Austin Journal of Nutrition and Food Sciences

Open Access

Austin Publishing Group

Short Communication

Effect of Diet on Lipid Levels in Children/Adolescents with Familial Hypercholesterolemia

Widhalm K* and Fallmann K
Austrian Academic Institute for Clinical Nutrition and Medical University of Vienna, Austria

***Corresponding author:** Widhalm K, Austrian Academic Institute for Clinical Nutrition and Medical University of Vienna, Austria

Received: October 26, 2022; **Accepted:** November 22, 2022; **Published:** November 29, 2022

Abstract

There is enough evidence, that children and adolescents with Familial Hypercholesterolemia (FH) should be treated in order to reduce elevated Total chol and LDL-c levels and therefore avoid the risk of early cardiovascular diseases. There are many papers published in the last years dealing with drug treatment, several publications describe guidelines for the therapy, however most without any data on the effect of recommended measures. The effect of diet on lipid levels in children with FH is not well documented. The goal of this paper was to search for data describing the effect of various dietary regimes in children and adolescents with FH. Surprisingly, there are only few papers studying the effect of various dietary regimes: in general, low fat-, fat substituted- or soy bean protein substituted diets are able to lower total chol and LDL-chol on average of 10–15 %. These effects should be documented and then used before starting drug treatment. Therefore, an effect of diet could reduce drug treatment or possibly postpone for some years. Anyhow, a carefully planned and performed diet for approx. 3 months should be the basis for the treatment of all children and adolescents with FH.

Keywords: Children/Adolescents; Familial Hypercholesterolemia; Diet; Drugs

Introduction

There is a body of evidence and general acceptance that children and adolescents affected with FH should be treated as soon as possible in order to lower elevated LDL-Chol levels. To achieve this goal, first dietary measures and secondary drug treatment is necessary [27,33]. Although there are several papers describing the effects of drug treatment, mainly for short periods, there is a paucity of studies describing the effect of dietary treatment in young subjects with FH. Principles of the diet are the reduction of saturated fats, substituted by mono- and polyunsaturated fatty acids, an increased intake of vegetables, fruits and legumes, and a low intake of simple carbohydrates. Surprisingly, there are many publications describing recommendations for the treatment of children and adolescents without any data.

Methods

In order to find out studies which describe dietary regimen and their effects in young subjects affected with FH we made a search on the scientific data banks and found only few publications in that field. Database searches were made on PubMed and Medline between December 2021 and May 2022. Searches were conducted with keywords as “Familial Hypercholesterolemia” and “Diet”.

Findings

The first paper judging the effect of diet on lipids in children with FH we found was published by Jakulj in 1974: They found a reduction of chol by 7, 5 and LDL-C by 9, 2% after a 4-week diet with daily 500ml low-fat yoghurt enriched with 2g stanols [1].

Laurin et al described a diet trial in 1991 in children with FH with a soy protein (35% of protein energy) compared with a low-milk protein drink. After some weeks the soy beverage reduced significantly triglycerides and low density lipoprotein ($p < 0,05$) whereas HDL-C increased significantly [2].

In 1993 our group in Vienna reported a dietary treatment in 23 children with FH or polygenic hypercholesterolemia using a soy protein substituted diet compared with a conventional diet for 8 weeks. In the soy group the lowering effect on LDL-C was significantly greater ($p < 0, 05$) than in the low fat, low cholesterol group [3].

Gylling and co-workers studied in 1995 the effect of sitostanol (3g/day) ester dissolved in rapeseed oil margarine in one homozygous and 14 heterozygous children with FH for 6 weeks within a double-blind design. Sitostanol margarine diet reduced total cholesterol, HDL-C and LDL-C by 11, 26 and 15% and increased HDL/LDL ratio by 27%. They did not use a group with a usual low-fat diet [4].

The next study in this field has been published in 2002 by Amundsen at al from Oslo [5]. They conducted a study using plant sterol esters enriched spread in a randomized double blind crossover study for 8 weeks: They were able to show a decrease of LDL-C by 10,2% ($p < 0,003$) after this diet compared with the control group.

Again, our group in Vienna reported in 2002 a study on 10 children with FH the effect of a 5 months diet containing rapeseed oil compound with a classical low-fat/low-cholesterol diet. It could be shown, that the rapeseed diet lowered TG by 29% [6].

