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Case Study *Open Access*

The biomarker of choice in association of dyslipidemia with osteoporosis: A case study

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ABSTRACT

Introduction

Association between dyslipidemia and osteoporosis has been reported in which certain reliable markers and risk factors such as presenting history and lab investigations influenced the diagnosis and optimal therapy of the diseases in the patient.

Case Presentation

The study reported a 55 year old retired male patient of associated conditions presented in a UK hospital with a history of pain in the lower limb. Family history of metabolic diseases and excessive alcohol consumption was reported. Patient was diagnosed of dyslipidemia due to genetic predisposition, disturbed lipid profile and presenting history. Osteoporosis was diagnosed by measurement of bone mineral density BMD which was lower than normal, measured a year and half later following a fracture. These findings were significant for proper diagnosis and management of these diseases.

Conclusion

The findings suggest that the biomarker of choice in association of dyslipidemia with osteoporosis is low HDL and high LDL levels in lipid profile. These markers predict both porosity of bones and dyslipidemia so it can be prioritized for screening and treatment as appropriate.

Keywords: Biomarker, Association, Dyslipidemia, Osteoporosis.

BACKGROUND

Biomarkers are key molecular or cellular events that link a specific internal or external biological exposure to a health outcome, this characteristic is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes or pharmacological responses to a therapeutic intervention. They play an important role in understanding the relationships between the development of chronic human diseases and the identification of subgroups that are at increased risk for disease. Identifying and validating new biomarkers can be used in population-based studies of diseases for the purpose of early diagnosis.[1]

INTRODUCTION

A promising biomarker should precede as well as accompany major clinical interventions that can measure a disease incidence. In a study conducted in a healthcare setting in the UK, a patient was presented with a case of dyslipidemia who was also observed to have low mineral bone density (BMD) that transitioned to the diagnosis of osteoporosis.[2] Dyslipidemia in the patient presented in the study was diagnosed by the observation of disturbed blood lipid profile, which is a hall mark for identification and measure of dyslipidemia.[3] The patient presented also had reported family history, habits and other lab investigations that may provide a logical scientific basis for validation for a choice of a biomarker that associates dyslipidemia with osteoporosis.[2]

CASE PRESENTATION

The study conducted reported a 55 year old retired male patient of normal physique and weight, having the associated conditions presented in a UK hospital with a history of pain in the lower limb. He was reported to have a family history of metabolic diseases, but no history of smoking, although excessive alcohol consumption was reported which may be along with other findings, a risk factor for the developed diseases in the patient.[4] Besides these, patient was diagnosed dyslipidemia due to genetic predisposition, lab findings such as low levels of HDL and high levels of LDL along with presenting history by the physicians.[2] The diagnosis of osteoporosis by measurement of bone mineral density (BMD) was made a year and half later following a fracture of the femur while walking as reported. The lab findings at the time of diagnosis of osteoporosis are reported as a low score of bone mineral density (BMD). Factors such as history of pain, history of metabolic diseases, excessive alcohol consumption, genetic predisposition, low HDL levels and high LDL levels, fracture and low bone mineral density (BMD) for dyslipidemia and osteoporosis were significant for proper diagnosis and management of the aforementioned case [2], it can be presumed that one or more of these factors may be a significant determinant or marker to identify dyslipidemia associated with osteoporosis.

MANAGEMENT AND OUTCOMES

For the management of this dyslipidemia, a proactive approach to lower the low density lipoprotein LDL and subsequently reduce cardiovascular risk was initiated. Drug therapy and therapeutic lifestyle changes TLC, the traditional two way approach was employed as therapy in which for first line drug therapy Simvastatin 40mg OD (at night), a cholesterol lowering HMG COA reductase inhibitor in accordance to the AACE Guidelines (20-40mg starting recommended dose of simvastatin) was given.[2] The major reported side effects of Simvastatin are head ache >15% and muscle pain >10%.[5]

In this case however, the pain reported was due to osteoporosis associated fracture[2], although the incidence of pain can be considered as a biomarker of ADR's resulting from statin therapy[5], since every biomarker has a certain characteristic that make it possible to check a particular disease condition, the clinicians had ruled out ADR associated pain and established fractureas the main cause for the skeletal muscle pain, due to the occurrence of low bone mineral density (BMD) as an initial investigation.[2]

The drug used to treat osteoporosis was a bisphosphonates i.e. Risendronate 35mg PO once weekly. The most common adverse effect of bisphosphonates is gastrointestinal problem such as dyspepsia.[6] The patient did suffer from dyspepsia [2], the incidence of which can be considered as a biomarker of ADRs resulting from pharmaco vigilance studies of patients under bisphosphonate and Risendronate therapy.[6]

Identification and measurement of other markers such as lab investigations of lipids proceeding with a follow up after 3-6 months in accordance with the conditions of the patient along with the measurement of CK, ALT/AST and signs of muscle soreness were conducted to monitor the condition of dyslipidemia.[2]

