Original Article

Diagnosis and Management of Dyslipidemia

Abdalrashid Faisal M Halawani[1*], Zubaidah Saad Alahmari[2], Dina Abdullah Asiri[2], Abdullah Ahmed Albraheem[3], Abdullah Munahi A Alsubaie[4], Abdulrahman Ghazi Alqurashi[5], Feher Mohammed Alturkistani[6], Mohammed Khamis Albalawi[6], Fahad Nasser Abdulrahman Alzaid[7], Mansour Musaad T Alsaluli[8], Mohammad Saleh Sahhab Alghamdi[8]

[1] Department of Medical Science, Faculty of Medicine, King Abdulaziz University, Jeddah, KSA. [2] Department of Medical science, Faculty of Medicine, King Khalid Univrsity, Abha, KSA. [3] Department of Medical Science, Faculty of Medicine, Alfaisal University, Riyadh, KSA. [4] Department of Medical Science, Faculty of Medicine, medical university of warsaw, Warszawa, Poland. [5] Department of Medical Science, Faculty of Medicine, Ibn Sina National College, Jeddah, KSA. [6] Ministry of Health, King Abdulaziz Hospital, Jeddah, KSA. [7] Ministry of Health, Almuzahimiyah Hospital, Riyadh, KSA. [8] Department of Medical Science, Faculty of Medicine, Al Baha University, Al Baha, KSA.

Abstract

Background: Nowadays, cardiovascular disease is considered as a leading cause of mortality worldwide, and dyslipidemia is one of its most common risk factors. Moreover, most of the ischemic heart diseases are said to be secondary to dyslipidemia and its effects. Dyslipidemia with a high prevalence has been the subject of multiple studies. As a family physician, the role of identification of people with this major risk factor has gained importance, especially with availability of screening and management. **Objectives:** In this study, we aim to provide summarized, yet comprehensive review focusing on screening, diagnosis and management of dyslipidemia. **Methodology:** PubMed database was used for articles selection using particular keywords. **Conclusion:** Dyslipidemia recognition, management and guidelines are ever changing with the recent breakthroughs. Thus, primary health care physicians shall be aware of the recent protocols regarding the screening of the population, diagnosis, management and especially follow-up. Moreover, family physician has to ensure the compliant of the patient in order to have the best outcome in these cases. Nevertheless, further studies with larger sample sizes and better design are necessary to establish the full effect of the recent drugs, which may change the way we approach this disease.

Keywords: dyslipidemia, primary health care, screening, diagnosis, management

Introduction

Nowadays, cardiovascular disease is considered as the leading cause of mortality worldwide, with estimations as high as 17 million deaths every year.[1] Thus, risk factors and leading causes to this disease has been widely studied in order to prevent development of this disease. One of the most associated and recognized factors is dyslipidemia, which has been strongly associated with CVD and all its complications. In fact, one-third of all the ischemic heart diseases are said to be secondary to dyslipidemia and its effects. Dyslipidemia has been one of the major subjects of screening, and management in the adult and children populations. The prevalence of such problem, in 2008, was as high as 39% in males and 40% in females in the developed countries.[2] Moreover, with the increasing number of people with dyslipidemia discovered due to the effective screening, primary health care physician role became pivotal in management and follow up. In this paper we will review dyslipidemia, its definition, screening protocols, how to diagnose it, the management with a special focus on the primary health care setting.

Methodology

PubMed database was used for articles selection using the following keywords: dyslipidemia, and its diagnosis, management, and screening. With regard to the inclusion criteria, the articles were selected based on the following topics; dyslipidemia, screening, diagnosis, management focusing on the primary health care setting. Exclusion criteria were all other articles which did not have one of these topics as their primary endpoint.