Another study carried out in Amsterdam on 41 children with FH has been published by de Jonghi at al in 2003: They also used a plant sterol spread (mainly sitosterol and campesterol) for 6 weeks and reported a decrease of total cholesterol by 11%, LDL-C by 14%

Citation: Widhalm K and Fallmann K. Effect of Diet on Lipid Levels in Children/Adolescents with Familial Hypercholesterolemia. Austin J Nutri Food Sci. 2022; 10(2): 1168.

Table 1: Overview of Studies on FH, with data on the effect of recommended measures.

Study	Results
[1]	Children at the age of 7-12 years Intake of 500ml low-fat yoghurt daily enriched with 2g stanols over 4 weeks TC decreased by 7.5% and LDL by 9.2% (compared to control group)
[2]	10 children Low-fat/low-cholesterol/high-protein diet, 20% protein, 28% fat, less than 200 mg cholesterol per day, 35% of the protein from soy products No effect on TC, LDL Apo-Lipoprotein but significant reduction in TG and VLDL
[3]	23 children average age of 9 years, Group 1 (G1): Soy protein diet over 8 weeks Group 2 (G2): low-fat, low-cholesterol diet After an interruption of 8 weeks each group was placed on the alternate regimen During the soy protein diet decrease in TC by 16% in G1 and 18% in G2; LDL decreased in G1 by 22% and in G2 by 25%. During the low-fat, low-cholesterol diet TC and LDL were reduced by 8% and 7% in G1 and by 12% and 13% in G2.
[4]	14 children Low-cholesterol diet for 6 weeks with an intake of 3g sitostanol per day via rapeseed oil or margarine; Reduction of TC, IDL and LDL by 11, 26 and 15%, respectively; 27% increase in HDL/LDL ratio
[5]	38 children Consumption of approx. 18g/d spread enriched with plant sterols (1.6g/d) over 8 weeks LDL decreased by 10.2%, TC and ApoB decreased by 7.4%
[6]	17 children and adolescents at the age of 4 – 19 years 5 months diet enriched with rapeseed oil (average 15 – 22 g/d) Decrease in TG by 29%, VLDL-chol by 27%, TC by 10%, LDL-chol by 7%
[7]	41 children Daily consumption of 15g spread enriched with 2.3g plant sterols for 4 weeks Decrease of TC by 11% and LDL by 14% compared to the control group
[8]	16 children with FH, average age 8.8 years, replacement of animal protein with soy products over 3 months; Reduction of TC, LDL and ApoB by 12.3, 11.8 and 10.6%
[9]	21 children at the age of 6 -18 years, fat-modified diet enriched with rapeseed or sunflower oil for 13 weeks; Reduction of TC by 9.4% in both, LDL by 12.7% (in rapeseed oil) and 11.3% (in sunflower oil)
[10]	34 children Group 1 diet supplemented with soy products; Group 2 Control group on a fat-modified diet for 13 weeks LDL decreased more significantly in the soy group compared to the control group (154.7 vs. 176.3)

Table 2: Overview of some Studies with Guidelines on FH, without any data on the effect of recommended.