In the diagnosis of osteoporosis, periodic BMD testing, which is a classical biomarker for the diagnosis of osteoporosis[7], was done along with assessment by GP to establish the diagnosis. Markers for the monitoring of drug therapy involving Risendronate, includes creatinine clearance CrCl, serum alkaline phosphate, serum calcium and serum phosphate were all measured as recommended.[2]

DISCUSSION

Biomarkers are classified as those of exposure, effect, and susceptibility. Due to limited ability to transform large datasets, (e.g. clinical data in diagnosis of disease) into meaningful information and knowledge of a disease process or impact of a drug in the treatment of disease, it is imperative for physicians to make accurate and decisive decisions. One approach to enhance an understanding of such issue has emerged in the form of biomarker discovery, validation and utilization.[1] Perspective of biomarkers in case of dyslipidemia associated with osteoporosis can be hypothesized by the provided information in the context of disease treatment and investigations of the precedent patient profile.

For instance, high LDL levels (levels of low-density lipoprotein cholesterol LDL-C and low HDL levels present in the patient lipid profile are core biomarkers for the diagnosis of dyslipidemia.[3] Simplified target lipid levels such as atherogenic lipoproteins, as reflected by the serum (or plasma) levels of low-density lipoprotein cholesterol LDL-C or apolipoprotien (apo B) are also secondary markers for diagnosis.[3] The evidence favoring LDL-C reduction for the prevention and treatment of dyslipidemia leading to atherosclerosis is strong and compelling, and is based on multiple randomized clinical trials.[3] Besides this Increased levels of all these parameters such as total cholesterol (TC) to high-density lipoprotein cholesterol (HDL-C) ratio, and the hs-CRP, non-HDL-C and serum (or plasma) triglyceride have been found to confer additional risk. However, clinical trial evidence is lacking on the importance of intervening on these variables to further reduce risk and thus, so they are considered secondary and optional markers for diagnosis.[3]

Family history of metabolic diseases as well as genetic predisposition present in the patient profile are conventional risk factors that explain the etiology of dyslipidemia, which can have both genetic and environmental determinants that can be considered markers of susceptibility. Importantly suggested by clinical trial investigations, 10% to 15% of patients with dyslipidemia have no apparent major risk factors. However, dyslipidemia-related events occur along a continuum of risk, and persons with no apparent exposure to traditional risk factors may be exceptionally susceptible to the presence of apparently physiological levels of those risk factors.[3]

Alcohol consumption can be considered a secondary yet important risk factor as it is positively associated with low-density lipoprotein cholesterol level in all populations; the lipid level in an alcoholic patient gives a graded response even over the low levels of alcohol consumption as well as less strong. Plasma-triglycerides also show a modest positive correlation with alcohol. So increased alcohol consumption gives disturbed lipid levels, hence causing dyslipidemia.[4]

Classification of prominent biomarkers in the case of osteoporosis includes low bone mass or the micro architectural deterioration measured as low bone mineral density (BMD) of bone tissue that results in increased risk for fracture.[7] The patient suffered fracture while under low energy stress exercise (i.e. walking), under such conditions, it is usually an indicator of high bone fragility as compared to fracture during high energy stress or impact.[7] Fracture under such conditions usually indicate low bone mass and also predict porosity[7]. For which the ideal assessment would be measurement of bone mineral density BMD (e.g., by dual-energy x-ray absorptiometry) which was measured that resulted to be lower than normal. Besides this other tests such as a biochemical index of bone turnover can provide different but complementary information that can aid in predicting risk of future bone loss and osteoporotic fracture.[8] In accordance to osteoporosis, skeletal muscle pain is induced by fracture due to the sensitized nerve endings at the junction of skeletal muscle and bone that signal release of pain mediators via brain. It can help predict fracture due to mobility that cause pressure changes in movements of skeletal muscle with bone of low porosity[9] but to qualify as a primary indicator, low bone mineral density (BMD) is a prominent and validated biomarker associated with osteoporosis, as provided by repeated biomarker investigational studies.[8]

The proposed association of dyslipidemia and osteoporosis attracts the critical question to adequately transform the data of lab investigations and risk factors that defines many aspects of disease prediction, onset and progression to single out a biomarker of significance which can identify the association of the two pathophysiologically separate diseases.[2] The relation between biomarkers of

dyslipidemia and osteoporosis can be viewed clearly in the light of biomarker investigational studies that reveal that in common risk factors for both cardiovascular disease and low bone densities, increased LDL and decreased HDL causes decreased bone mineral density (BMD).[3] Statins are said to increase bone mineral density while having beneficial effect on plasma lipid levels in a patient hence, underlying this theory it is evident that this drug can benefit plasma lipids along with BMD, the lipid levels then would be much closely associated with bone mineral density.[10] Besides this, the investigation of lipid profiles with bone mineral densities among men and women indicated that the total body and hip BMD were significantly related to serum lipids in both women and men.[11]