Discussion

Address for correspondence: Abdalrashid Faisal M Halawani. Department of Medical Science, Faculty of Medicine, King Abdulaziz University, Jeddah, KSA.
E-mail: Abdulrasheed.halawani @ gmail.com

How to cite this article: Faisal M Halawani, A., Saad Alahmari, Z., Abdullah Asiri, D., Ahmed Albraheem, A., Munahi A Alsubaie, A., Ghazi Alqurashi, A., and et al. Diagnosis and Management of Dyslipidemia. Arch Pharma Pract 2019;10(4):67-70.

Dyslipidemia is one of the most common risk factors noted in patients with cardiovascular disease (such as atherosclerosis). Unfortunately, this disease is generally asymptomatic, and usually presents with complications, such as ischemic heart disease, and stroke. Defining this condition is important in order to classify and recognize cases with abnormal lipid profile. The main patterns in patients with dyslipidemia are their high concentrations of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and the low level of high-density lipoprotein cholesterol (HDL-C). Another pattern seen in dyslipidemic patients is high triglyceride levels, and these cases usually are referred to as hypertriglyceridemia.

Definition

Dyslipidemia is an abnormal metabolic status leading to persistent high plasma concentration of lipids. This condition can be divided into three different presentations, hypercholesterolemia (high cholesterol), hypertriglyceridemia, and mixed hyperlipidemia (both triglyceride and cholesterol are high). The general pattern noted with total cholesterol is that they increase from birth till 2 years of age, and then stabilize. Afterwards, they start to be increased again till reaching a peak just before puberty, afterwards, in adolescent, these levels go down slightly. [3] Dyslipidemia can be inherited genetically that examples include familial combined hyperlipidemia, familial hypertriglyceridemia, and familial hyperapobetalipoproteinemia. However, are multiple factors that have been associated with this disease such as high BMI, alcohol use and waist circumference. Moreover, dyslipidemia can be secondary due to another medical condition like; diabetes, hypothyroidism, Cushing's syndrome, inflammatory bowel disease, and severe infections. Accordingly, we can divide dyslipidemia into primary (mainly familial –genetics-) and secondary (as a result of lifestyle or medical condition). [4]

Screening

Screening for dyslipidemia has been suggested for a while as a part of the community health strategies applied in many other diseases e.g. diabetes. The main goals behind such approach are to identify the affected cases as s as possible, thus reducing long-term cholesterol impact (with early intervention), and prevention or delay of complications (such as cardiovascular events). Unfortunately, dyslipidemia screening rates are low overall (2.5% - 3.2%), even though a diagnosis of cases was present in 4.8% to 12.3% of the screened population.[5] Many studies and guidelines have been suggested regarding this topic, with different approaches to screening. Guideline from the National Heart, Lung, and Blood Institute in 2011 suggested a universal screening for dyslipidemia starting from 9 years of age (till 11), and a second screening at 17 years till 21, but a selective screening at other ages. [6] Moreover, other studies recommended a universal screening test for any patient above 5 years of age. [7]

The idea behind the selective screening is identifying the high risk population, which are mainly the ones with a positive family history regarding dyslipidemia, premature CVD, early CVA deaths, and /or other cardiovascular disease risk factors (e.g. diabetes). Studies showed that people with afore mentioned factors had a higher prevalence of the disease; however, classically the very early (or infant) screening is primarily for detecting familial hypercholesterolemia cases. On the other hand, European guidelines, and American Academy of Pediatrics (AAP) suggest screening for this condition only if the patient has the risk factors (rather than universally) in people younger than 21 years old. However, people older than 21 years old shall undergo the universal testing, and the frequency in general for fasting lipid test is every 4 to 6 years. [8] Screening mainly assesses triglyceride, total cholesterol, HDL-C, LDL-C and non-HDL-C levels. [9] Since recent guidelines are suggesting a more focused screening criteria for population less than 21 years old, we recommend it as well. Some reasons behind difficulty of implementing the universal screening are ethical considerations, needle stick risk, and resources availability especially in the primary health care setting. [10]

