley: http://onlinelibrary.wiley.com/cochranelibrary/search); Embase (http://www.embase.com/); MEDLINE (http://www.ncbi.nlm.nih.gov/pubmed). PICO, population, intervention, comparison, and outcome.

TABLE 2
Summary of findings

Outcome	Comparison/risk factor	Effect size	No. of participants (experimental, control)	Reference
Change in mean values of LDL cholesterol (mmol/L), according to MNS status at 6 mo from baseline	Low-fat diet compared with normal dietary regimen	*MN* genotype Intervention: 4.1955 − 4.2469 = −0.0514 Control: 4.4949 − 4.6217 = −0.1268 *MM* genotype Intervention: 4.1316 − 4.4026 = −0.271 Control: 4.6256 − 4.5923 = 0.0333 *NN* genotype Intervention: 3.8909 − 4.2364 = −0.3455 Control: 4.1261 − 4.2280 = −0.1019 Significant difference between MN and MM/NN intervention groups in ANOVA; $P = 0.0031$	Total: 254 (127, 127) *MN* genotype: 128 (67, 61) *MM* genotype: 78 (38, 40) *NN* genotype: 48 (22, 26)	Birley et al, 1997 (29)
Change in mean values of LDL cholesterol (mmol/L) according to MNS status at 12 mo from baseline		*MN* genotype Intervention: 4.1508 − 4.2469 = −0.0961 Control: 4.3915 − 4.6217 = −0.2302 *MM* genotype Intervention: 4.2056 − 4.4026 = −0.1970 Control: 4.4538 − 4.5923 = −0.1385 *NN* genotype Intervention: 3.8752 − 4.2364 = −0.3612 Control: 4.3615 − 4.2280 = −0.1335 Difference between MN and MM/NN intervention groups in ANOVA; $P = 0.0936$		
Change in mean values of LDL cholesterol (mmol/L) according to MNS status at 18 mo from baseline		*MN* genotype Intervention: 4.2516 − 4.2469 = 0.0047 Control: 4.3847 − 4.6217 = −0.2370 *MM* genotype Intervention: 4.0389 − 4.4026 = −0.3637 Control: 4.4897 − 4.5923 = −0.1026 *NN* genotype Intervention: 3.8045 − 4.2364 = −0.4319 Control: 4.1200 − 4.2280 = −0.1280 Significant difference between MN and MM/NN intervention groups in ANOVA, $P = 0.0002$		

assignment was unclear, and there was a lack of participant blinding (which is somewhat unavoidable in dietary interventions). A total of 315 patients were randomly assigned (intervention: $n = 157$; control: $n = 158$); however, only 254 patients were analyzed, which indicated an incomplete accounting of patients and outcome events.

Because the study was a randomized experimental trial, the initial grade for the quality of evidence was high (A). However, this level was downgraded because of study limitations (a lack of adequate random assignment and allocation concealment along with an incomplete accounting of patients), imprecision (a small study size), and indirectness (the analysis provided an indirect outcome because it did not directly assess the current PICO question). Overall, the strength of the evidence, according to the GRADE approach, was determined as low (C) to very low (D).

DISCUSSION

Blood type diets have maintained significant popularity for more than a decade. They have been heavily endorsed on claims of health improvement, but to our knowledge, no studies have been performed to specifically examine resulting health effects. This situation is despite it being mentioned within D'Adamo's books (published in 1996 and 2004) that ABO blood type diet trials were expected to be completed within 2 y and 12 wk, respectively (44, 45).

This current systematic review was performed by using sensitive search strategies within well-established life sciences and biomedical information databases. Of the 16 articles identified on the basis of titles and abstracts (Table 1), only 4 articles presented experimental or observational studies. Of these 4 articles, only one article met all of the inclusion and exclusion criteria; Birley et al (29) compared the variation in LDL-cholesterol concentrations between different MNS blood types (which are functionally distinct from ABO blood types) in response to a low-fat diet. The analysis within the article compared the variation between responses of the experimental groups across different MNS blood types; however, a comparison between intervention and control groups for each blood type at each time interval (6, 12, and 18 mo) would have provided information more pertinent to this review. Although these results did not provide direct evidence for the current PICO question, relevant information concerning the variation in response to the diet was shown across the intervention arms of the study; a significant difference in LDL-cholesterol reduction was shown between combined MM and NN blood types and the MN blood type. This result suggests that individuals with either an MM or NN blood type may respond

more effectively (in relation to LDL-cholesterol reduction) to a low-fat diet than would their MN counterparts. The result also suggests that MNS blood typing should perhaps be considered when developing a diet designed to lower cholesterol; however, there appear to be other factors that may also require consideration.

A systematic review has considered the association between genetic variation and lipid response to a dietary intervention (46). Published in 2003, the review identified 74 studies that investigated the presence of a relation between lipid responses and variations in genes including genes associated with apolipoproteins, genes coding for enzymes, the LDL-receptor gene, and other genes. It was the latter category (other genes) that included genotypic variations in blood type, and Birley et al (29) was the only article listed. The systematic review concluded that the results tended to suggest that a variation in the genes encoding apolipoproteins may be associated with dietary-induced lipid-response variations. However, the conclusion also stated that the evidence was limited, and the effects of genetic variation have not been consistently shown and were sometimes conflicting (46). It was recommended that future studies should include larger sample sizes and investigate effects of polymorphisms in multiple genes rather than effects of polymorphisms in single genes (46). It seems that there may potentially be a variety of genetic aspects to be considered when the inconsistency of responses to a dietary change is evaluated, which make a diet developed specifically for one of the many genetic variations (blood type or otherwise) even more prone to challenges of validity.

Studies such as these, which compare responses between intervention groups, are useful to show, eg, a heterogeneous response according to the genotypic variation. However, the results do not provide any evidence of the purported health benefits of the dietary intervention. To specifically validate the health benefits of a promoted diet (ie, a blood type diet), studies must focus on the outcome of an experimental group (adhering to the diet) compared with that of a control group (continuing with a standard diet) within a specific population (ie, grouped according to blood type).

The other 3 studies that did not meet the inclusion-exclusion criteria of the current systematic review [Langmann et al (31), Mäkivuokko et al (34), and Power (41)], all lacked an appropriate diet as an intervention, and Langmann et al (31) and Mäkivuokko et al (34) also lacked a health measurement as an outcome. Power (41) claimed to show a clear pattern between ABO blood type and food allergies and hypersensitivities, which were detected after the intervention of food-allergy tests. Some of the results presented by Power (41) tended to contradict the recommendations made by the ABO blood type diets designed by D'Adamo (9). Although the article by Power (41) was excluded from our review (because it did not meet our PICO question), an overt potential bias was noted because the author directs readers of the article to a website that promotes her research along with her upcoming book.

In conclusion, a standard PICO question and a systematic search of established medical and scientific databases yielded no evidence regarding the validity of blood type diets. Evidence exists that links an increased vulnerability of certain blood types to particular diseases (3), and studies that considered an association between genetic variation and responses to specific diets are also available (46). However, there is currently no evidence that an adherence to blood type diets will provide health benefits, despite the substantial presence and perseverance of blood type diets within the health industry. Until the health effects of blood type diets have been substantiated, the widespread claims should be clarified so that consumers are aware that the advertised health benefits are theoretical and not supported by scientific evidence.

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