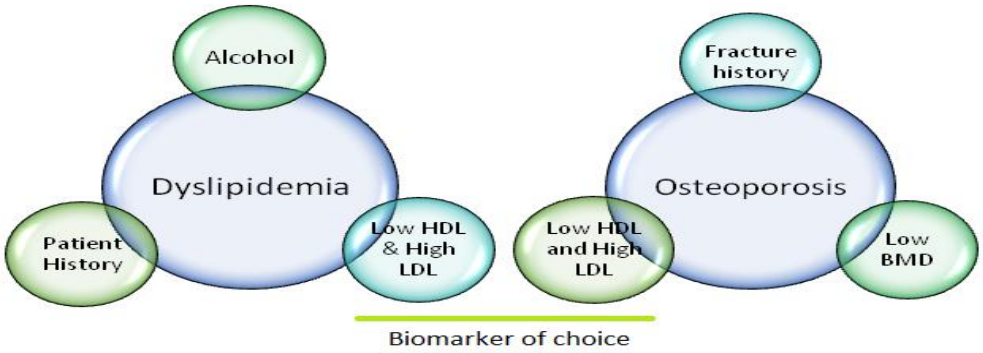

Figure 1. The association between two diseases highlighted by a biomarker

CONCLUSION

The association of dyslipidemia and osteoporosis gives a strong conspicuous background to investigate the choice of a single biomarker that predicts the onset of both these diseases found together in this cohort investigation to provide clinical meaningfulness that may strengthen decision making in diagnosis. The core biomarkers for dyslipidemia are disturbed lipid profile (low HDL and high LDL)[3], risk factors such as history of metabolic diseases, epigenetic factors and alcohol consumption[3], whereas biomarkers for osteoporosis are low bone mineral density BMD[7], skeletal turnover and an incontestable and distinct finding of low HDL and high LDL that may predict porosity in bones[10, 11]. Therefore the biomarker of choice in association of dyslipidemia with osteoporosis is low HDL and high LDL levels in lipid profile.

STATEMENT OF CONSENT

The clinical information was obtained with the consent of the patient.

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Conflict of Interests

The authors declare they have no conflict of interests.

REFERENCES

[1]. Ananya Mandal. Biomarker - What is a Biomarker? [Internet] 2014. [updated 2014 Feb: cited 2014 Feb] News-Medical. Available from: http://www.tsalliance.org/documents/UnlockBiomarkersDescription.pdf

[2]. Atta Abbas. The association of dyslipidemia with osteoporosis: A case report. 2013. El Mednifico Journal. 1(3); 82-83 P. Available from: http://www.mednifico.com/index.php/elmedj/article/view/43

[3]. Genest, J., McPherson, R., Frohlich, J. 2009 Canadian Cardiovascular Society/Canadian guidelines for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease in the adult–2009 recommendations. 2009. Canadian Journal of Cardiology. 25(10): 567-579 P.

[4]. Castelli, W., Gordon, T., Hjortland, M., Kagan, A., Doyle, J., Hames & Zukel, W. Alcohol and blood lipids: the cooperative lipoprotein phenotyping study.1977. The Lancet. 310(8030): 153-155 P.

[5]. Kiortsis, D. N., Filippatos, T. D., Mikhailidis, D. P., Elisaf, M. S., & Liberopoulos, E. N. Statin-associated adverse effects beyond muscle and liver toxicity. 2007. Atherosclerosis. 195(1): 7-16 P.

[6]. Papapetrou, P. D. Bisphosphonate-associated adverse events. 2009. Hormones Athens. 8(2): 96-110 P.

[7]. Eyre, D. R. Bone biomarkers as tools in osteoporosis management. 1997. Spine. 22(24): 17S-24S.

[8]. McCormick, R. K. Osteoporosis: integrating biomarkers and other diagnostic correlates into the management of bone fragility. 2007. Alternative Medicine Review. 12(2): 113 P.

[9]. Jimenez-Andrade, J. M., Martin, C. D., Koewler, N. J., Freeman, K. T., Sullivan, L. J., Halvorson, K. G., ... & Mantyh, P. W. Nerve growth factor sequestering therapy attenuates non-malignant skeletal pain following fracture. 2007. Pain. 133(1), 183-196 P.

[10]. Burnett, J. R., & Vasikaran, S. D. Cardiovascular disease and osteoporosis: is there a link between lipids and bone. 2002. Annals of clinical biochemistry. 39(3): 203-210 P.

[11]. S. Adami. Relationship between Lipids and Bone Mass in 2 Cohorts of Healthy Women and Men. 2004. Calcified Tissue International. 74(2): 136-142 P.