Diagnosis

As mentioned before, dyslipidemia is generally asymptomatic and is diagnosed accidentally or via screening. However, in severe cases the patient can present with one of the symptoms of the complications (either coronary or peripheral artery disease) such as leg pain, chest pain, dizziness, palpitations, swelling of lower limb or veins (e.g.in neck, or stomach) and fainting. The main laboratory test for diagnosis is fasting lipid test (profile), and the patient must fast for at least 12 hours before taking the blood sample. This test gives the fasting total cholesterol, triglyceride, and HDL-C values, and the LDL-C concentration can be calculated using the Friedewald equation. This equation is used as long as triglyceride values are less than 400 mg/dL(4.5 mmol per L); however, if the value is higher, the clinician shall order an LDL-C direct assay. Another initial test that some clinicians carry out is the non-fasting lipid profile; however, if it reveals a high value (triglyceride higher than 400 mg/dL) fasting lipid profile shall be done after. The exact values to consider each of the four lipids high, optimal or low (in case of HDL) are marked in Table 1. [3]

The clinician shall be aware of any co- risk factors in patients with borderline values, and this is vital to choose the next optimal step. If the patient has a borderline high cholesterol values with low HDL, a lipoprotein analysis should be carried out. The analysis is also indicated if the patient has a high cholesterol, or present with two risk factors. These risk factors include age (more than 45 in men, and 55 in women), premature menopause (with no estrogen replacement therapy), family history of CVD, diabetes, smoking, hypertension, and cerebrovascular or peripheral vascular disease. If the family physician establishes the diagnosis, secondary causes must be investigated properly and ruled out [3, 5, 9].

Table 1: The Criteria for Diagnosis of Dyslipidemia

	Low	Optimal Value	Borderline high	High	Very high
Total Cholesterol	-	Less than 200 mg/dL	Between 200 and 239 mg/dL	Equal to or higher than 240 mg/dL	-
low-density lipoproteins (LDL)	-	Less than 100 mg/dL	Between 130 and 159 mg/dL	Equal to or higher than 160 up to 189 mg/dL	Equal to or higher than 190 mg/dL
Triglycerides	-	Less than 150 mg/dL	Between 150 and 199 mg/dL	Equal to or higher than 200 up to 499 mg/dL	Equal to or higher than 500 mg/dL
high-density lipoproteins (HDL)	Less than 40 mg/dL	Above 40 mg/dL	-	Equal to or higher than 60 mg/dL	-

Childhood dyslipidemia has different cut-off points which are derived from their population norm. Generally, total cholesterol equal to or more than 200 mg/dL or LDL-C values equal to or higher than 130 mg/dL are considered diagnostic (high). Even though the dyslipidemia in childhood is typically multifactorial, genetic causes present usually in this age with very high lipid concentrations. [8, 10]

Management

The approach to dyslipidemia has been changing a lot in the last few decades, this is attributed to the advances in our understanding of the CVD, and the new modalities of management. The clinician has to approach the patient as a whole to offer the optimum care, thus enquiring about any other risk factors, medical conditions, and possible contraindications to the therapy. Recent American College of Cardiology (ACC)/American Heart Association (AHA) guidelines, recommended calculating the atherosclerotic cardiovascular disease (ASCVD) lifetime risk to establish the baseline and guide the therapy for these cases. The general approach to management is that in young adult patients (20 - 39 years) promoting a healthy lifestyle can suffice and improve dyslipidemia. Pharmacological therapy in this population is usually indicated in patients with LDL-C levels (starting from 160 mg/dL or higher than 100 mg/dL in high risk patients). [11] Patient stratification into very high, high and low ASCVD risk depends on multiple factors such as major events like recent acute coronary syndrome (within 1 year), history of myocardial infarction or ischemic stroke, symptomatic peripheral arterial disease. The other high-risk conditions include age (older than 64 years), DM, HTN, smoking, CKD, and congestive heart failure. Patients between 40 and 75 year old are more dependent on their 10-year ASCVD risk to guide the management, with higher risk indicating likely higher benefit from pharmacological therapy. Older patients need to be approached carefully with full-risk assessment and discussion with the patient to weigh the advantages and disadvantages of initiating (or continuing) the drug therapy. On the other hand, youths are not recommended to start lipid lowering drugs in treating multifactorial dyslipidemia. Treating this condition is very beneficial, with every 1 mmol/L (38.6 mg/dl) reduction in LDL-C associated with reduction by 23% of the relative risk of major vascular events in five years. Moreover, every 1 mg/dL increase in HDL-C showed a reduction by 2-3% in coronary heart disease events. [12] Non-pharmacological management is the first line in the management in all age groups, this include endorsing a healthy lifestyle, changing into a more healthy diet, reduction of weight, and cessation of smoking.