Study	Guideline
[13]	Guideline on Diagnosis, Guidance on lifestyle modification and keeping appropriate body weight, initiate lipid-lowering therapy at the same time; offering maximum tolerated dose of statin and/or ezetimibe in combination; if insufficient effect add PCSK9 inhibitor and/or resin and/or probucol; if insufficient effect LDL-apheresis; No data on the effect of the recommended measures
[12]	Review of diagnosis, screening and treatment; Summary of recommendations: Management on FH: 1. Reduce LDL level by ≥ 50% from baseline, 2. Use high-dose statin as first-line therapy, 3. In patients who fail to achieve the reduction of ≥ 50% in LDL levels with statin therapy other LDL-lowering agents should be added as ezetimibe, bile-acid sequestrants, fibrates or niacin No data on the effect of the recommended measures.
[25]	Overview of currently approved therapeutics for lipid lowering with expected effects on lipid profiles from data on pooled analysis; e.g. HMG-CoA reductase inhibitors (statins) – LDL lowering up to 50%, HDL increase up to 10%, TG lowering up to 20% Bile acid sequestrants – LDL lowering about 18%, HDL no significant change, TG variable Nicotinic acids – LDL lowering 12%, HDL increase 16%, TG lowering 20% Fibrates – LDL lowering 8%, HDL increase 9 – 10%, TG lowering 30-36% No data on the diet.
[18]	Position Paper on Guidelines on diagnosis and management of FH; Summary of Recommendations: Management should focus on a combination of lifestyle, statin therapy and lipoprotein apheresis; the lipid-lowering therapy should start as soon as possible; LDL apheresis can be considered in all patients with HoFH, and can be started at the age of 5 and not later than 8 years; Lomitapide and mipomersen should be considered as additional treatments to further lower plasma LDL-c levels No data on the effect of the recommended measures
[22]	Guideline for the Management of FH, Diagnostic criteria: LDL-c ≥ 180 mg/dl, tendon/skin xanthoma and a family history of FH or premature CAD Treatment: intensive lipid control with statins and if necessary, with other drugs Control other risks of CAD such as smoking, DM and hypertension No data on the effect of the recommended measures
[20]	Review of Guidelines on Genetic Testing and Management of FH Ten Guidelines were considered appropriate and of good quality Most important thing: a early detection of affected patients for effective prevention of CVD No data on the effect of the recommended measures
[19]	Guideline for new horizons for Diagnosis and Effective Management; Summary of management options for FH with expected effect on lipid metabolism; Low cholesterol diet – to reduce the cholesterol intake – reduction of LDL up to 10% Plant Sterols Statins – should affect cholesterol absorption – no defined results Statins – inhibition of HMG-CoA reductase - LDL reduction up to 80% in HeFH and 20% in HoFH, Ezetimibe – blocks the intestinal absorption of cholesterol – reduction of LD up to 15 -20% No data on the effect of the recommended measures. Bile acid sequestrants – Increase of feacal excretion of bile acids and LDL-R up regulation – Reduction of LDL up to 18-25% Fish Oils – improve the lipid profile (fewer/larger LDL, more/larger HDL particles) – Reduction of TG up to 20% and decrease in ApoB Lipoprotein apheresis – selective mechanical lipid removal – LDL Reduction up to 25%, Lp(a) reduction up to 50-70%

as compared to placebo, but no effect on the endothelial function has been found. A reduction of total cholesterol by 10%, LDL-C by 7% compared to the classical low-fat diet an additional pronounced lowering effect of TG and HDL-C could be shown [7].

In 2008 our group in Vienna published a study of the effect of a standard diet compared to a soy substituted diet (0, 25-0,5g/kg body weight) in 23 children with FH during 3 months. After the standard diet chol and LDL-C decreased by 11, 8% and 11,8%, whereas during soy substituted diet an additional decrease of 7,7% and 7,6% could be shown [8].

In a trial comparing the effect of rapeseed oil with sunflower oil substituted low-fat diet our group was able to show that the cholesterol and LDL-C could be lowered by 10-12%, both significantly. The rapeseed diet showed more favorable effects in regard to the total cardiovascular risk profile [9].

Discussion

It is surprising that in contrast to adult studies only 10 diet studies on children with FH have been published during the last 30 years. From these studies it is evident that a strict dietary regime is able to lower total cholesterol and LDL-cholesterol in children with FH. This is important because lifestyle modification which includes not only diet but also physical activity and other factors that influence the behavior are essential factors in regard to prevent atherosclerotic processes in young age. From a psychological point of view, it seems fundamental for the whole family is motivated to adhere to a healthy lifestyle. Also unaffected family members could have a benefit from a healthy lifestyle and behavior.

In this regard it is very interesting, that between 2000 and 2020 at least 31 papers have been published describing recommendations and guidelines for the treatment of children and adolescents with FH without any data of the effect of diet [11-41) (Table 2).

Conclusion

Although there are no long-term studies on the effect of dietary regiments in children with FH, it could be clearly shown several times, that diet can lower total chol and LDL-Chol in children with FH between approximately 10-15%.

On the other hand, it has to be mentioned that diet studies for a longer period are very difficult to carry out because parents have to be very strict in regard to protocols and in regard to the adherence to a periodical diet for children. It should be taken in consideration, that also very few studies on the effect of drug-treatment for a longer period are available to far in children. However, the fact, that it has been shown in several studies, that dietary regiments are able to lower chol and LDL-chol should be taken in account especially that possibly the use of drugs could be postponed or the dosage could be reduced in order to reach the acceptable levels for total and LDL-chol. Finally, the adherence to a diet is one main part of a healthy lifestyle.