Pharmacological therapy is based on statin as the cornerstone, with other medications such as ezetimibe, PCSK9 Inhibitors, and fibrin used along with it. Extreme risk patients (According to ASCVD) shall have a target of LDL-C of less than 55 mg/dL; however, a very high risk patient has a goal of less than 70 mg/dL. If patients have a high risk (CAD, DM, and any aneurysm or stenosis or more than 2 other risk factors) , they will have an LDL-C goal of less than a 100 mg/dL, moderate risk include patients with 2 or less risk factors with an LDL-C goal of less than 130 mg/dL. Lastly, cases with one or less risk factor shall aim for LDL-C less than 160 mg/dL. [13] Statin with high-intensity (up to maximum) is started in very high risk patients and patients who are not very high risk and younger than 76 years old with a general goal of lowering LDL-C by at least 50%. Family physician shall follow the patient and if treatment was not tolerated, then the dosage shall be lowered into a moderate with a goal of reaching a reduction of 30% to 49% in LDL-C. However, if the LDL levels are still high (more than 70mg/dL) on maximal statin, adding ezetimibe is the next step. Last step in the management is adding PCSK9 inhibitor (or bile acid sequestrant) if the combination of statin and ezetimibe was not effective and LDL levels were still high. In high intensity statin therapy, atorvastatin and rosuvastatin are the main examples, and lower intensity therapy can include

other varieties such as simvastatin, pravastatin, lovastatin, and fluvastatin. Even though statin is widely recognized as the first line in the management of dyslipidemia, many side effects are associated with it includin: myalgia, myositis, myopathy, rhabdomyolysis, hepatic failure and new onset DM. Thus, family physicians have a major role in advising and teaching the patient about the exact dosage, possible side effects and follow-up plan to ensure the best results.

If triglyceride concentration remains equal to or higher than 500 mg/dL after ruling out all secondary causes, fibrate (or omega-3 fatty acid) therapy shall be started to prevent pancreatitis. However, if the triglyceride level is between 200 to 499 mg/dL statin is started especially if LDL level was high. Combining both drugs (and/or omega-3 fatty acid) is usually reserved in cases where hypertriglyceridemia (equal to or higher than 200 mg/dL) persists even after lifestyle modifications and statin. However, the exact effect of this combination therapy on the mortality and CVD incidence remained controversial, with some studies showing no change in the mortality rates. [14]

Monitoring and Follow up

Family physician shall monitor the patients with dyslipidemia on a regular intervals. Lipid profile shall be done 4 to 12 weeks after starting the therapy in order to assess the response and compliance. Then, if the results were satisfying, testing shall be at 3 to 12 months interval. Selection of the exact months will be up to the clinician based on depending on the patient's cardiovascular risk and his response to the therapy. Other tests that shall be done in these cases include liver function and creatinine kinase (CK) levels. If the patient shows any abnormal liver function test values and/or CK levels increased more than 10-fold, then the drugs shall be discontinued immediately. [3, 15]

Conclusion

In conclusion, managing one of the most prevalent causes of mortality and morbidity in our modern days (CVD) starts with its risk factors. Dyslipidemia is one of the most common risk factors and with recent breakthroughs and therapy the protocols and guidelines are ever changing. Primary health care physicians shall be aware of the recent protocols regarding the screening of the population, diagnosis, management and especially follow-up. Family physician has to be able to carry out this pivotal role, and ensure the compliant of the patient in order to have the best outcome in these cases. Nevertheless, further studies with larger sample sizes and better design are necessary to establish the full effect of the recent drugs, which may change the way we approach this disease.