References

1. Jakulj L, Vissers MN, Rodenburg J, Wiegman A, Trip MD, et al. Plant stanols do not restore endothelial function in pre-pubertal children with familial hypercholesterolemia despite reduction of low-density lipoprotein cholesterol levels. J Pediatr. 2006; 148: 495-500.
2. Laurin D, Jacques H, Moorjani S, Steinke FH, Gagne C, et al. Effects of a soy-protein beverage on plasma lipoproteins in children with familial hypercholester-olemia. Am J Clin Nutr. 1991; 54: 98-103.
3. Widhalm K, Brazda G, Schneider B, Kohl S. Effect of soy protein diet versus standard low fat, low cholesterol diet on lipid and lipoprotein levels in children with familial or polygenic hypercholesterolemia. J Pediatr. 1993; 123: 30-34.
4. Gylling H, Siimes MA, Miettinen TS. Sitostanol ester margarine in dietary treatment of children with familial hypercholesterolemia. J Lipid Res. 1995; 36: 1807-1812.
5. Amundsen AL, Ose L, Nenseter MS, Ntanios FY. Plant sterol ester-enriched spread lowers plasma total and LDL cholesterol in children with familial hypercholesterolemia. Am J Clin Nutr. 2002; 76: 338-344.
6. Gulesserian T, Widhalm K. Effect of Rapeseed Oil Substituting Diet on Serum Lipids and Lipoproteins in Children and Ado-lescents with Familial Hypercholesterolemia. J Am Coll Nutr. 2002; 21: 103-108.
7. de Jongh S, Vissers MN, et al, Plant sterols lower LDL cholesterol without improving endothelial function in prepubertal children with familial hypercholesterolemia, J Inherit Metab Dis. 2003; 26: 343-351.
8. Weghuber D, Widhalm K, Effect of 3-month treatment of children and adolescents with familial and polygenic hypercholesterolemia with soy-substituted diet. Br J Nutr. 2008; 99: 281-286.
9. Negele L, Schneider B, Risti R, Stulnig TM, Ehringer AW, et al. Effect of low-fat enriched either with rapeseed oil or sunflower oil on plasma lipoproteins in children and adolescents with familial hypercholesterolemia. Results of a pilot study. Eur J Clin Nutr. 2015; 69: 337-343.
10. Helk O, Widhalm K. Effects of low-fat dietary regimen enriched with soy in children affected with heterozygous familial hypercholesterolemia. Clin Nutr ESPEN. 2020; 36: 150–156.
11. Raal FJ, Hovingh GK, Catapano AL. Familial Hypercholesterolemia treatment: Guidelines and new therapies. Atherosclerosis. 2018; 277: 483-492.
12. Turgeon RD, Barry AR, Ishigaki Y. Familial hypercholesterolemia: Review of diagnosis, screening and treatment. Can Fam Physisian. 2016; 62: 32-37.
13. Harada-Shipa M, Arai H, Ishigaki Y, Ishibashi S, Okamura T, et al. Guidelines for Diagnosis and Treatment of Familial Hypercholesterolemia 2017. J Atheroscler Thromb. 2018; 25: 751-770.
14. Goldberg AC, Hopkins PN, Toth PP, Ballantyne CM, Rader DJ, et al. Familial hypercholesterolemia: screening, diagnosis and management of pediatric and adult patients: clinical guidance from the National Lipid Association Expert Panel on Familial Hypercholesterolemia. J Clin Lipidol. 2011; 5: 133-140.
15. Hopkins PN. Familial hypercholesterolemia – improving treatment and meeting guidelines. Int J Cardiol. 2003; 89: 13-23.
16. Reiner Z. A comparison of European and US guidelines for familial hypercholesterolemia. Curr Opin Lipidol. 2015; 26: 215-220.
17. Civeira F. Guidelines for the diagnosis and management of heterozygous familial hypercholesterolemia. Atherosclerosis. 2004; 173: 55-68.
18. Cuchel M, Bruckert E, Ginsberg HN, Raal FJ, Santos RD, et al. Homozygous familial hypercholesterolaemia: new insights and guidance for clinicians to improve detection and clinical management. A position paper from the Consensus Panel on Familial Hypercholesterolaemia of the European Atherosclerosis Society. Eur Heart J. 2014; 35: 2146-2157.
19. Mytilinaiou M, Kyrou I, Khan M, Grammatopoulos DK, Rendeva HS, et al. Familial Hypercholesterolemia: New Horizons for Diagnosis and Effective Management. Front Pharmacol. 2018; 9: 707.
20. Migliara G, Baccolini V, Rosso A, Andrea ED, Massimi A, et al. Familial Hypercholesterolemia: a systematic Review of Guidelines on Genetic Testing and Patient Management. Front Public Health. 2017; 5: 252.
21. Lloyd-Jones DM, Morris PB, Ballantyne CM, Birtcher KK, Daly DD, et al. 2017 Focused Update of the 2016 ACC Expert Consensus Decision Pathway on the Role of Non-Statin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk: A Report of the American College of Cardiology Task Force on Expert Consensus Decision

Pathways. J Am Coll Cardiol. 2017; 70: 1785-1822.