References

1. World Health Organization. Geneva: World Health Organization; c2019. Global Health Observatory (GHO) data; 2019 Jun 20.
2. OMS. Cadre Global Mondial de Suivi, Comprenant des Indicateurs, et Série de Cibles Mondiales Volontaires Pour la Lutte Contre les Maladies non Transmissibles. Geneva, Switzerland: OMS; 2012.
3. Rhee EJ, Kim HC, Kim JH, et al. 2018 Guidelines for the management of dyslipidemia. Korean J Intern Med. 2019;34(4):723–771. doi:10.3904/kjim.2019.188.
4. G.B. John Mancini, Robert A. Hegele, Lawrence A. Leiter. Dyslipidemia. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee; April 2013; Volume 37, Supplement 1, Pages S110–S116.
5. Vinci SR, Rifas-Shiman SL, Cheng JK, Mannix RC, Gillman MW, de Ferranti SD. Cholesterol testing among children and adolescents during health visits. JAMA. 2014;311(17):1804-1807.
6. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents. National Heart, Lung, and Blood Institute Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: summary report. Pediatrics. 2011;128 Suppl 5:S213–S256.
7. Bell MM, Joseph S. Screening 1140 fifth graders for hypercholesterolemia: family history inadequate to predict results. Journal American Board Fam Pract. 1990 Oct-Dec; 3(4):259-63.
8. O'Loughlin J, Lauzon B, Paradis G, Hanley J, Lévy E, Delvin E, Lambert M. Usefulness of the American Academy of Pediatrics recommendations for identifying youths with hypercholesterolemia. Pediatrics. 2004 Jun; 113(6):1723-7.
9. Catapano AL, et al. ESC Scientific Document Group. 2016 ESC/EAS Guidelines for the Management of Dyslipidaemias. Eur Heart J. 2016 Oct 14; 37(39):2999-3058.
10. Kelishadi R, Haghdoost AA, Moosazadeh M, Keikha M, Aliramezany M. A systematic review and meta-analysis on screening lipid disorders in the pediatric age group. J Res Med Sci. 2015;20(12):1191–1199. doi:10.4103/1735-1995.172989.
11. Donna K. Arnett et al. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease. J Am Coll Cardiol. 2019 Sep, 74 (10) e177-e232. DOI: 10.1016/j.jacc.2019.03.010.
12. Baigent C, Keech A, Kearney PM, Blackwell L, Buck G, Pollicino C, Kirby A, Sourjina T, Peto R, Collins R, Simes R, Cholesterol Treatment Trialists' (CTT) Collaborators. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. Lancet. 2005 Oct 8; 366(9493):1267-78.
13. Garber AJ et al. Consensus statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the comprehensive type 2 Diabetes management algorithm- 2018 Executive summary. Endocr Pract. 2018 Jan; 24(1):91-120.
14. Ginsberg HN et al. ACCORD Study Group. Effects of combination lipid therapy in type 2 diabetes mellitus. N Engl J Med. 2010 Apr 29; 362(17):1563-74.
15. Ko A, Choi S, Chang J, Park SM. Effect of Lipid-Testing Interval on Stoke Risk among Newly Diagnosed Dyslipidemia Patients Initiated on Statins. J Clin Med. 2019;8(5):742. Published 2019 May 24. doi:10.3390/jcm8050742.