22. Harada-Shiba M, Arai H, Oikawa S, Ohta T, Okada T, Okamura T, et al. Guidelines for the Management of Familial Hypercholesterolemia. J Atheroscler. 2012; 19: 1043-1060.

23. Palma L, Welding M, O'Shea J. Diagnosis and Treatment of familial hypercholesterolemia: The impact of recent guidelines, Nurse Pract. 2016; 41: 36-43.

24. Feldmann DI, Blaha MJ, Santos RD, Jones SR, Blumenthal RS, et al. Recommendations for the management of patients with familial hypercholesterolemia. Curr Atheroscler Rep. 2015; 17: 473.

25. Sjouke B, Kusters DM, Kastelein JJP. Familial Hypercholesterolemia: Present and Future Management. Curr Cardiol Rep. 2011; 13: 527-536.

26. Knowles JW, Stone NJ, Ballantyne CM. Familial Hypercholesterolemia and the 2013 American College of Cardiology/American Heart Association Guidelines: Myths, Oversimplification and Misinterpretation Versus Facts. Am J Cardiol. 2015; 116: 481-484.

27. Harada-Shiba M, Ohta T, Ohtake A, Ogura M, Dobashi K, et al. Guidance for Pediatric Familial Hypercholesterolemia 2017. J Atheroscler Thromb. 2018; 25: 539-553.

28. Mata P, Alonso R, Ruiz A, Juanatey JRG, Badimon L, Diaz JL, et al. Diagnosis and treatment of familial hypercholesterolemia in Spain: consensus document. Aten Primaria. 2015; 47: 56-65.

29. Robinson JG. Management of familial hypercholesterolemia: a review of the recommendations from the National Lipid Association Expert Panel on Familial Hypercholesterolemia. J Manag Care Pharm. 2013; 19: 139-149.

30. Alonso R, Mata P, Zambon D, Mata N, Jimenez F, et al. Early diagnosis and treatment of familial hypercholesterolemia: improving patient outcomes. Expert Rev Cardiovasc Ther. 2013; 11: 327-342.

31. Mysliwiec M, Walczak M, Malecka-Tendera E, Dobrzanska A, Cybulska B, et al. Management of familial hypercholesterolemia in children and adolescents. Position paper oft he Polish Lipid Expert Forum. J Clin Lipidol. 2014; 8: 173-180.

32. Waters DD, Boekholdt SM. An Evidence-Based Guide to Cholesterol-Lowering Guidelines. Can J Cardiol. 2017; 33: 343-349.

33. Ramaswami U, Humphries SE. Management of familial hypercholesterolemia in childhood. Curr Opin Pediatr. 2020; 32: 633-640.

34. Illingworth DR. Management of hypercholesterolemia. Med Clin North Am. 2000; 84: 23-42.

35. Ose L. Diagnostic, clinical and therapeutic aspects of familial hypercholesterolemia in children. Semin Vasc Med. 2004; 4: 51-57.

36. Daniels SR. Pediatric guidelines for dyslipidemia. J Clin Lipidol. 2015; 9: 5-10.

37. Humphries SE. Guidelines for the identification and management of patients with familial hypercholes-terolemia (FH): are we coming to a consensus?. Atheroscler Suppl. 2011; 12: 217-220.

38. Toth PP. Novel Therapies for Low-Density Lipoprotein Cholesterol Reduction. Am J Cardiol. 2016; 118: 19-32.

39. Masana L, Civeira F, Pedro-Botet J, et al. Expert consensus on the detection and clinical management of familial hypercholesterolemia. Clin Investig Arterioscler. 2013; 25; 182-193.

40. Tonstad S, Sivertsen M. Dietary adherence in children with familial hypercholesterolemia. Am J Clin Nutr. 1997; 65: 1018-1026.

41. Ito MK, McGowan MP, Moriarty PM. Management of familial hypercholesterolemia in adult patients: recommendations from the National Lipid Association Expert Panel on Familial Hypercholesterolemia. J Clin Lipidol. 2011: 38-45.